IASLC 2022 World Conference on Lung Cancer
AUGUST 6-9, 2022 | VIENNA, AUSTRIA

Lung cancer screening and tobacco control

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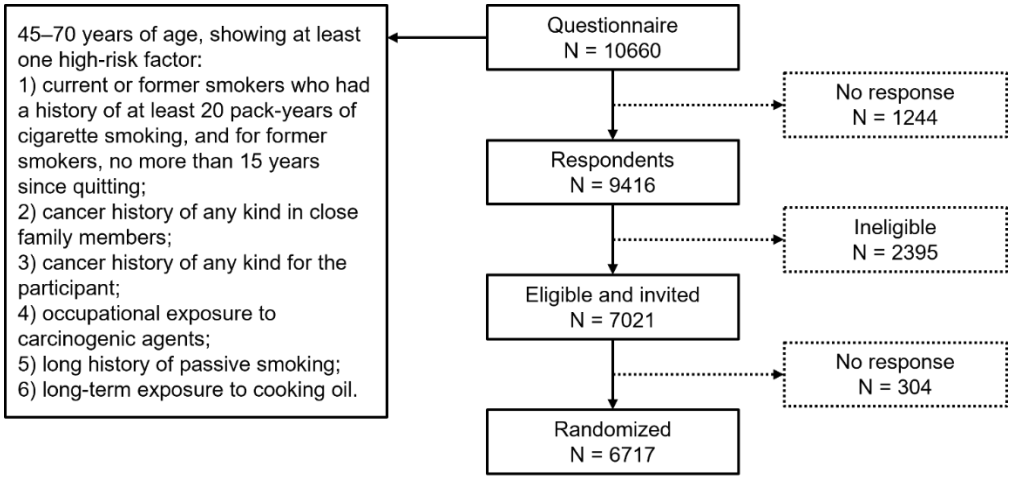
DISCLOSURES

Company	Relationship(s)
Intuitive Surgical	Consultant
Intuitive Foundation	Research grant
Centese	Research grant

Lung cancer risk assessment

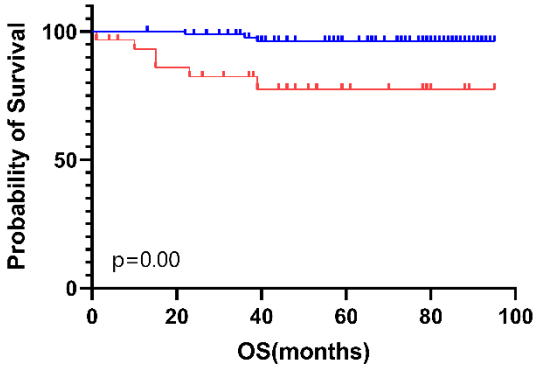
China Lung Cancer Screening (CLUS) version 1.0

- From November 2013 to November 2014
- 6717 eligible participants with high-risk factors
- LDCT vs Nature cases
- Screening interval: biennial
- Screening rounds: three
- Data cut-off date: February 28, 2022

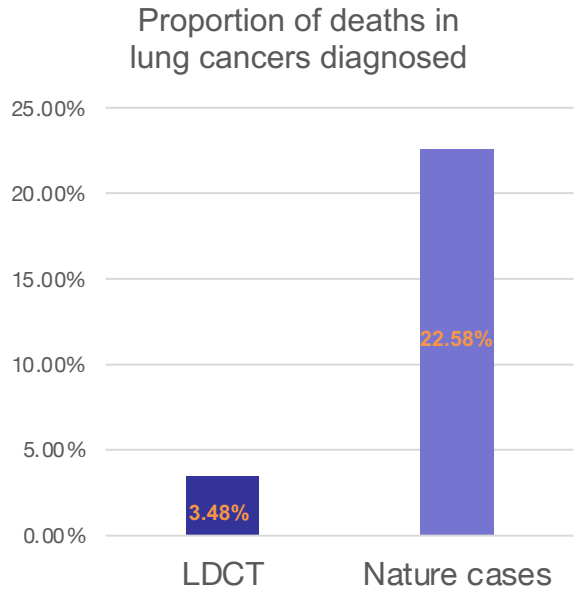


Clinical characteristics, stage and histologic features of lung cancers diagnosed

	LDCT			Nature cases
	Screening-detected	Non-Screening-detected	All	
No.			3512	3145
Lung cancers (No.)	79	7	86	31
Mortality of lung cancer (No.)	2	1	3	7



5-years overall survival: 97.3% vs 75.0%
Median follow-up time: 73.65 months



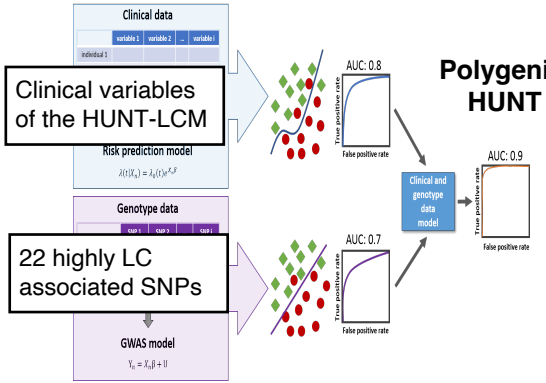
HUNT Lung-SNP model

Model development

Cohort: HUNT2

N = 30 746 ever smokers (median follow up 15,26 years).

N = 160 individuals were diagnosed with LC within 6 years



Polygenic Risk Model: HUNT Lung-SNPs

External validation:

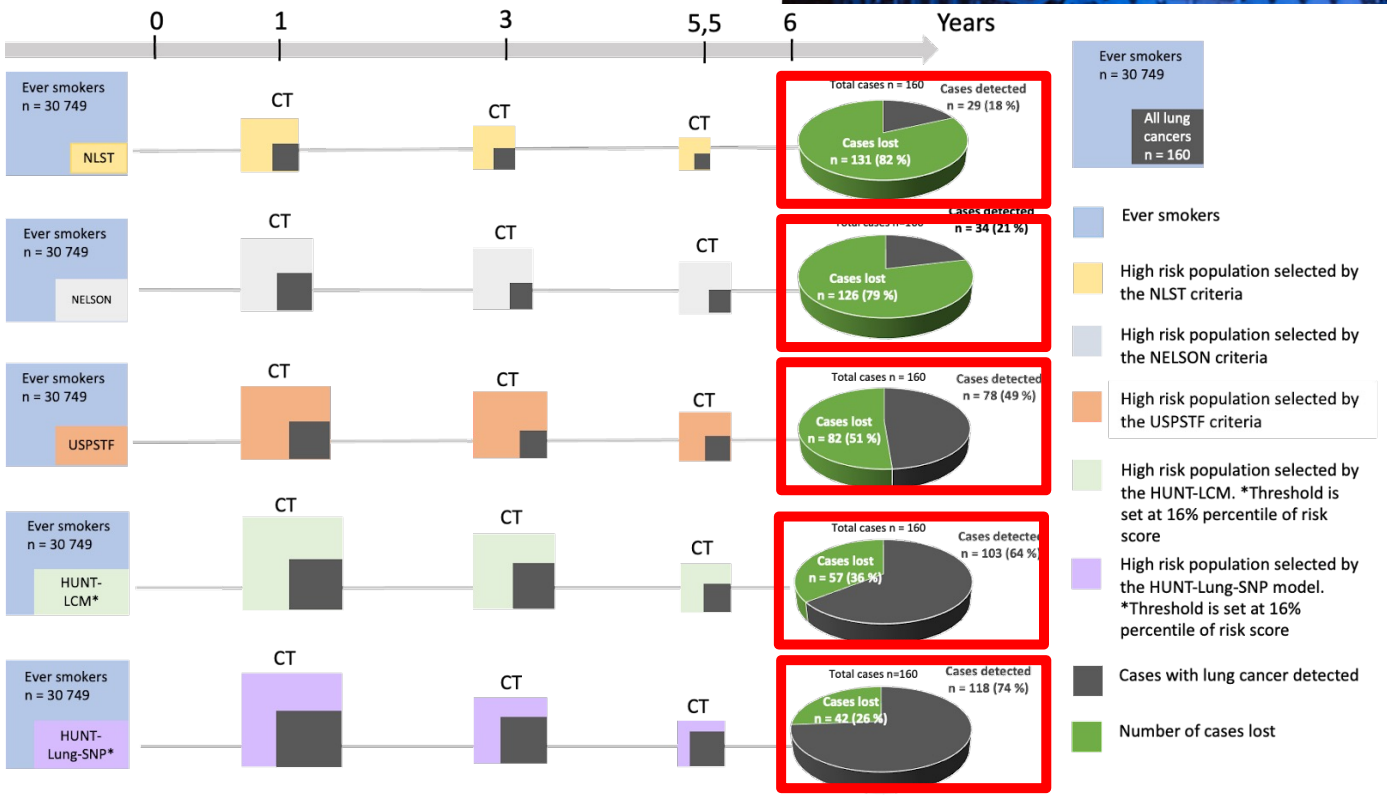
Cohort: Tromsø study

N = 3074 ever smokers (median time to event 3.04 years)

N = 39 individuals were diagnosed with LC within 6 years

Results

Model \ Cohort	Discovery (HUNT2)	Validation (Tromsø)
	N = 30749	N = 3074
HUNT-LCM		
AUC (95% CI)	0·844 (0·82-0·869)	0·893 (0·848-0·931)
C-index (95% CI)	0·849 (0·824-0·873)	0·89 (0·848-0·933)
HUNT-Lung-SNP		
AUC (95% CI)	0·875 (0·854-0·896)	0·926 (0·891-0·955)
C-index (95% CI)	0·88 (0·86-0·9)	0·924 (0·892-0·955)


0
1
3
5,5
6
Years
Ever smokers n = 30 749
NLST
CT
Total cases n = 160
Cases detected n = 29 (18 %)
Cases lost n = 131 (82 %)
Ever smokers n = 30 749
NELSON
CT
Cases detected n = 34 (21 %)
Cases lost n = 126 (79 %)
Ever smokers n = 30 749
USPSTF
CT
Total cases n = 160
Cases detected n = 78 (49 %)
Cases lost n = 82 (51 %)
Ever smokers n = 30 749
HUNT-LCM*
CT
Total cases n = 160
Cases detected n = 103 (64 %)
Cases lost n = 57 (36 %)
Ever smokers n = 30 749
HUNT-Lung-SNP*
CT
Total cases n=160
Cases detected n = 118 (74 %)
Cases lost n = 42 (26 %)
Ever smokers n = 30 749
All lung cancers n = 160
Ever smokers
High risk population selected by the NLST criteria
High risk population selected by the NELSON criteria
High risk population selected by the USPSTF criteria
High risk population selected by the HUNT-LCM. *Threshold is set at 16% percentile of risk score
High risk population selected by the HUNT-Lung-SNP model. *Threshold is set at 16% percentile of risk score
Cases with lung cancer detected
Number of cases lost

The INTEGRAL project

1000+ proteins
Proximity extension assay (Olink)

731 cases and 731 matched controls with a history of daily smoking

Pre-diagnostic blood collected up to 3y before diagnosis

6 cohort studies from 12 countries

The Lung Cancer Cohort Consortium (LC3)

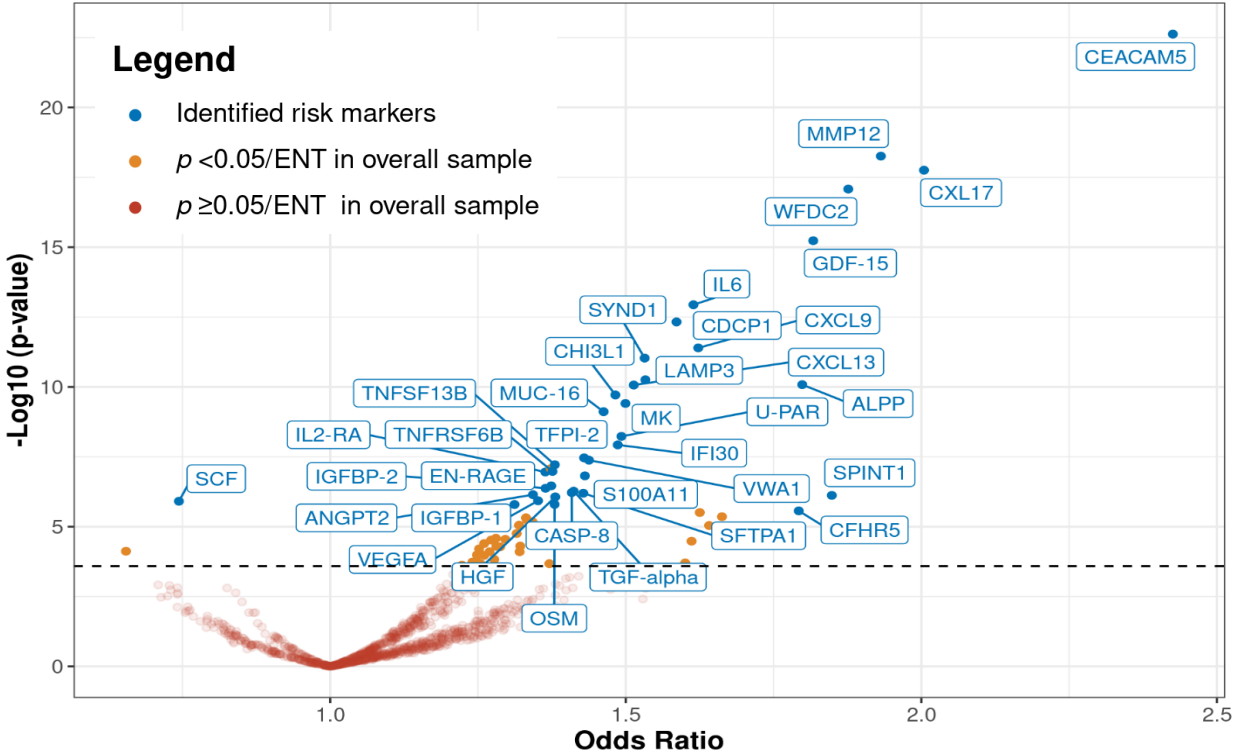
The Lung Cancer Cohort Consortium, *medRxiv* 2022
Robbins et al, *medRxiv* 2022

Proteins associated with lung cancer risk

67 proteins
Corrected for multiple comparisons

↓

36 ‘robust’ proteins
Resampling algorithm

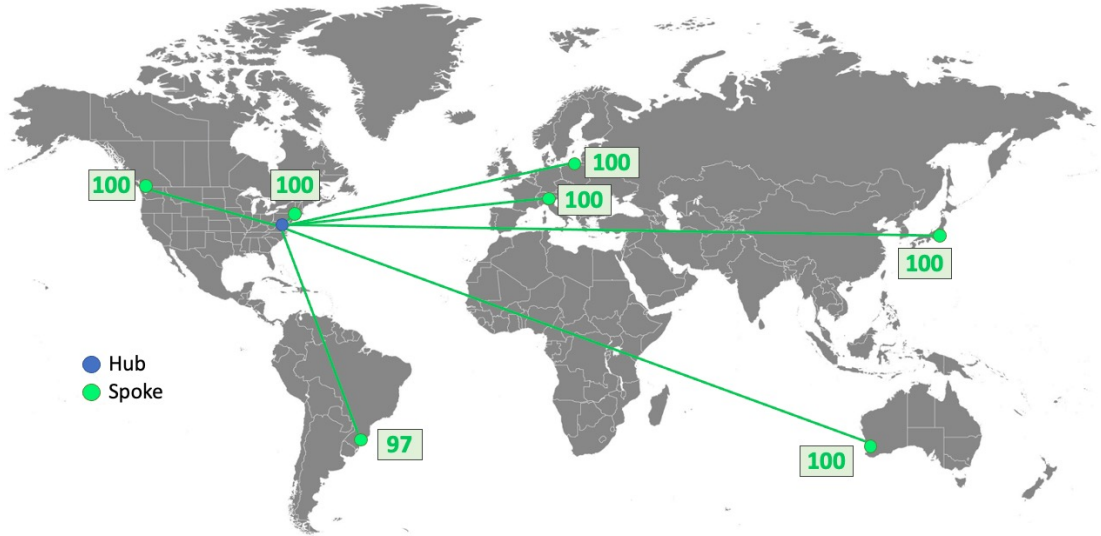


The Lung Cancer Cohort Consortium, *medRxiv* 2022
Robbins et al, *medRxiv* 2022

Nodule detection and reporting

Early Lung Imaging Confederation

- **Participating Sites (Spokes) Provide 100 cases of de-identified high quality screening CT scan images and metadata at 2 time points to IASLC ELIC hub for analysis within a highly secure and strictly controlled environment**
- **All Spoke Provided Data Stays Within Their Country/Region By Using The Amazon Web Services (AWS) Global Cloud Infrastructure**
- **AI Algorithm Developers Can Securely Send a Lung Analysis Algorithm To The Spokes To Run Computational Experiments And Receive Back Analysis Results.**
- **Selected data set for an initial feasibility study**



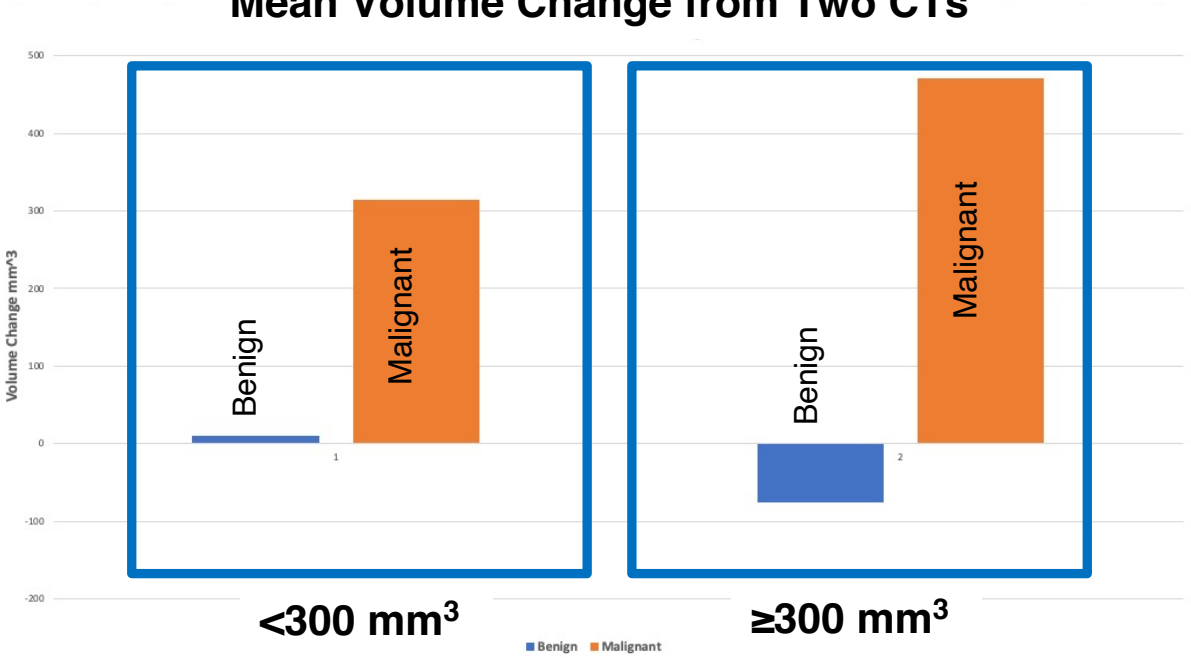
ELIC Is Now Running Globally Distributed Deep Learning AI and Quantitative Imaging Experiments
These First Analyses Show The Potential Of ELIC

Semi-automated Volumetric Measurements of Change in Solid & Part-solid Nodules in 2 CTs from Same Individual

	Volume mm^3	Mean	COV
Benign	<300	9.3	5.35
	≥300	-75.4	-6.68
Malignant	<300	313.9	0.91
	≥300	471.3	1.57

COV = Coefficient of Variation

Mean Volume Change from Two CTs



STUDY DESIGN

2053 baseline CT from International Lung Screening Trial (Vancouver, 2016- 2019, ever smoker, 55-80 yo, meet the USPSTF 2013 screening criteria or with a PLCOm2012 6-years lung cancer risk >1.5%)

Arm #1: Radiologist & CAD concurrent reading
(1 combined report, 1 radiologist reading time)

PanCan malignancy score

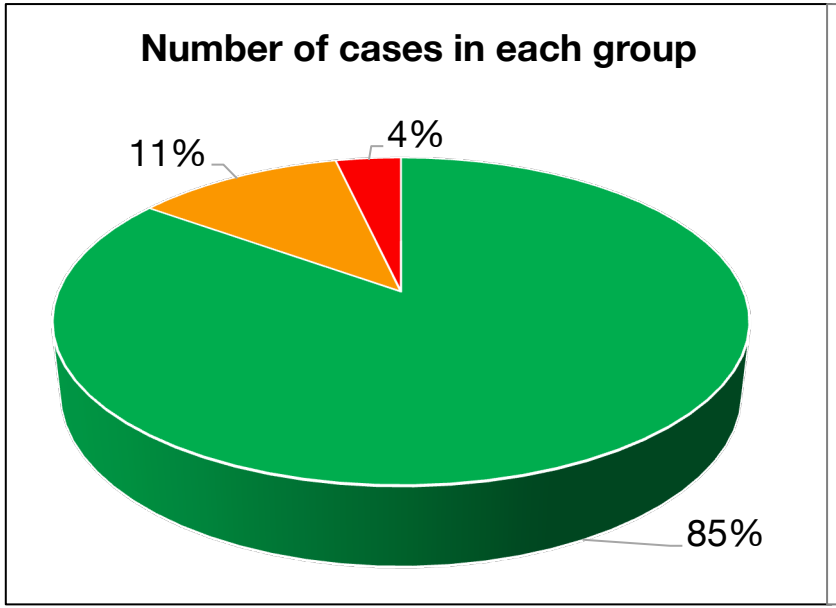
Arm #2: Radiologist-1st -> adding CAD -> combined reading
(2 reports: manual and combined; Rad-alone reading time)

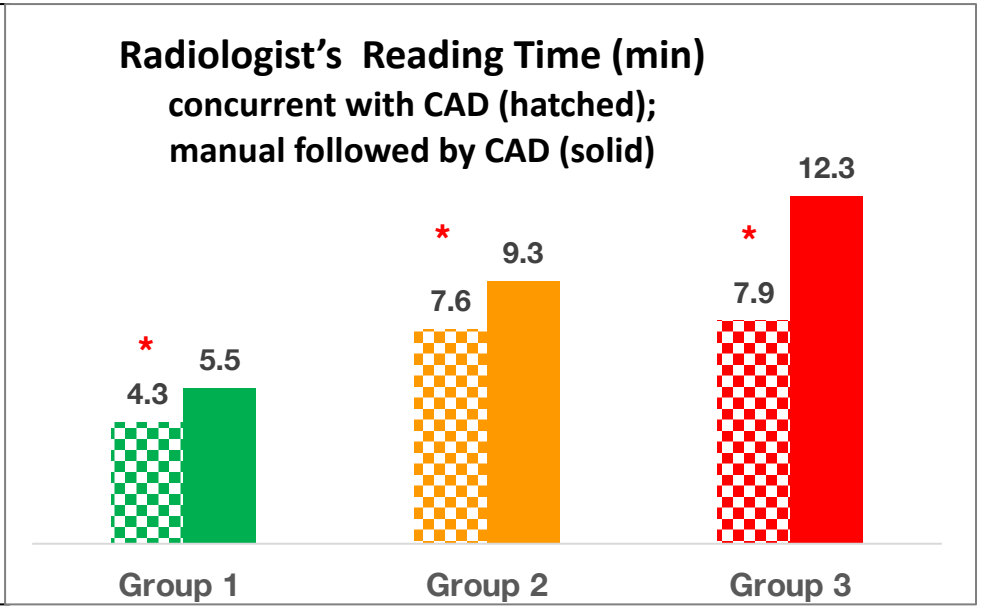
Group 1: (Biennial/Annual FU CT) **Group 2: (Early FU CT in 3 months)** **Group 3: (Diagnostic work-up)**

Q1: Rad's Reading Time between 2 arms, in: Group1, Group 2, Group3, respectively

Q2: Any change in management (i.e., "group") between Rad-alone and combined reading? If so, which direction?

RESULTS – 1) Radiologist's Reading Time





Methods:

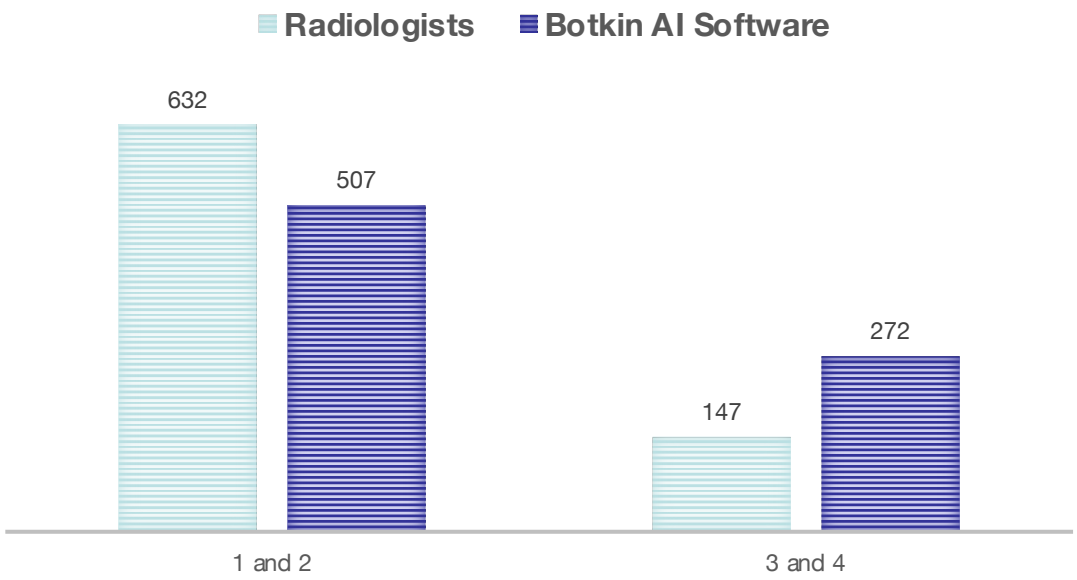
Retrospective study based on the reanalysis of LDCT performed in the first lung cancer screening program in Brazil (BRELT1).

LDCT were evaluated by radiologist and analyzed using artificial intelligence software (BOTKIN IA – Russia)

In each exam, LungRADS™ was evaluated.

General methodology primarily focuses on outcomes-based training, full volume approaches, and directly comparable clinical performance evaluation.

ASSESSMENT OF THE MAIN NODULE - LUNG RADS™



LungRADS™ 3 and 4

Sensibility of 92.5%

Specificity of 78.5%

PPV 50%

NPV 97.8%

Overall accuracy of 81.1%

Cost effectiveness

Methods

We assumed that screening reduces lung cancer mortality (per NELSON and NLST) and calculated the costs and QALYs implied by that assumption.

Modelling procedure

1. Identify the eligible population in Australia and model death from lung cancer or other-causes.
2. Apply the lung cancer mortality benefit observed in trials to estimate life years gained.
3. Estimate lung cancer cases by stage, with and without screening (accounting for overdiagnosis).
4. Apply costs and disutilities relating to screening, false positives, and treatment.
5. Estimate incremental costs per QALY.

Inputs

Australian data

- Composition of eligible population estimated from the *45 and Up Study*, a longitudinal cohort study (n = 267,153).
- Hazard ratios for LC and all-cause mortality in the *45 and Up Study* using linked records on cancer diagnoses and deaths.
- Lung cancer costs[1] and cost of CT scan ($307).
- SF-6D utility values[2-4]

Trial-related outcomes

- LC mortality reductions (by length of follow-up)
- Stage-shift
- False positive rates
- Overdiagnosis rates

1. Goldsbury et al. Health services costs for lung cancer care in Australia: Estimates from the 45 and Up Study. PLOS ONE. 2020 Aug;15(8):e0238018.
2. Ngo et al. Health utilities for participants in a population-based sample who meet eligibility criteria for lung cancer screening. Lung Cancer. 2022 May 13.
3. Ngo et al. Large-Scale Population-Based Surveys Linked to Administrative Health Databases as a Source of Data on Health Utilities in Australia. Value in Health. 2022 May 6.
4. Tramontano et al. Catalog and Comparison of Societal Preferences (Utilities) for Lung Cancer Health States. Medical Decision Making. 2015 Apr;35(3):371–87.

Results

NELSON

Base case: AU**$39,250**/QALY

95% CI: AU**$18,150-108,300**/QALY

P(ICER < AU$30,000/QALY) = **15%**

P(ICER <AU$50,000/QALY) = **60%**

NLST

Base case: AU**$76,300**/QALY

95% CI: AU**$41,750–236,500**/QALY

P(ICER < AU$30,000/QALY) = **0.5%**

P(ICER < AU$50,000/QALY)= **6.7%**

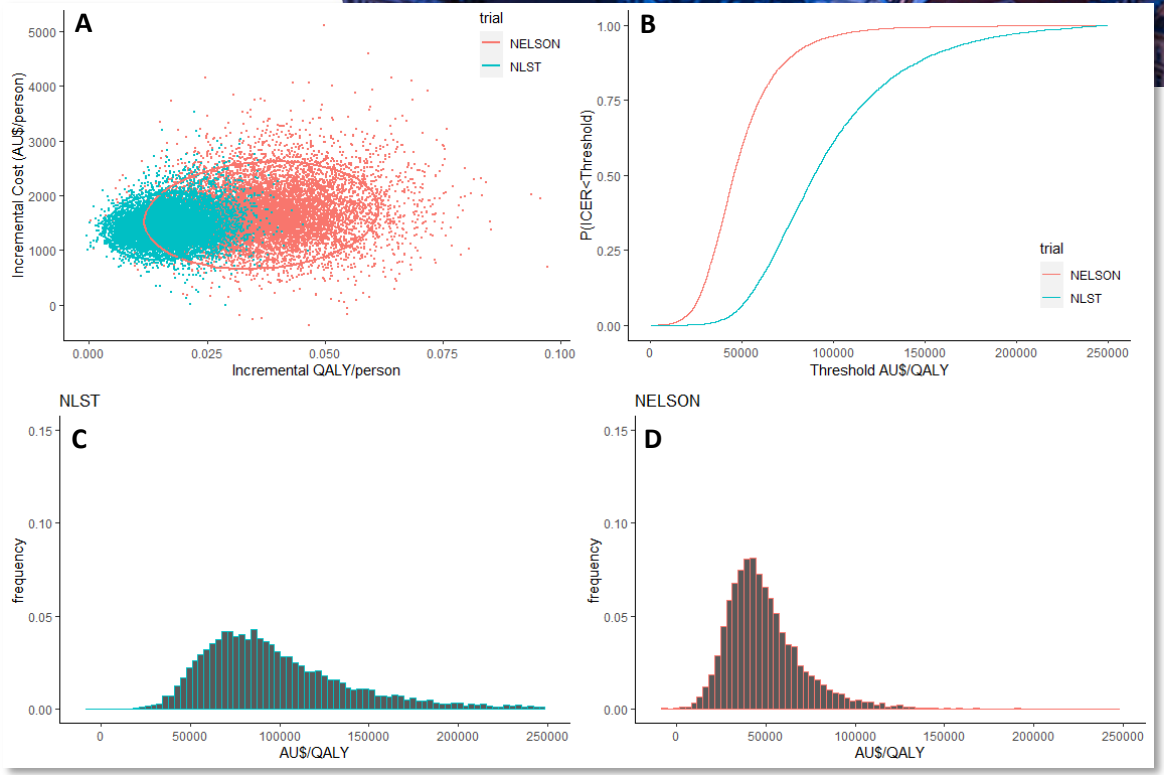


Figure 1. (A) Scatter plot of incremental costs (in AU$/person) vs incremental QALYs/person obtained from the PSA for the NELSON and NLST settings. (B) Corresponding estimated cost-effectiveness curve given the ICER distributions obtained from the PSA. (C and D) Histograms showing the ICER distributions obtained from the PSA for the NLST and NELSON settings, respectively.

Surveillance

Patients diagnosed with biopsy-confirmed lung cancer in the NLST
N = 1,971

Patients in NLST diagnosed with clinical stage I-III initial primary lung cancer
N = 1,405

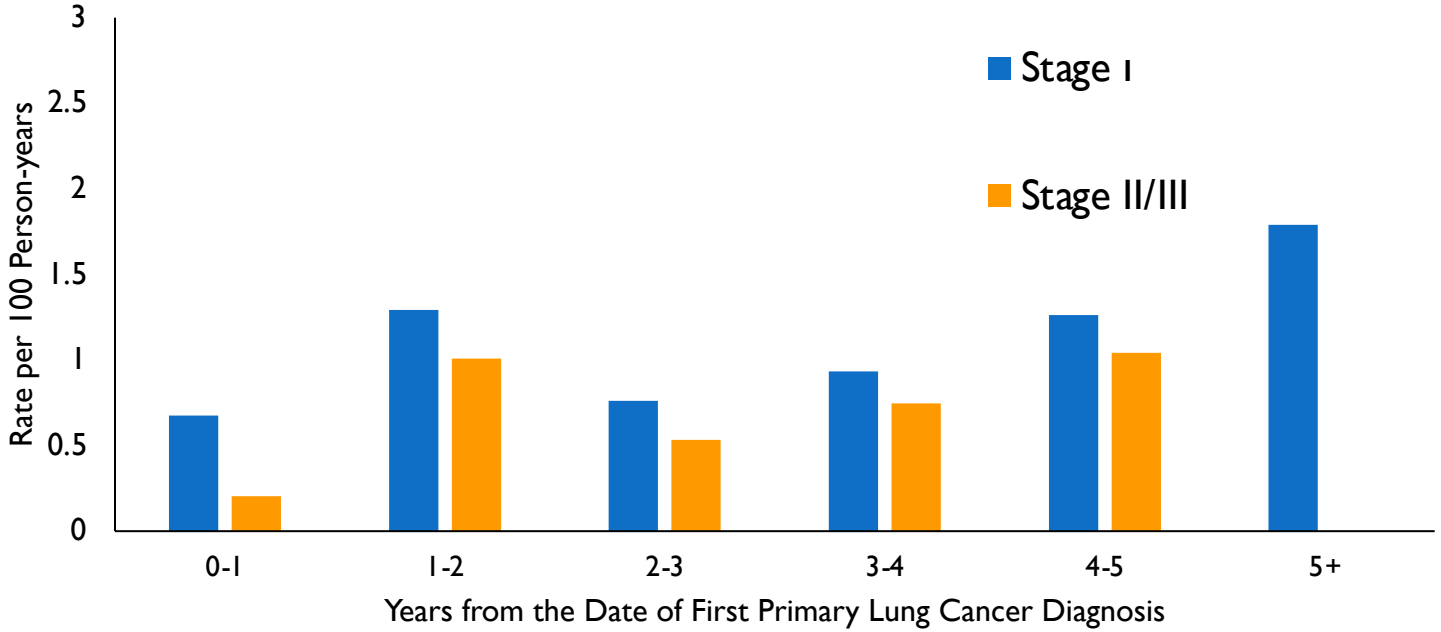
No Second Primary Lung Cancer
N = 1,323 (94.2%)

Second Primary Lung Cancer
N = 82 (5.8%)

Synchronous
N = 45 (54.9%)

Metachronous
N = 37 (45.1%)

Incidence of Metachronous Primary Lung Cancer from the Date of Initial Primary Lung Cancer Diagnosis



Smoking cessation

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Current smokers attending lung health check
- Immediate consultation with smoking cessation practitioner
  - Behavioural support, pharmacotherapy/e-cigarette
  - Explanation of trial and information sheet provided

4-week follow up: control
- Informed consent
- Smoking status (CO in quitters)
- 1-1 and ongoing pharmacotherapy + behavioural support

4-week follow up: intervention
- As control group + personalised risk information (CT images of own heart & lungs) + supportive communication

3 and 12 month follow up
- Smoking status (CO validation in quitters)
- Psychological change variables
- Quality of life
- Healthcare usage

Yorkshire Stop Smoking Study

Yorkshire Cancer Research

7-day validated point prevalent abstinence 4 weeks after the LHC: **12.4%**
(15.0% self-reported)
Cost per validated quitter: £523.76*

7-day validated point prevalent abstinence 4 weeks after the LHC: **16.5%**
(20.1% self-reported)
Cost per validated quitter: £414.95*

Participants attending for LCS that currently smoke (n=2248)

Eligible for SCP referral (n=2150)

Seen by SCP on mobile unit (n=1905, 89%)

Agree to ongoing SCP support (n=1609, 84%)

R

Consent to YESS (n=1003)

Control arm (ongoing behavioural support + pharmacotherapy) (n=476,47%)

Intervention arm (personalised feedback + supportive communication + ongoing behavioural support + pharmacotherapy) (n=527, 53%)

Ineligible for SCP:
- Ineligible for CT screening
- Unable to consent
- SCP not available

Refused to see SCP on mobile unit (n=245, 11%)

Decline ongoing SCP support (n=296, 16%)

Decline consent to YESS (n=606)

*cost per quitter includes smoking cessation consultations, pharmacotherapies and e-cigarettes dispensed from the co-located service

Opt-In vs Opt-Out Tobacco Treatment in Hospital

Changing the Default (N=1,000)

Opt In

Offer in-patient med

↓

Provide Brief Advice to quit

↓

Ready or Willing to quit?

↓ Yes

Offer Treatment plan/ post dc Meds/Support

→ No

Motivational Intervention

Opt Out

Provide in-patient med

↓

Provide Brief Advice to quit

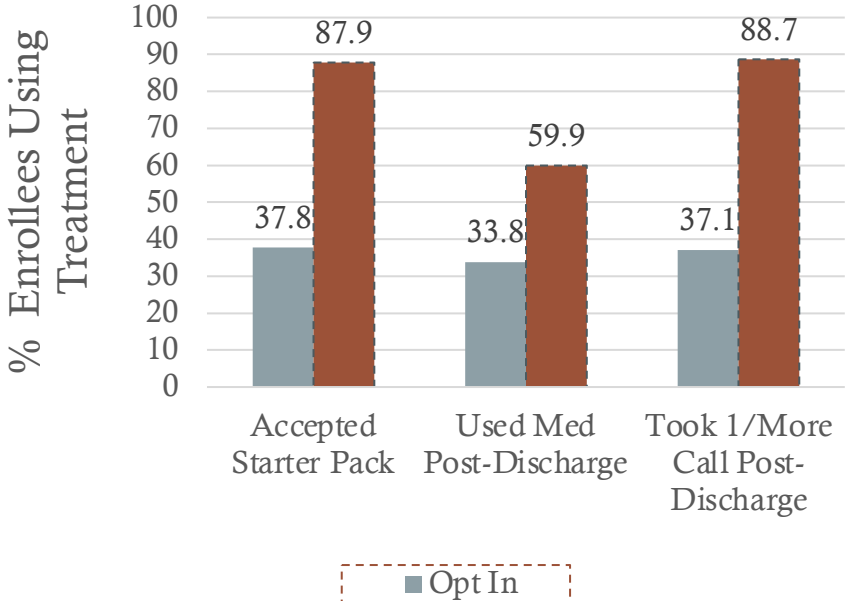
↓

Provide Treatment plan/ post dc Meds/Support

- Randomized clinical trial
- Primary outcome: Verified quit
  - 1 month post dx

Richter & Ellerbeck, 2015; Faseru et al., 2017; Faseru et al. 2022

Medication & Counseling Use (N=739)



	Abstinence Rates (95% Credible Interval)		Bayesian Posterior Probability Opt Out better than Opt In
	Opt In	Opt Out	
	15.8 (11.8, 20.5)	21.5 (17.9, 25.4)	**.971**

Smoking Cessation Programs

Site	Description
A	Ottawa Model for Smoking Cessation: 12 weeks of weekly counselling with follow-up at 6 months; pharmacotherapy as appropriate, self-help materials
B	3 options: • On-site group session (1.5 hr), follow-up at 3 months by SC champion • Referral back to primary care provider • Community pharmacists
C	4 face-to-face sessions (baseline, 3 & 8 weeks, 6 months), 15 min with trained navigator; access to free NRT

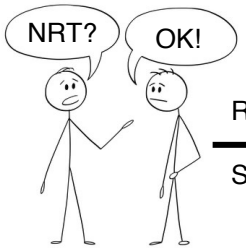
Results

Smoking cessation program participation:

4,451 had baseline LDCT scan
- 3,063 (68.8%) current smokers
- 2,736 (89.3%) attended counselling on day of LDCT screening

Program results:

1,689 had a 12-month follow-up LDCT with complete data
- Quit rate (30-day abstinence): 15.5% (range 10.5%–20.0%)
- Relapse rate 6.3%: (3.1%–7.3%)



Randomization

Single Blinded

Meet Smoking Cessation Counsellor
- Design quit plan
- Select quit date
- $50

Quit Date

Grace Period 3 Months

Tobacco Free 1 Month

Follow Up 6 months

Reward Group

Pay for Performance

Questionnaires
1. Demographics
2. Fagerström Test Nicotine Dep. (FTND)
3. Minnesota Nicotine Withdrawal (MnNWS)
4. Beck's Anxiety Index
5. Beck's Depression index
6. Pgh Sleep Quality Index (PSQI)
7. PTSD PCL5
8. Kirby's Delayed Discounting

Weekly smoking tests by exhaled Carbon Monoxide (COex)
- COex ≤6 PPM => Pass & $40
- COex >6 PPM => Strike & $0

Allowed two Strikes

Third Strike disqualifies
- Reward Group: keep all money
- Banked Money Group: lose all earned money

Biweekly smoking tests

Any strike disqualifies

Smoking test at 3 and 6 months

Questionnaires

$20 compensation

Currently ongoing

Banked Money Group

Modified Commitment Contracts

$40 $200 $360 $480

REWARD

Subject No.	GRACE				PERIOD	(3 MONTHS)				TOBACCO	FREE	(1 MONTH)
25					X			X				
28					X							
33												
35												
36												
22			X			X						X
9			X	X	X							
17		X	X	X								
19		X	X	X								
21		X	X	X								
24		X	X	X								
29		X	X	X								
15												
26												
27												
	GP1	GP2	GP3	GP4	GP5	GP6	GP7	GP8	GP9	TF1	TF2	TF3

BANKED

Subject No.	GRACE				PERIOD	(3 MONTHS)				TOBACCO	FREE	(1 MONTH)
2						X						
3			X									
7												
10								X				
16							X		X			
23												
32												
4			X									✦
11								X	X	X		
6		X	X		X							
18		X		X	X							
1		X	X	X								
14		X	X	X								
5												
8												
13												
	GP1	GP2	GP3	GP4	GP5	GP6	GP7	GP8	GP9	TF1	TF2	TF3

Trial design is feasible
31/36 (86.1%) Enrolled
25/36 (69.4%) First clinic visit
6/36 (16.7%) saw smoking cessation, received $50 and quit

12/36 (33.3%) quit rate amongst both groups
- Reward Group: 5/15 (33.3%)
- Banked Money Group: 7/16 (43.8%)
- P = 0.82

Take home points

- Lung cancer screening implementation is challenging globally – every step needs analysis and optimization, with goals of equitable care and using technology

- Smoking cessation programs require creativity – more intensive programs, opt out instead of opt in, integrating with screening, financial incentives