LDCT Screening for BIG-3

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I-ELCAP International Early Lung Cancer Action Program

IELCART Initiative for Early Lung Cancer Research on Treatment

Icahn School of Medicine at Mount Sinai

Disclosures

I have no financial interests to disclose

THE BIG-3

Lung Cancer

- **#1** cause of cancer death globally
- **#1** cause of cancer death in **Taiwan**
- 53% of Taiwan cases in never-smokers

Cardiovascular Disease

- **#1** cause of death globally
- **#2** cause of death in **Taiwan**

(One death every 26 minutes)

COPD / Emphysema

- **#4** cause of death globally
- **#8** cause of death in **Taiwan**

44% of all global premature deaths are caused by these three diseases combined: lung cancer, cardiovascular disease, and COPD.

CT Screening for Lung Cancer – Evidence of LDCT screening benefits

CT detected more early stage LC than CXR;
85% of people diagnosed were in **Stage I**

N=1,000

THE LANCET • Vol 354 • July 10, 1999

1999

I-ELCAP
International Early Lung Cancer Action Program

2006

The NEW ENGLAND JOURNAL of MEDICINE

2015

NLST
National Lung Screening Trial
NATIONAL CANCER INSTITUTE

20% reduction in LC mortality in CT arm

N=53,439

N Engl J Med 2013;368:1980-91.

2013

NELSON
Lung Screening Trial

N=15,789

24% reduction in LC mortality

2020

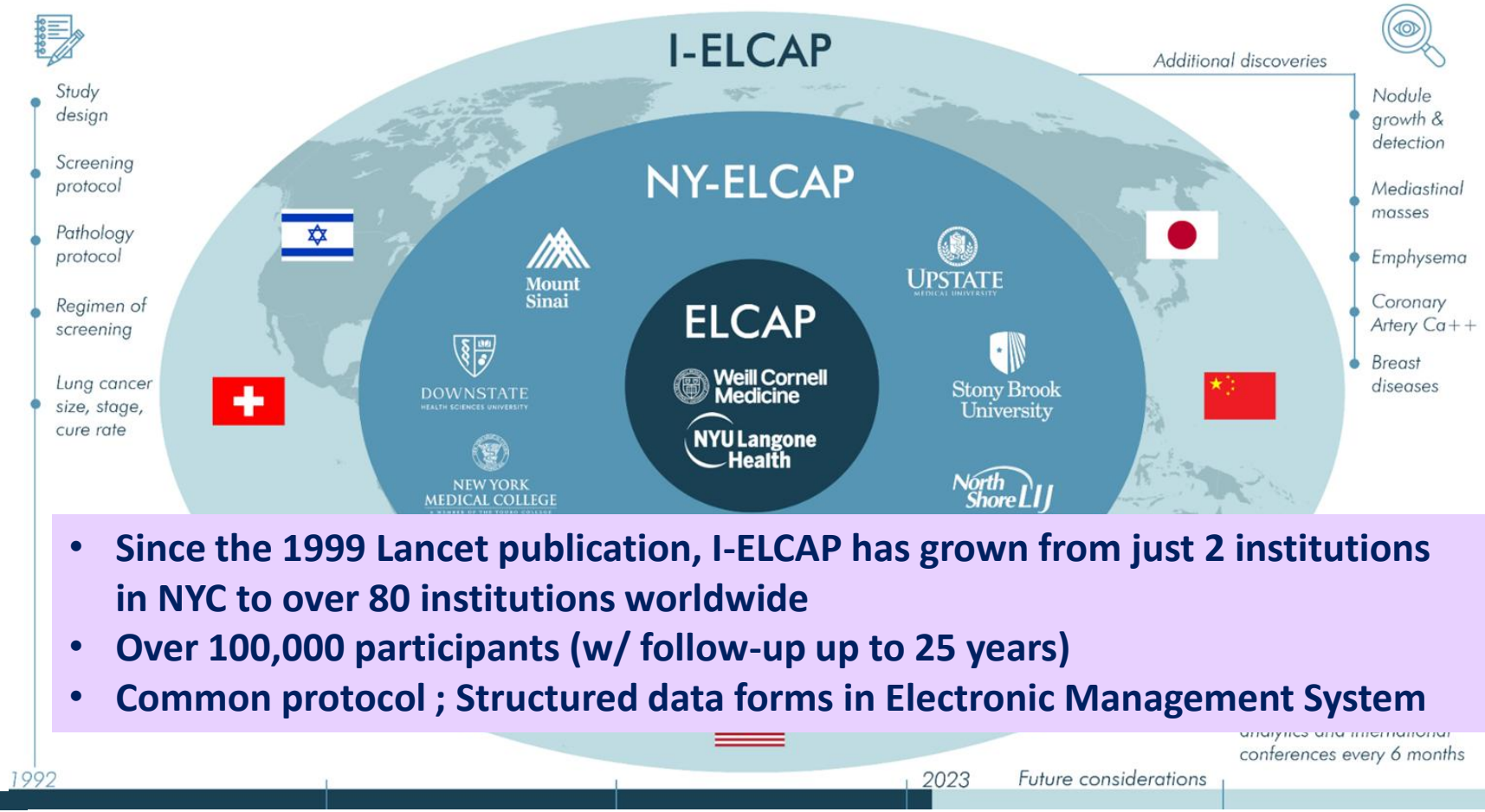
N Engl J Med 2020;382:503-13.

LDCT Screening is proven to save lives.

Annual LDCT screening has now been accepted as a viable screening tool for early lung cancer detection

10-year LCS survival= 80%

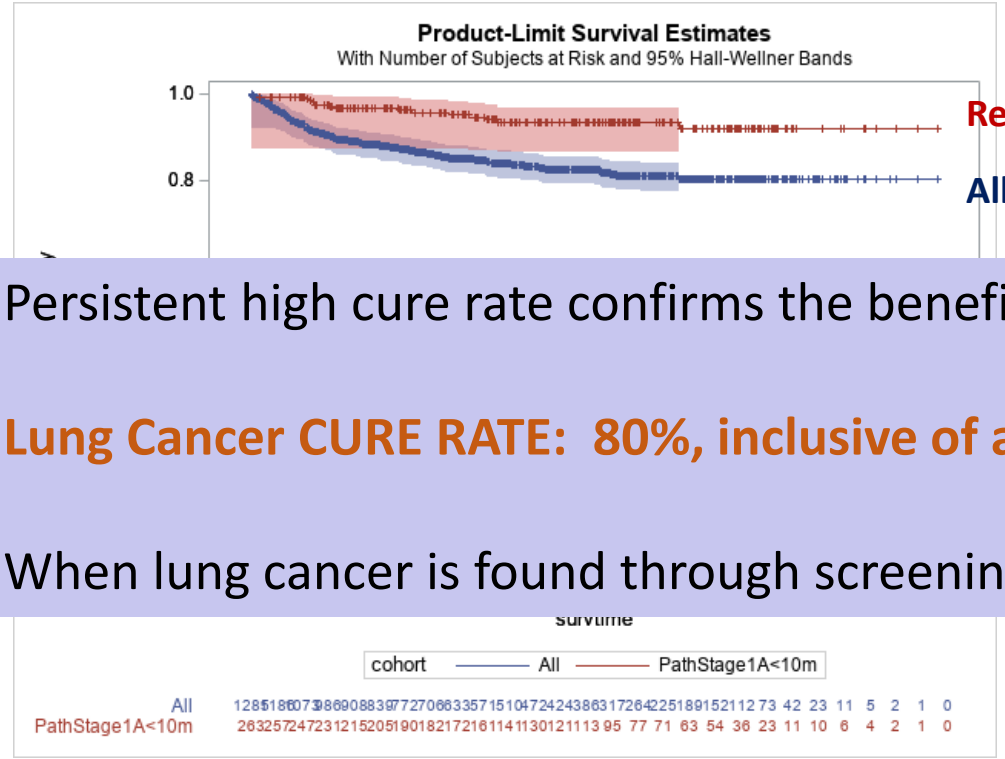
*Ages 55 to 77, have at least a 30 pack-year history of smoking, and currently smoke or have quit within the past 15 years.



- **Since the 1999 Lancet publication, I-ELCAP has grown from just 2 institutions in NYC to over 80 institutions worldwide**
- **Over 100,000 participants (w/ follow-up up to 25 years)**
- **Common protocol ; Structured data forms in Electronic Management System**

I-ELCAP reported on the 20-Year Lung Cancer Survival Rate

in 1285 Participants diagnosed with lung cancer under annual screening



Resected Path T1a N0M0<10mm **95%**

All cases 80.5%

Persistent high cure rate confirms the benefit of annual LDCT screening

Lung Cancer CURE RATE: 80%, inclusive of all stages and treatments

When lung cancer is found through screening, **4 out of 5 people will be cured**

Henschke CI*, Yip R*, Shaham D, et al. Radiology 2023. PMID: 37934099 . PMCID: PMC10698500

European Heart Journal (2014) **35**, 2792–2796
doi:10.1093/eurheartj/ehu296

CURRENT OPINION

Combined detection of coronary artery disease and lung cancer

Harvey S. Hecht*, Claudia Henschke, David Yankelevitz, Valentin Fuster, and Jagat Narula

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Introduction

Coronary artery disease (CAD) and lung cancer have several important features in common. First, their dramatic increases are in large part attributable to societal ills, including worsening dietary patterns, obesity, and tobacco use. Secondly, as these behaviours permeate the world, the diseases are disproportionately increasing in the poorer societies with limited resources for healthcare. Consequently, it is necessary to develop cost-effective strategies. Both disease states may be amenable to early detection by a single low radiation dose CT scan.

In an attempt to simplify cholesterol treatment, the 2013 ACC/AHA Guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults[6] restricted the use of CAC to the patients who did not fall into four designated conventional risk factor-based categories. Coronary artery calcium was downgraded to a Class IIb status (recommendation's usefulness/efficacy less well established),[7] ignoring the robust CAC literature that initially engendered the Class IIa recommendation, and the more recent data from three prospective, population-based outcome trials that the CAC Net Reclassification Index of the FRS is extremely high, particularly for the intermediate-risk group (52–66%) (*Table 1*).[8–10] The guide-

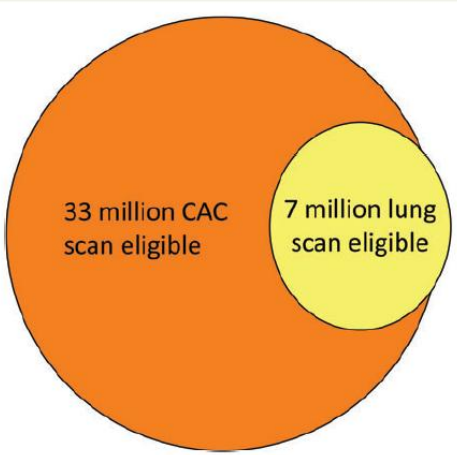


Figure 1 USA estimates, and overlap, of coronary artery calcium and lung scan eligible patients. The number of eligible patients in the USA is estimated at 33 million for coronary artery calcium scanning (orange)[28] and 7 million for lung scanning (yellow).[27] Excluding lung scan eligible patients who have established coronary disease (5.3%, unpublished data from the I-ELCAP database) yields an overlap of 6.6 million lung scan patients who would be expected to benefit from coronary artery calcium scanning.

Hecht HS, Henschke C, Yankelevitz D, Fuster V, Narula J.
Combined detection of coronary artery disease and lung cancer.
European Heart Journal 2014; 35:2792-6 PMID:25112665

Ordinal Coronary Artery Calcification Score
Frequency of CAC on LDCT Screenings

- Coronary calcium detected by chest CT has been shown to be the most reliable determinant of cardiovascular risk
- **The ELCAP-CAC score,** independently scored CAC in the four coronary arteries (main, left anterior descending, circumflex, and right coronary) was classified as

  0 = absent, 1 =mild, <⅓ of artery, 2 = moderate, ⅓ – ⅔), or 3 = severe, >⅔

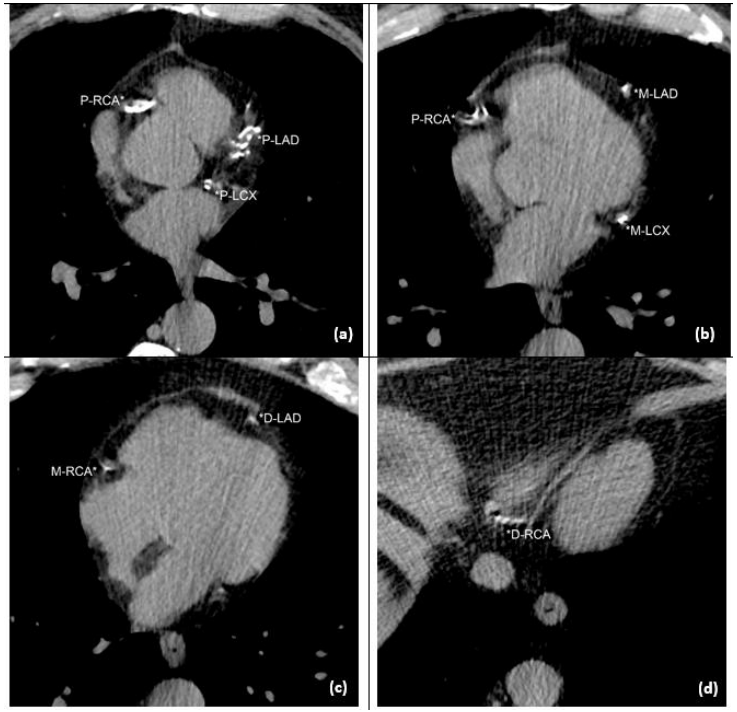
  Total score 0-12, categorized as: 0 = low risk , 1-3 = intermediate,

  4-6 = moderate , 7-12 = high

- Three Ordinal CAC score categories of 0, 1-3 and 4-12 were *highly correlated with*

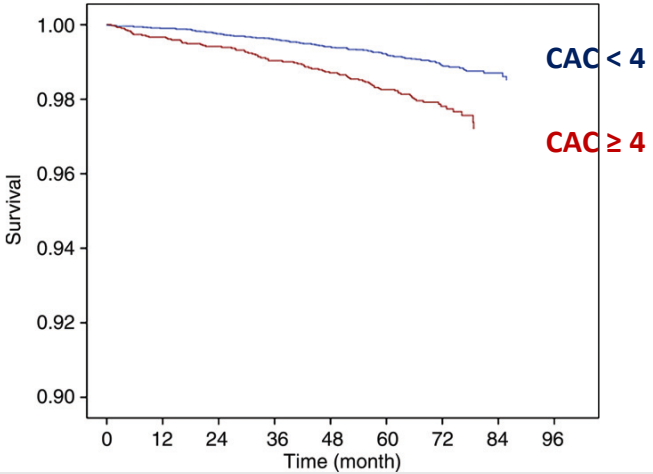
  Agatston score categories of 0 (low risk), 1-400 (intermediate risk) and 400+ (high risk)

Quantify Extent of CAC and CVD Survival



CVD-specific Survival Rates

adjusted by age, sex, smoking history and diabetes, N=8,782



Parameter	Category 0 (n = 3573)	Category 1–3 (n = 3569)	Category 4–12 (n = 1640)
Mortality rate*	43 (1.2)	66 (1.8)	84 (5.1)
Cox hazard ratio†			
Unadjusted	NA‡	1.6 (1.1, 2.4)§	4.7 (3.3, 6.8)‖
Adjusted#	NA‡	1.0 (0.7, 1.5)	2.1 (1.4, 3.1)§

Shemesh J, Henschke CI, Shaham D, et al. Ordinal Scoring of Coronary Artery Calcifications on LDCT Scans of the Chest is Predictive of Death from Cardiovascular Disease. Radiology 2010; 257(2): 541-8. PMID:20829542

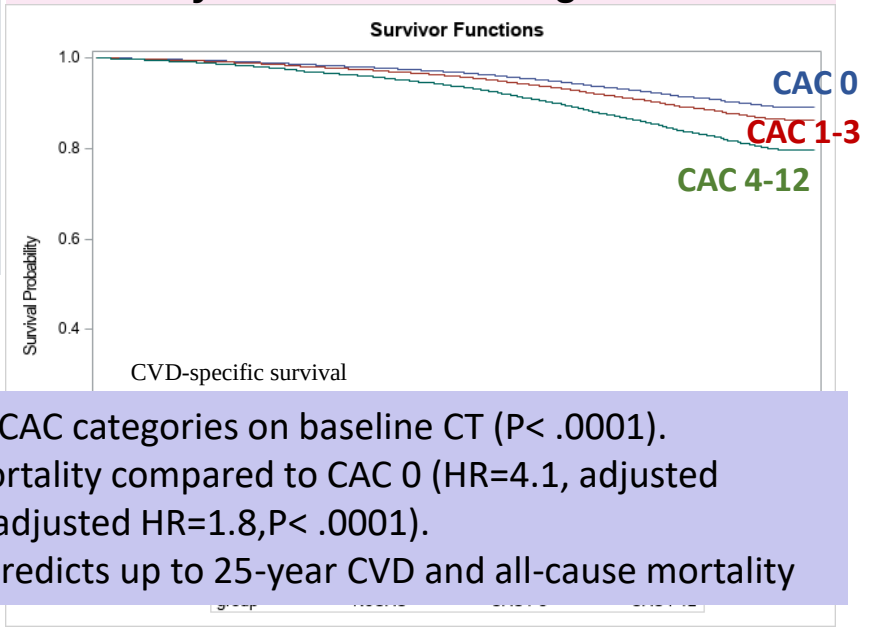
Survival after 25 years of follow-up (N=8782)

CAC Score at LDCT Predicts Long-Term Mortality

CAC category	CVD mortality		All-cause mortality	
	23-yr incidence	Adjusted HR (95% CI)	23-yr incidence	Adjusted HR (95% CI)
ELCAP-CAC 0 Low risk · n = 3,573	9.4%	Ref.	30.3%	Ref.
ELCAP-CAC 1–3 Intermediate · n = 3,569	16.5%	1.28 95% CI 1.11 – 1.48	44.5%	1.22 95% CI 1.13 – 1.32
ELCAP-CAC 4–12 High risk · n = 1,640	30.5%	1.98 95% CI 1.68 – 2.32	63.2%	1.70 95% CI 1.55 – 1.86

Adjusted for age, sex, pack-years of smoking, and diabetes mellitus. All p < .0001. Shemesh & Yip et al., Radiology 2025.

Cardiovascular (CVD) survival by Ordinal CAC categories



- CVD and all-cause mortality increased with higher Ordinal CAC categories on baseline CT (P< .0001).
- Participants with CAC 4-12 had significantly higher CVD mortality compared to CAC 0 (HR=4.1, adjusted HR=2.1, P< .0001) and higher all-cause mortality (HR=3.2, adjusted HR=1.8,P< .0001).
- Our study shows that a single baseline Ordinal CAC score predicts up to 25-year CVD and all-cause mortality

Shemesh J, Yip R, Cham M, et al. ELCAP Coronary Artery Calcium Score at Lung Cancer Screening CT Predicts Up to 25-Year Mortality. Radiology 2025; 316(23):250090

Visual Assessment of Emphysema

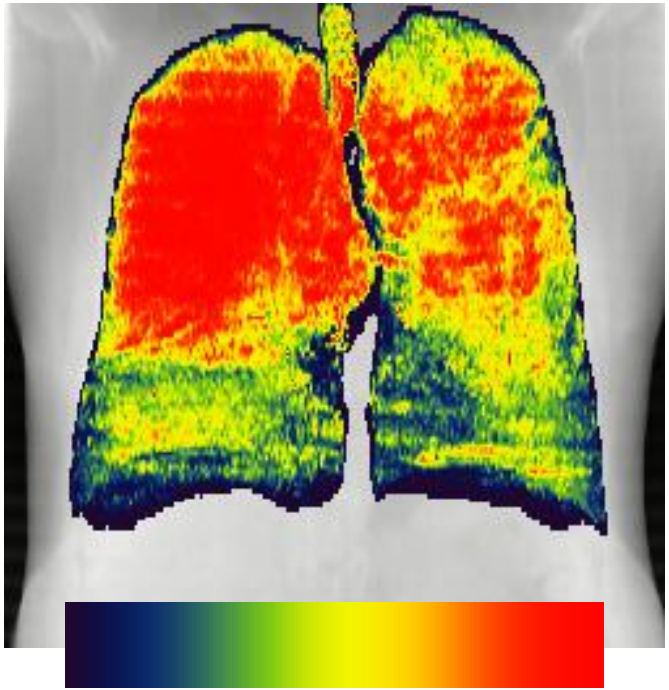
None: none of the findings below

Mild: no distinct areas of reduced attenuation were visible on the CT Scan, but vascular splaying suggested parenchymal expansion, or if only occasional discrete low-attenuation areas were observed

Moderate: presence of identifiable low-attenuation areas affecting <50% of the lung parenchyma

Severe: presence of identifiable low-attenuation areas involved ≥ 50% of the lung parenchyma.

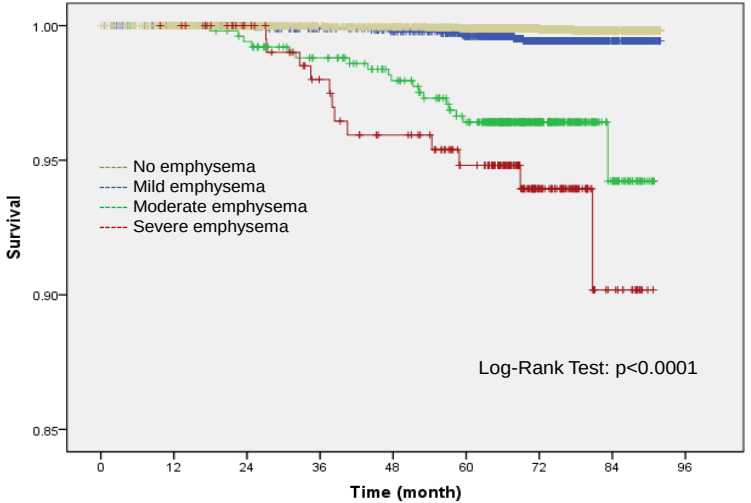
Quantify Extent of Emphysema and COPD Survival



severe emphysema shown in red

COPD-specific Survival Rates

adjusted by age, sex, smoking history and diabetes, N=9,047



Presence of emphysema Increases risk of lung cancer

Moderate: HR=17.3 (9.5-52.3)

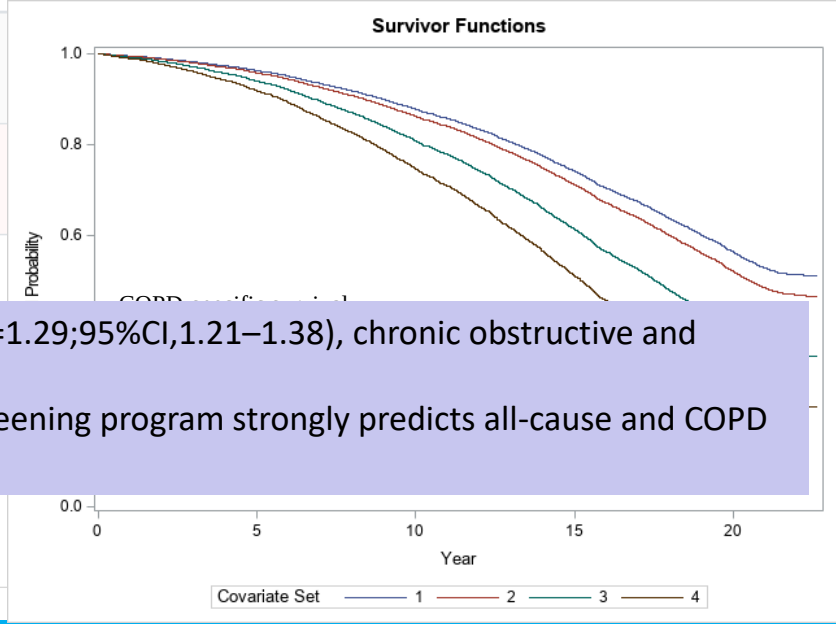
Marked: HR=43.7 (13.9-86.1)

Henschke CI, Yip R, Boffetta P, Markowitz S, Miller A, Hanaoka T, Zulueta JJ, Yankelevitz DF. CT screening for lung cancer: importance of emphysema for never smokers and smokers. Lung Cancer 2015; 88:42-7 PMID:25698134

Emphysema at Baseline LDCT Predicts 25-Year Mortality

	All-cause mortality		COPD mortality	
Emphysema category	Adjusted HR	95% CI	Adjusted HR	95% CI
Any emphysema *vs. none*	**1.29**	p = <.001	**3.29**	p = <.001
	1.21 – 1.38		2.59 – 4.18	
by severity (dose-response) **Mild emphysema** *vs. none · model 5*	1.15	p = <.001	2.07	p = <.001
	1.06 – 1.24		1.56 – 2.76	
Moderate emphysema *vs. none · model 5*	1.54	p = <.001	**5.31**	p = <.001
	1.36 – 1.74		3.82 – 7.38	
Severe emphysema *vs. none · model 5*	**2.28**	p = <.001	**12.06**	p = <.001
	1.94 – 2.69		8.43 – 17.27	

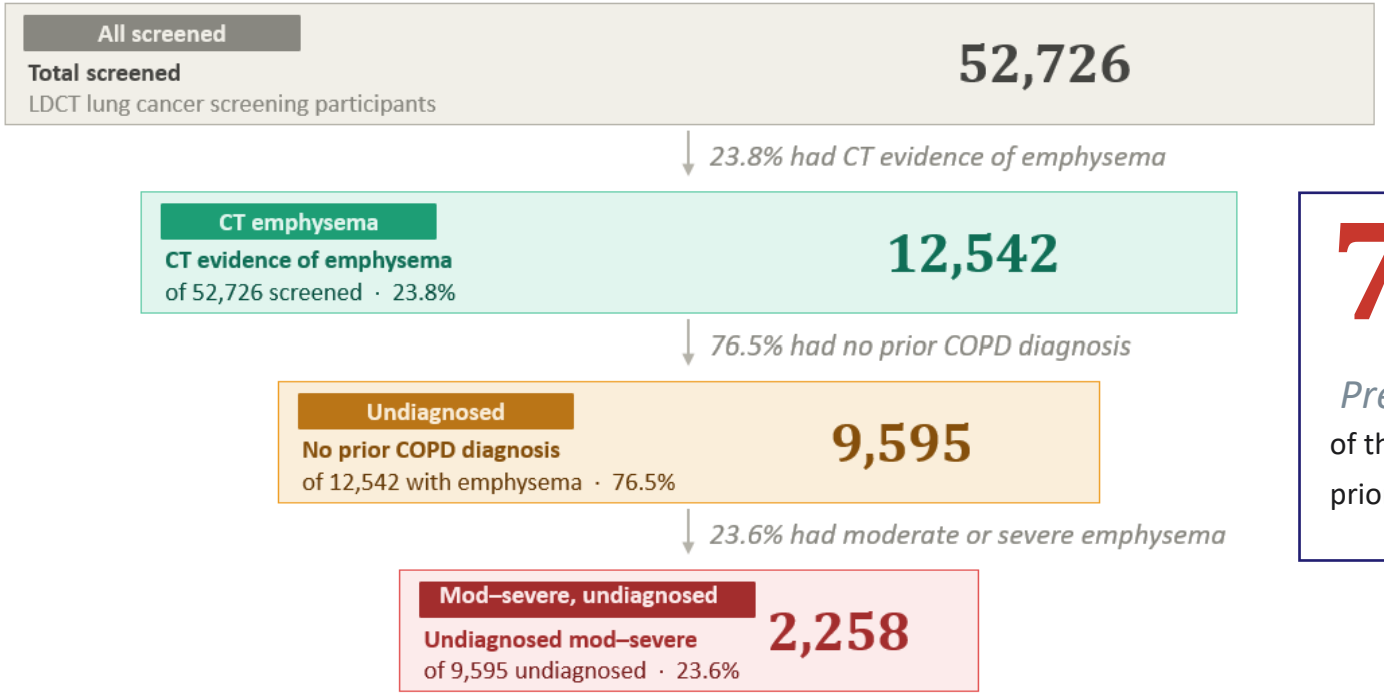
Adjusted for sex, age, pack-years of smoking, and years since quitting.



- Emphysema was a significant predictor of all-cause mortality (HR=1.29;95%CI,1.21–1.38), chronic obstructive and pulmonary disease(COPD) mortality (HR=3.29;95%CI,2.59–4.18).
- Emphysema at baseline on low-dose chest CT in a lung cancer screening program strongly predicts all-cause and COPD mortality up to 25 years later.

González Gutiérrez & Yip et al., Radiology 2025 · n = 9,047 ·

Emphysema on LDCT: a finding most people don't know they have.



76.5%

Previously undiagnosed

of those with emphysema had no prior COPD diagnosis

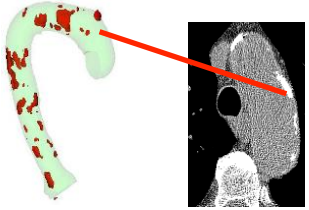
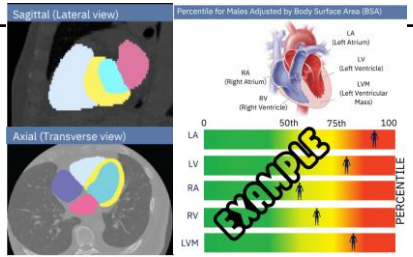
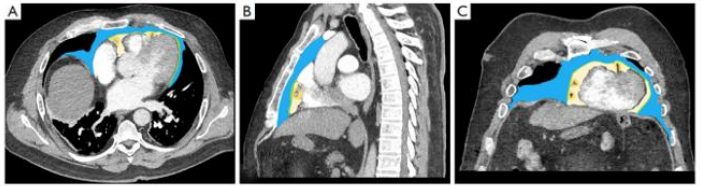
LDCT provides an opportunity to identify emphysema, and recommend smoking cessation.

Steiger et al. The importance of LDCT screening to identify emphysema in asymptomatic participants with and without a prior diagnosis of COPD. Clin Img 2021

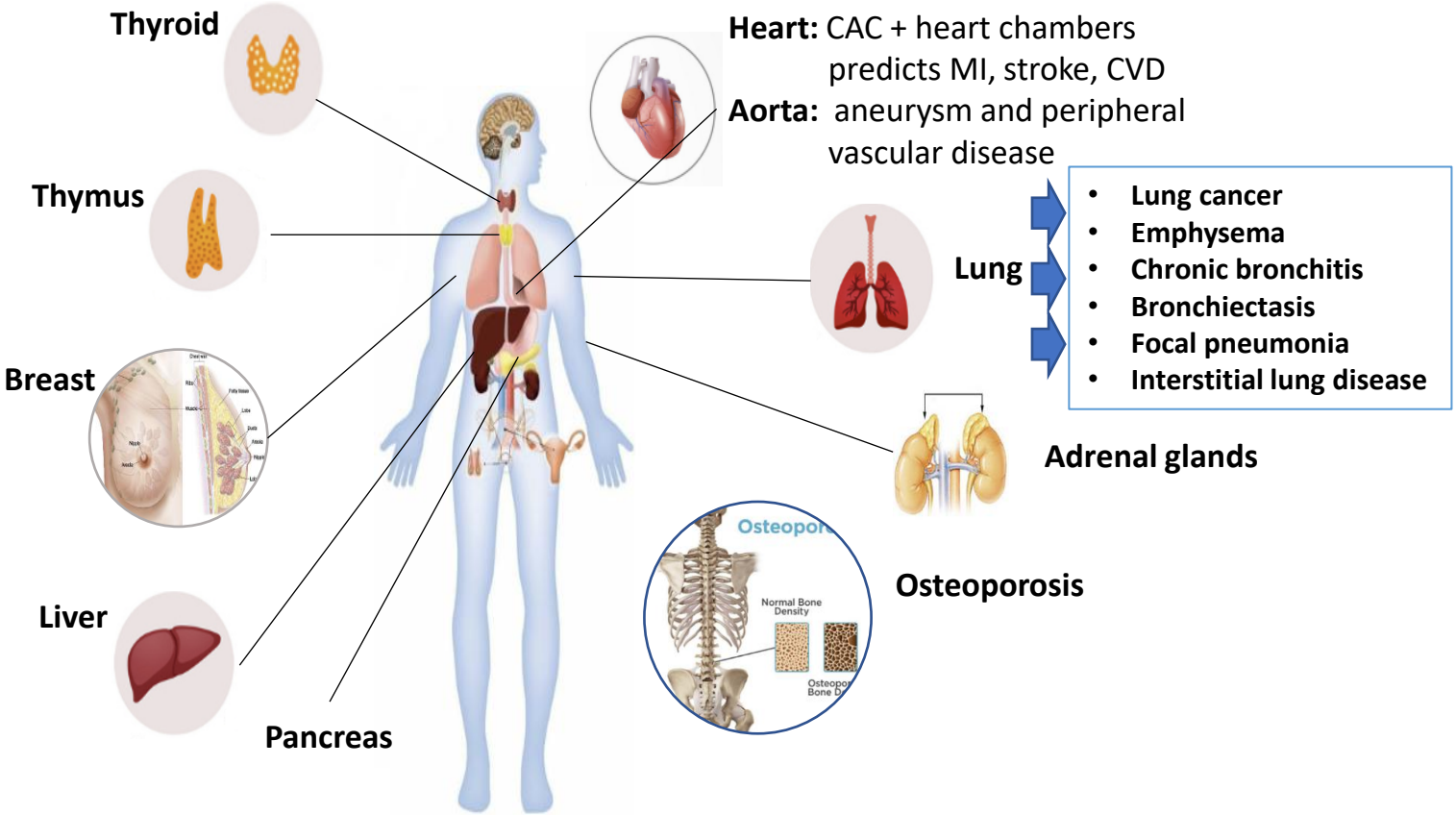
AI enabled detection & quantification

Other cardiovascular findings on LDCT

Nodule growth assessment

Aortic value calcification *Marker of aortic stenosis*	
Pulmonary hypertension	
Cardiac Chamber Volumetry *AFib, Stroke, HF*	
Pericardial and epicardial fat *cardiovascular events and mortality*	 **Figure 2** Thoracic CT on axial (A), sagittal (B) and coronal (C) planes. See regions of interest (ROIs) of PCAT (light orange ROI), EAT (light yellow ROI), pericardial adipose tissue (green ROI) and paracardial adipose tissue (light blue ROI). CT, computed tomography; PCAT, pericoronary adipose tissue; EAT, epicardial adipose tissue.

LDCT is an Annual Health Check – *Comprehensive Screening*



I-ELCAP Investigators 2000-2020; Added benefits: TLCR 2021
Developed Multidisciplinary Recommendations

Infrastructure that makes evidence possible

01 — Standardised protocol
Annual LDCT with consistent acquisition

02 — Structured reporting
CAC · emphysema · nodule findings documented

03 — Rigorous workup
Growth assessment before diagnosis minimises overdiagnosis

04 — Timely treatment
Median 1 month from diagnosis to surgery

05 — Long-term follow-up
Annual return · NDI linkage · 23+ year data

The same infrastructure that produced the 81% cure rate is what makes 25-year CAC and emphysema outcome data possible.

- Integrated management protocol? Comprehensive screening adds value only when detected CAC and emphysema findings trigger appropriate follow-up care, e.g. statin, smoking cessation, referral
- common CT acquisition protocol?

Looking ahead

- **The disease burden**

  44% of global premature deaths. All three are tobacco-related, co-occurring, and largely undiagnosed until symptoms appear late when treatment is unlikely to be curative.

- **The opportunity**

  The scan is already paid for. Same scan already contains CAC and emphysema data. Greater public health benefit requires moving beyond the single-disease silo.

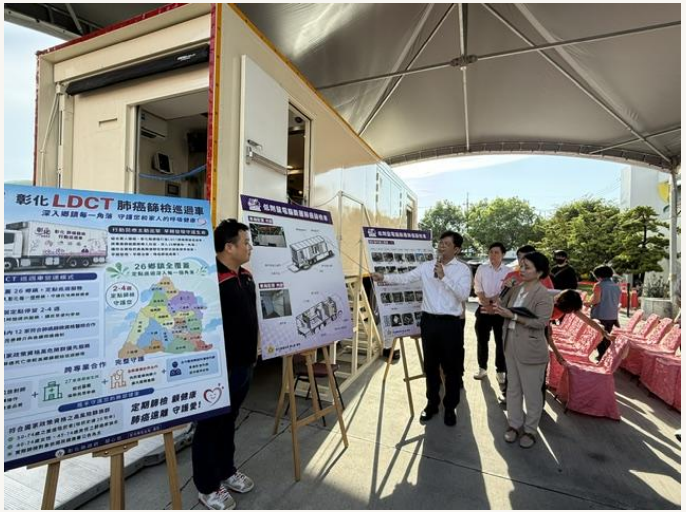
- **Screening as a teachable moment**

  People aware of their CAC score, emphysema grade, and lung cancer risk are more open to preventive measures -> Motivates smoking cessation, increase adherence to statin/lifestyle and screening adherence.

- **Implementing multiple disease endpoints brings potential cost economies, convenience, and health benefits for screening participants.**

BIG-3 Screening in Changhua

Taiwan launched its national LDCT lung cancer screening program (TALENT) in July 2022 — the first to screen by smoking history and family history. Now,



4-IN-THE-LUNG-RUN [ENROLLING] 5-country European trial, 26,000 participants, is the first implementation trial to prospectively integrating CAD and COPD to LDCT.

AGILE DxRx

Save the Date

4th AGILE DxRx April 1-3, 2027

Vancouver, Canada

The Alliance for Global Implementation of Lung and Cardiac Early Disease Detection and Treatment.

Our Mission

The early detection of lung cancer using thoracic CT has been widely demonstrated in multiple international trials to objectively increase cure rates. Now the international focus is on effective and economical implementation. Increasingly, it is emerging that thoracic CT screening is also detecting a range of early tobacco-related diseases including cardiovascular disease and chronic obstructive pulmonary disease. These three diseases comprise the ‘BIG3’, as they collectively account for close to half of the premature deaths globally. Thoracic CT screening presents a unique opportunity to integrate care for this high risk cohort with a single imaging examination. We plan to develop optimized protocols for evaluation of these major diseases, explore challenges and define solutions in enabling implementation, especially for economically disadvantaged countries across the world. A core strategy in achieving this ambitious goal is to leverage the use of AI processes across the continuum of care, including its use for risk assessment, disease detection and managing disease interventions.

https://agiledxrx.org

THANK YOU