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UK NSC Lung Showcase: Modelling

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Outline

- Existing lung cancer screening modelling studies
- Exeter model (2022 version)
  - Structure
  - Key inputs
  - Natural history model
- Results
- Discussion

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Existing LCS modelling studies

CISNET (Cancer Intervention and Surveillance Modelling Network)

Several lung cancer models developed in CISNET initiative to address lung cancer screening and tobacco control

All include a disease natural history component (substantial variation between)

Used for several comparative modelling assessments

- If models with diverse assumptions agree it suggests robustness

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Systematic reviews of standalone studies

Peters JL, Snowsill TM, Griffin E, Robinson S, Hyde CJ. Variations in model-based economic evaluations of low-dose computed tomography screening for lung cancer: a methodological review. Value in Health 2022; 25(4):656-665

Grover H, King W, Bhattarai N, Moloney E, Sharp L, Fuller L. Systematic review of the cost-effectiveness of screening for lung cancer with low dose computed tomography. Lung Cancer 2022; 170:20-33

Over 40 model-based economic evaluations of lung cancer screening

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UK-based economic evaluations

Whynes DK. Could CT screening for lung cancer ever be cost effective in the United Kingdom? Cost Eff Resour Alloc 2008; 6(1):5

Field JK, Duffy SW, Baldwin DR, et al. The UK lung cancer screening trial: a pilot randomised controlled trial of low-dose computed tomography screening for the early detection of lung cancer. Health Technol Assess 2016; 20(40)

Snowsill T, Yang H, Griffin E, et al. Low-dose computed tomography for lung cancer screening in high-risk populations: a systematic review and economic evaluation. Health Technol Assess 2018; 22(69)

Hinde S, Crilly T, Balata H, et al. The cost-effectiveness of the Manchester 'lung health checks', a community-based low-dose CT screening pilot. Lung Cancer 2018; 126:119-124

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What can we learn from previous CEA?

Non-UK studies will not give us “the answer” as CEA do not generalise easily

- But we can learn from them

Natural history components important

Only one UK-based study used natural history component and it had flaws

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Exeter model (2022 version)

Changes from 2018 version

Parameter updates

- Screening programme admin cost
- LDCT cost
- Cancer treatment cost
- Effect of cancer on QALY weights

Structure updates

- Separate SCLC and NSCLC
- Cancer stages revised
- Cancer mortality/survival assumptions revised
- New natural history model

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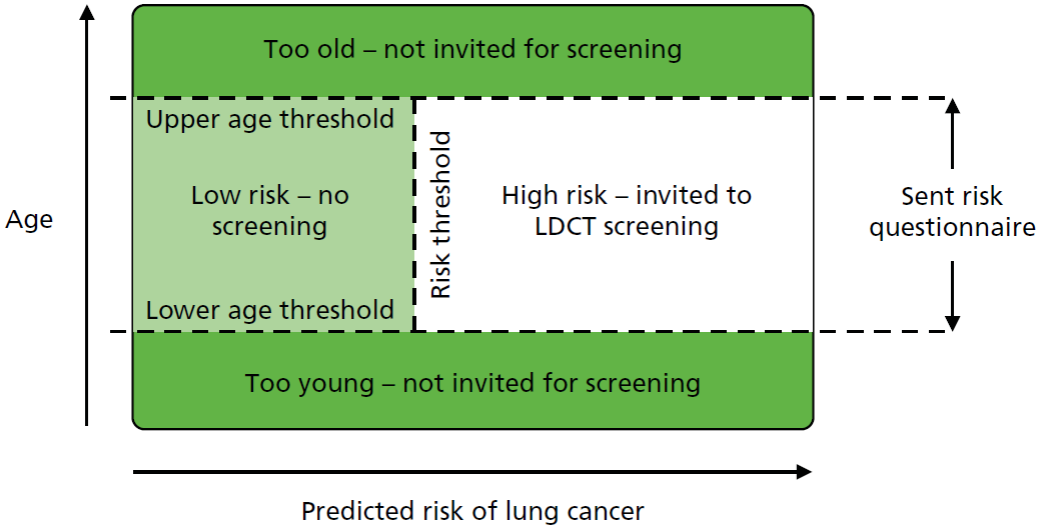
Model structure

Assumptions encoded in mathematics

Targeted population



Requirement	Options
Minimum age	55, 60
Maximum age	75, 80
Risk threshold ($PLCO_{m2012}$)	1.5%, 2.5%, 5%

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Screening schedules

No screening

Single

Triple (0, 12 and 24 months from start)

Biennial to age 80

Annual to age 80

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Predicted risk in the model

We model the $PLCO_{m2012}$ predicted risk for the population

Associated with age and smoking status

Smoking status (% of ever smokers aged 55-80)	>1.5%	>2.5%	>5%
Current (22%)	58%	46%	28%
Former (78%)	21%	10%	2%

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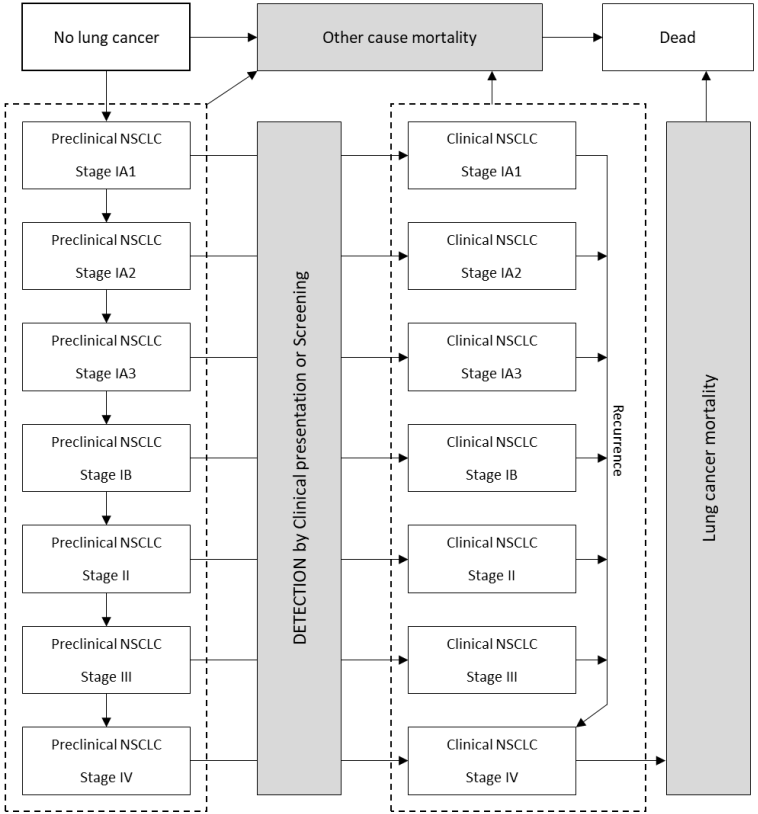

Health states and events

At any point in time a simulated person is either

- Alive without lung cancer
- Alive with preclinical NSCLC
- Alive with clinical NSCLC
- Alive with preclinical SCLC
- Alive with clinical SCLC
- Dead

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Prevalent cancer

- Some people have lung cancer when they first enter screening (prevalent cancer)
- The model includes a prevalent cancer component
- $PLCO_{m2012}$ risk is incorporated (slightly stronger association for SCLC)

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Incident cancer

- People who start screening without cancer are at risk of subsequently developing cancer
- We assume they develop no more than one lung cancer
- $PLCO_{m2012}$ risk is incorporated (slightly stronger association for SCLC)

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Cancer progression

- Cancer progresses through stages sequentially
- Constant hazard of progression to next stage but
  - Stage dependent
  - Heterogeneity (NSCLC) – some cancers progress much slower, some much faster

Cancer clinical detection

- Cancer can be detected outside of screening (i.e., presenting with symptoms, incidental detection)
- Constant hazard of presentation but
  - Stage dependent

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Screen-detection

- If a person has lung cancer it will be detected by an LDCT screen with a certain probability (true sensitivity)
  - Sensitivity increases as cancer becomes more advanced
  - Assumed perfect for metastatic cancer
- If they do not have lung cancer there is a chance of a false positive or indeterminate findings meaning they have one or two follow-up LDCT

Cancer survival

- Modelling cancer survival in screening interventions is tricky
- Observed survival of screen-detected cancers is extremely good
  - Detected in earlier stages than usual
  - Lead time
  - Over-representation of slow-growing cancers
- We model survival from time of diagnosis according to whether it is
  - Screen-detected
  - Interval
  - Post- / outside screening

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Other-cause mortality

An unfortunate consequence of targeting people with a strong smoking history is that they are also more likely to die from other smoking-related disease

This is incorporated in the model, including a relationship between $PLCO_{m2012}$ and the rate of death from other causes

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Key inputs

Screening uptake

Parameter	Value
Proportion of those contacted by post about the programme who have $PLCO_{m2012}$ risk assessment (by telephone)	50.8%
Proportion of those eligible after risk assessment who take up screening	83.6%
Adherence to screening (assumed)	100%

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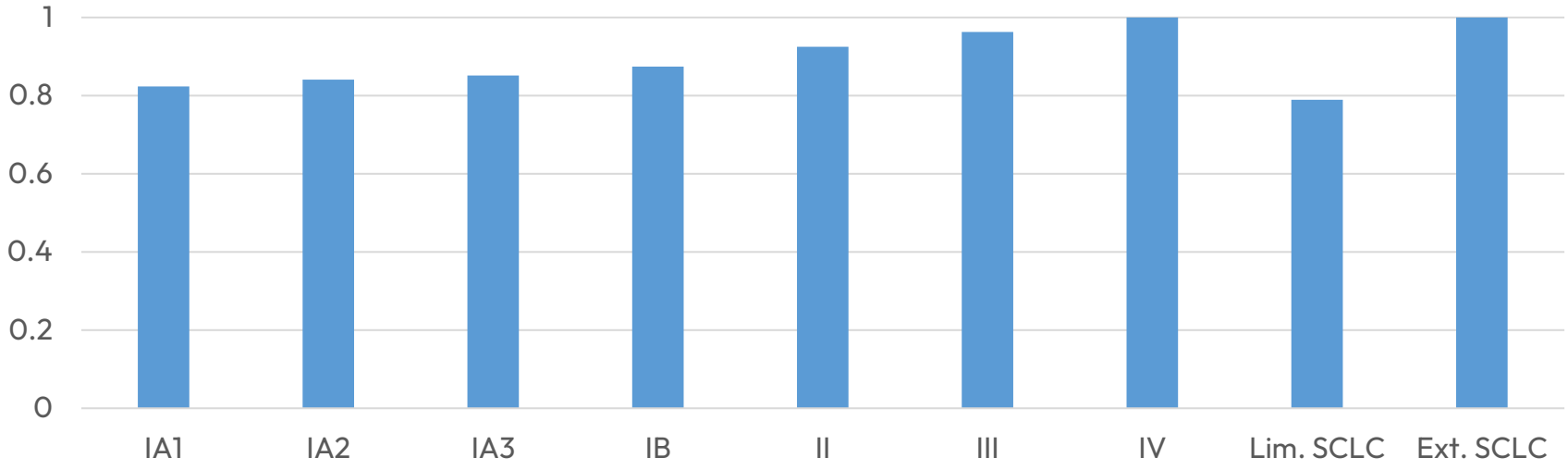
LDCT sensitivity



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LDCT specificity

False positives

- Definition: a referral to MDT but no cancer
- False positive rate = 0.037 (1 in 27; specificity = 0.963)

Indeterminate result

- Definition: requiring follow up LDCT at 3 and 12 months (or just at 12 months)
- Indeterminate result rate = 0.14 (1 in 7)

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Costs

Screening visit

- Nurse support: £7.75
- Scan cost: £77.31

Follow-up costs

- Indeterminate nodules: 1× or 2× scan cost
- False positive: £434.47

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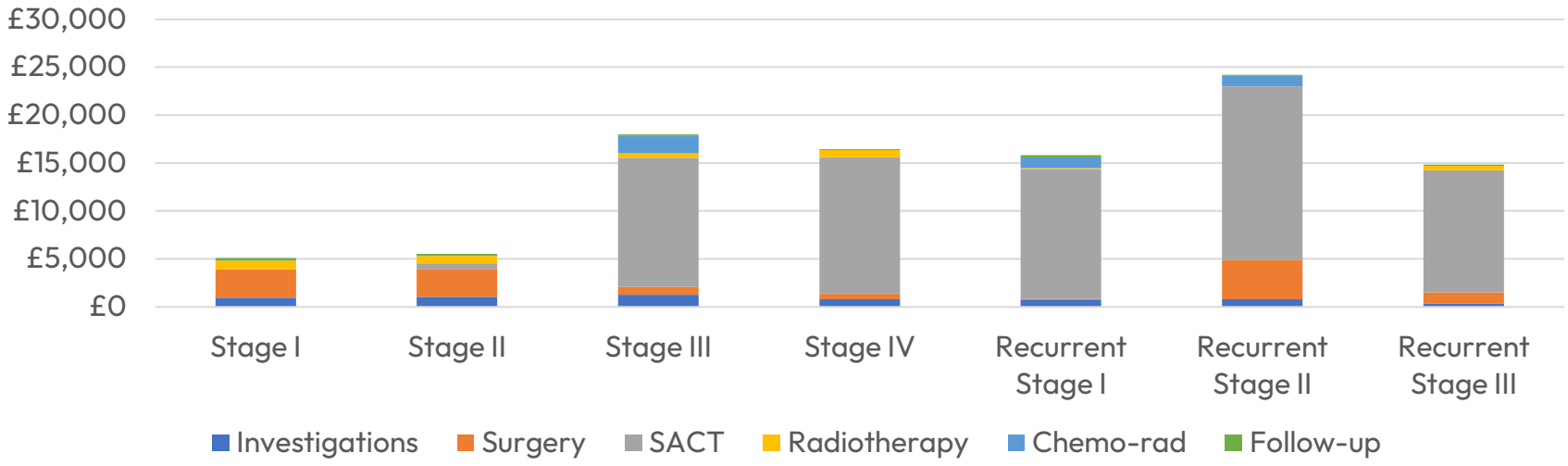
Costs (lung cancer)



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QALY weights

Baseline utilities

- Current/ex-smoker: male 0.820, female 0.791

Modifiers

- Stage II/III NSCLC (post-diagnosis): -0.04
- Stage IV or recurrent NSCLC (pre- and post-diagnosis): -0.05
- Extensive or recurrent SCLC: -0.08

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Natural history model

Structure

Contains the following from the economic model

- Cancer prevalence
- Cancer incidence
- Cancer presentation
- Cancer progression
- Screen-detection
- Other-cause mortality

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Data source

The natural history model was **calibrated** to patient-level data from the National Lung Screening Trial (NLST)

- Largest RCT of lung cancer screening by LDCT (N = 53,454)
- US-based
- Triple screen plus follow-up

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Results

Naming convention

Frequency – Lower age limit – Upper age limit – Risk threshold

E.g., S-55-75-1.5 means a single screen for people aged 55 to 75 with a predicted risk of at least 1.5%

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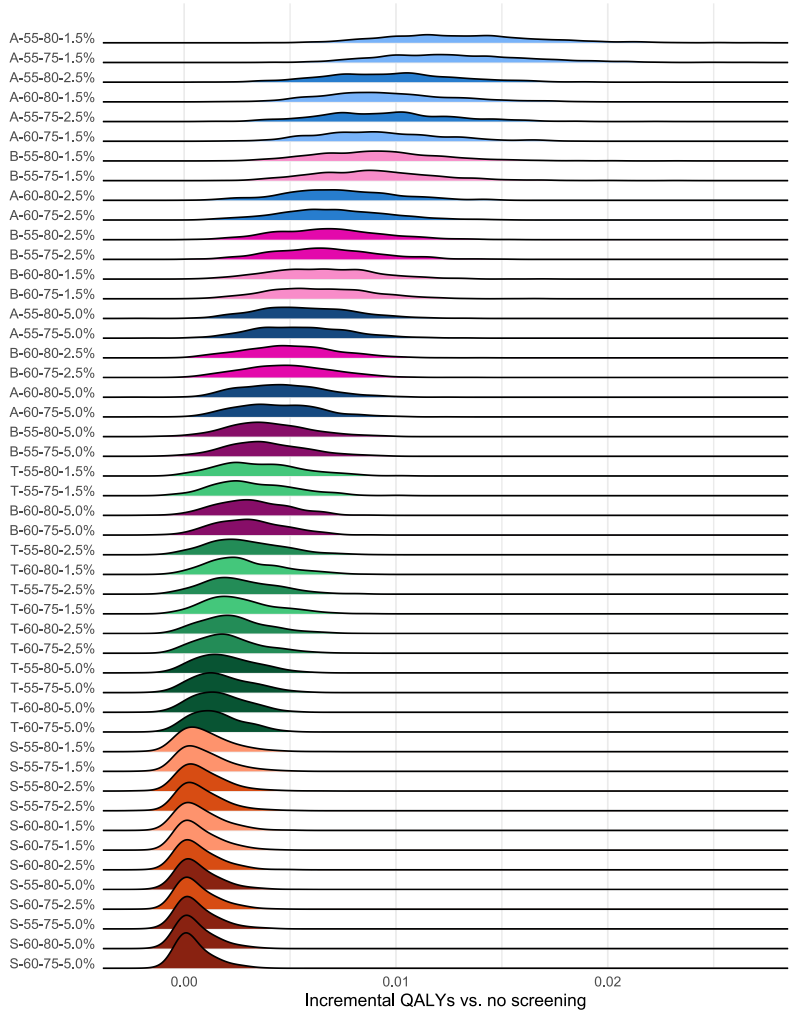

Clinical effectiveness

- Single screen generates very little health benefit
- Triple screen somewhat better
- Maximum health benefit achieved through prolonged regular screening in a broadly targeted population
- Greater benefits are more uncertain

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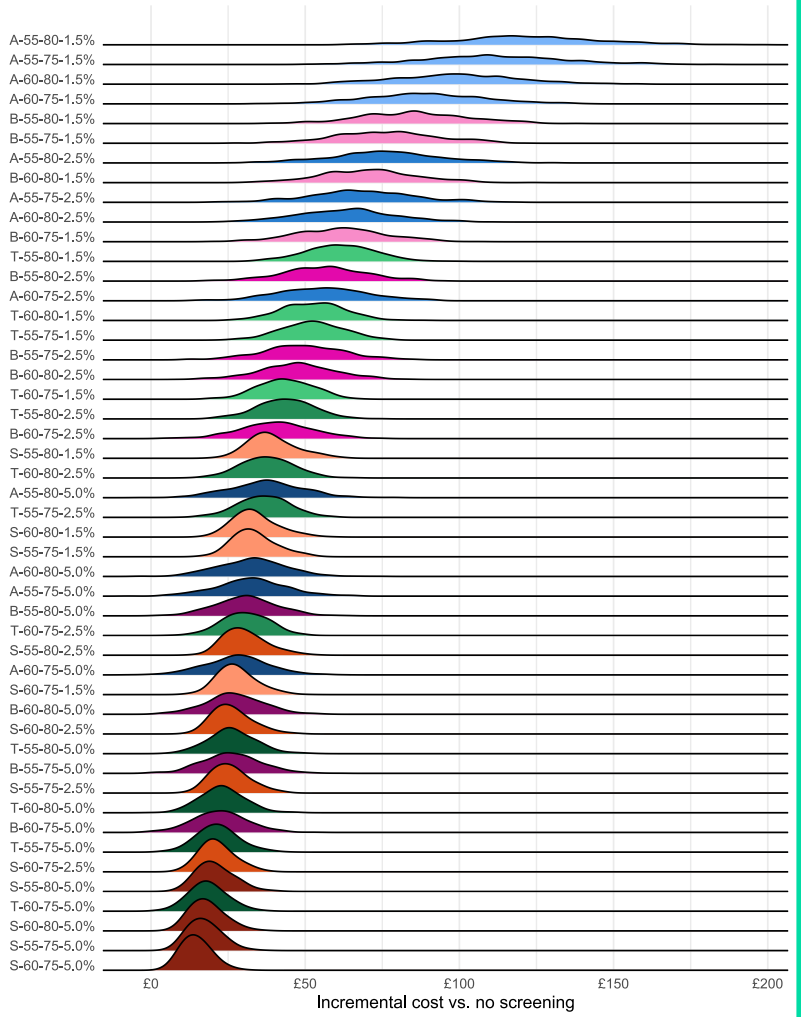

Costs

- Screening always increases costs
  - Cost of programme administration
  - Cost of scans (and false positives)
  - Cost of cancer treatment
- Costs can be contained by targeting narrowly and/or keeping the number of screens low

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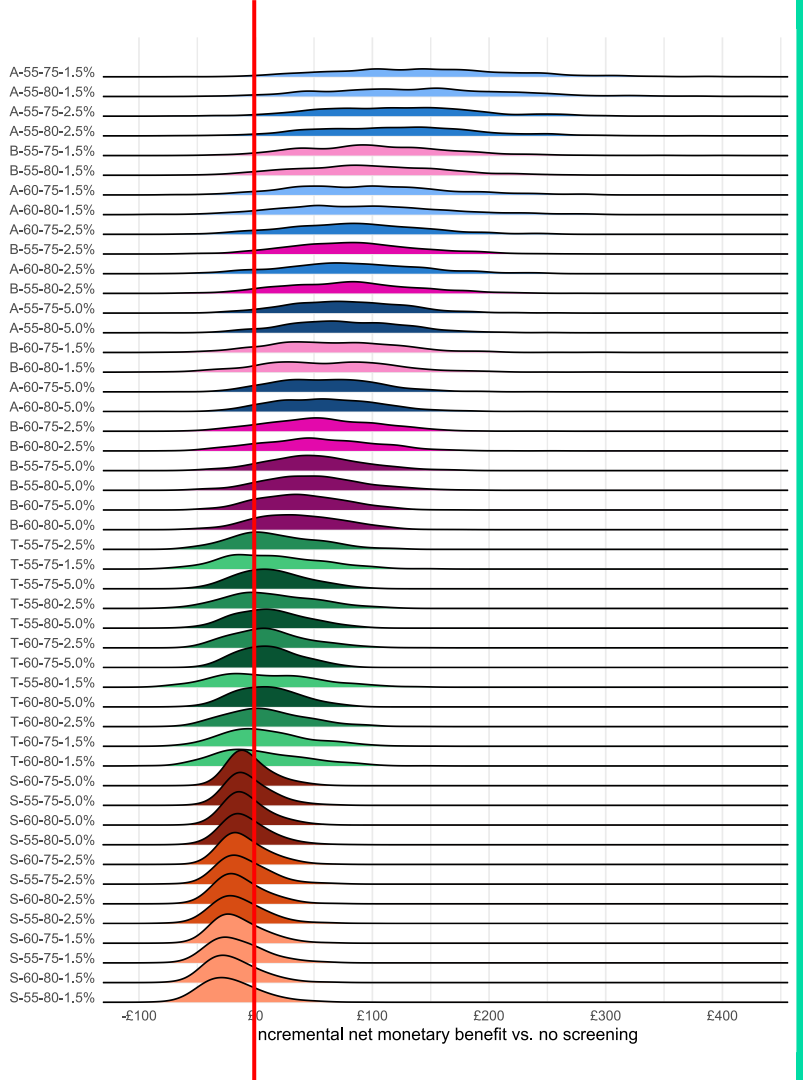
Cost-effectiveness analysis

Cost-effectiveness analyses use a threshold, e.g., £20,000 per QALY

This means that a new technology is cost-effective if it has a ratio of **additional** costs to **additional** QALYs no greater than £20,000 : 1 QALY

If we have more than two technologies being compared it can be a lot easier to look at the **net monetary benefit** – the technology with the highest net monetary benefit is economically optimal



Cost-effectiveness

Compared to no screening

- Single screen is not cost-effective
- Triple screen is possibly cost-effective (at the margin)
- Biennial and annual screen are cost-effective

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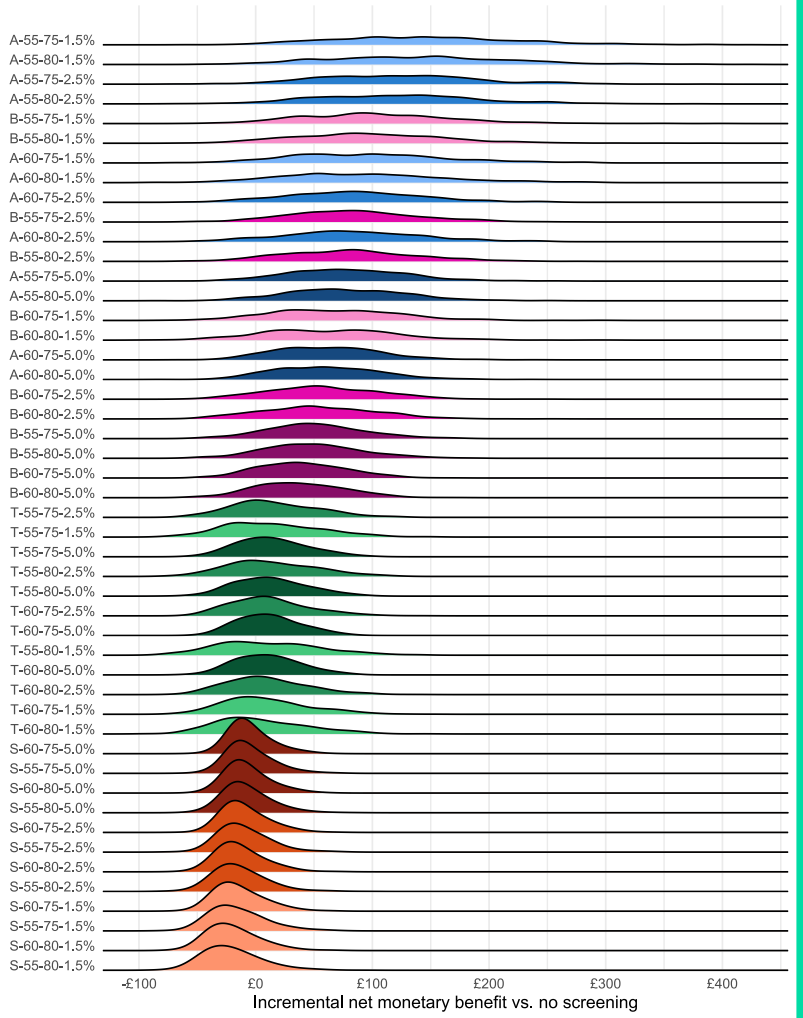

Cost-effectiveness

Compared to all options

- Annual and biennial strategies are “most cost-effective”
- Maximum economic benefit from annual screening in broad population (aged 55-75 years, risk at least 1.5%)

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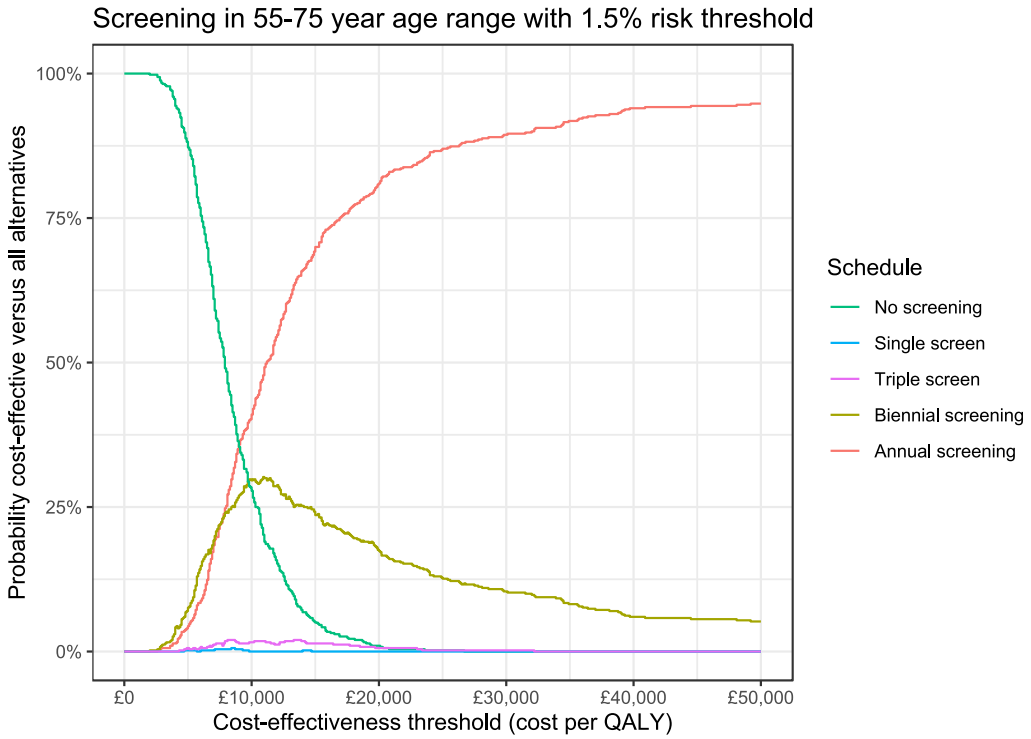
Screening in 55-75 year age range with 1.5% risk threshold
Probability cost-effective versus all alternatives
100%
75%
50%
25%
0%
£0
£10,000
£20,000
£30,000
£40,000
£50,000
Cost-effectiveness threshold (cost per QALY)
Schedule
No screening
Single screen
Triple screen
Biennial screening
Annual screening

A-55-75-1.5% (optimal?)

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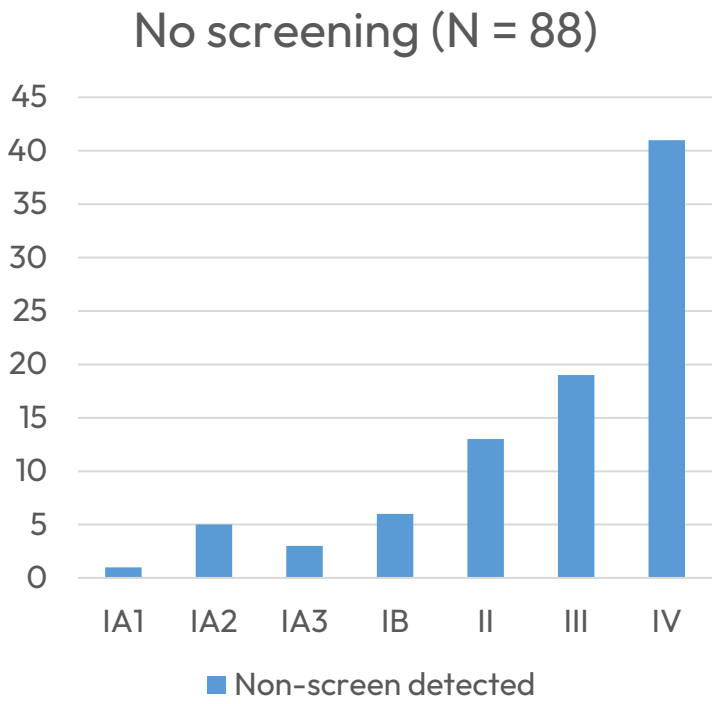
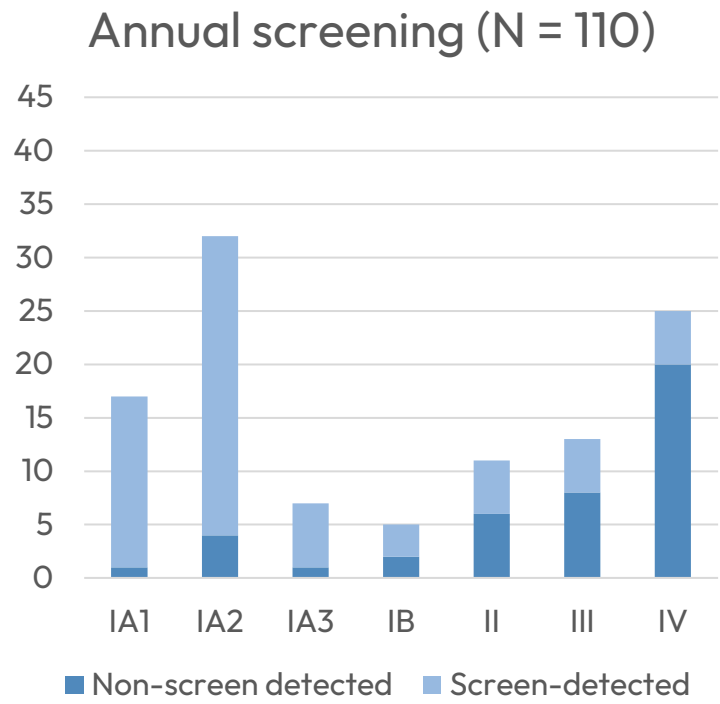
Life expectancy	+0.257
QALYs	+0.108
Average number of screens	11.4
Average number of false positives	0.4
Lung cancer mortality rate ratio	0.860

Stage distribution





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Discussion

Annual versus Biennial

Strategy	Costs	QALYs	INMB	ICER
No screening	£1,092	9.795		
Biennial screening	£1,168	9.804	£103	£8,500/QALY
Annual screening	£1,203	9.808	£145	£9,200/QALY

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True cost of LDCT

- Is the assumed cost an accurate **accounting cost**?
- Does the accounting cost represent the true **opportunity cost**?
- Is the cost fixed or dependent on quantity?

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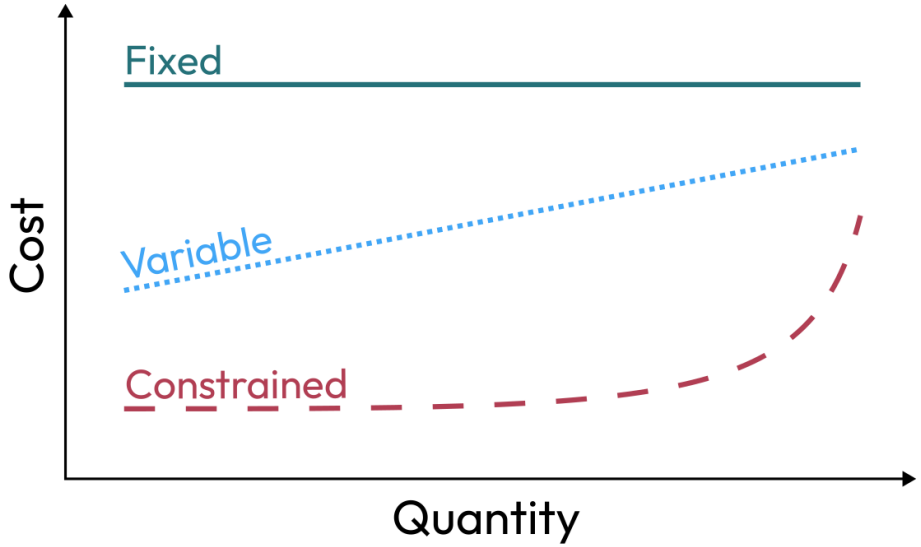
True cost of LDCT



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Time for questions