

# Comparing changes in solid component diameter and mass for detecting invasive adenocarcinoma in sub-solid pulmonary nodules: The SUMMIT study

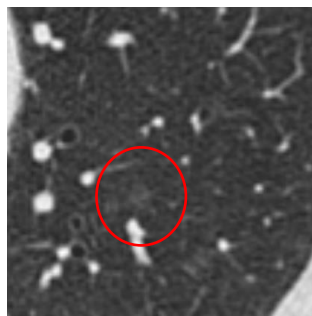
CR Khaw, DO Cheng, A Creamer, H Hall, A Bhamani, P Verghese, R Predecki, M Mullin, JL Dickson, C Horst, S Tisi, A Pennycuik, H Selway-Clarke, Z Frazer, KEJ Davies, C Percival, K Gyertson, A Hacker, L Hughes, S Galani, L Farrelly, J McCabe, W Ricketts, J Jacob, A Hackshaw, A Devaraj, SUMMIT consortium, A Nair, SM Janes

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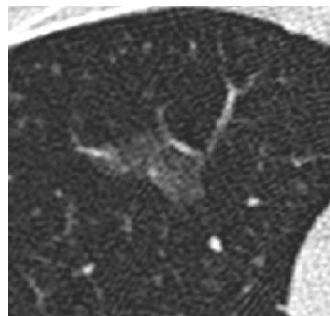
Persistent SSNs 3-5x more likely to be lung cancer compared to solid<sup>1</sup>

### Adenocarcinoma spectrum lesions



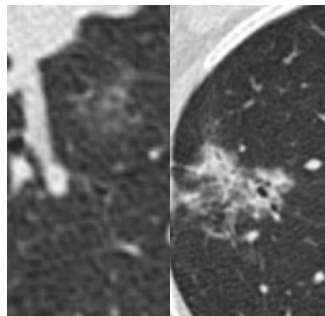
**AAH**

Atypical adenomatous hyperplasia



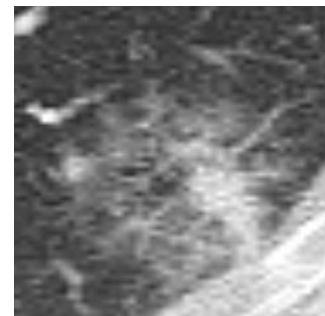
**AIS**

Adenocarcinoma in situ



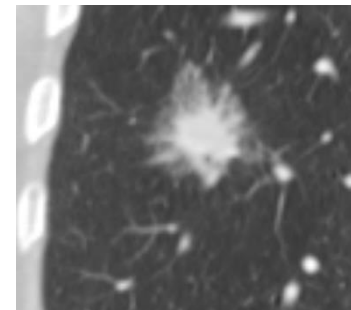
**MIA**

Minimally invasive adenocarcinoma

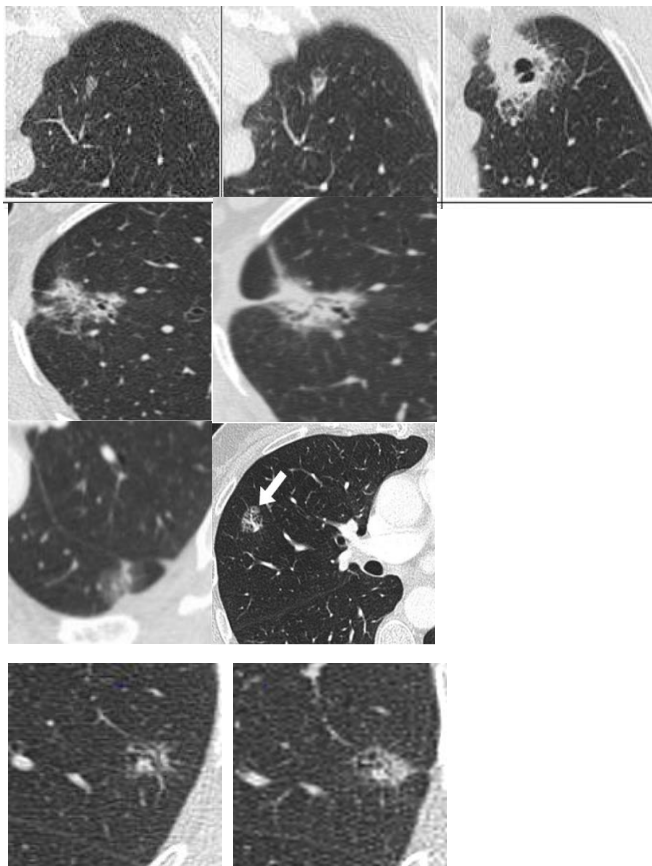


**LPA**

Lepidic predominant adenocarcinoma



**Invasive adenocarcinoma**



AIS

MIA

Size ↑

Density ↑

Morphology change (eg. pleural indentation, bubble lucency)

“Consider using changes in mass to assess growth” (BTS, 2015)

*Mass (mg) = volume x density*

Formula:

$volume (mm^3) \times [(Hounsfield Units + 1000)/1000]$

# Introduction

## Solid component diameter

CT image on HRCT						
Solid part	0 cm	0 cm	≤0.5 cm†	0.6-1.0 cm†	1.1-2.0 cm†	2.1-3.0 cm†
Total tumor size including GG	≤0.5 cm	0.6-3.0 cm‡	≤3.0 cm‡	0.6-3.0 cm‡	1.1-3.0 cm‡	2.1-3.0 cm‡
Pathologic Differential Diagnosis	AAH‡, AIS, MIA	AIS, MIA, LPA	MIA, LPA, AIS	LPA, Invasive AD, MIA	LPA, Invasive AD	Invasive AD
Clinical Stage*		cTis‡	cT1mi‡	cT1a	cT1b	cT1c
Invasive part	0 cm	0 cm	≤0.5 cm‡	0.6-1.0 cm†	1.1-2.0 cm†	2.1-3.0 cm†

Travis et al. *Journal of Thoracic Oncology* Vol. 11 No. 8: 1204-1223

### Absolute solid component diameter (SCD)

Lung-RADS, 2022; Fleischner Society, 2017  $\geq 8\text{mm}$

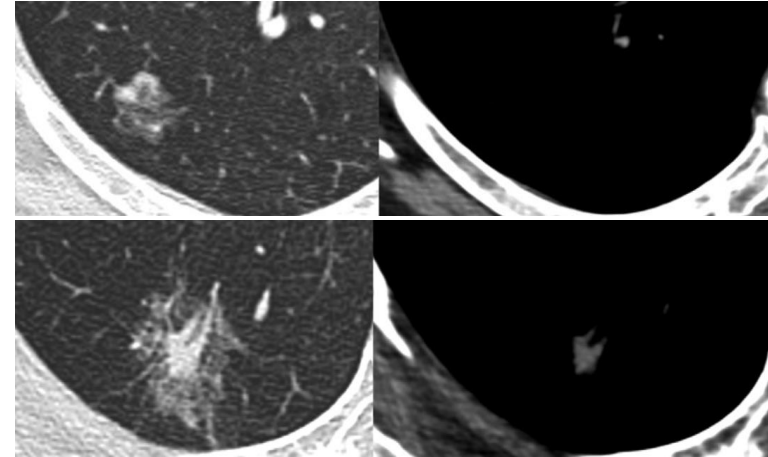
### Solid component diameter change (SCD change)

BTS, 2015; Cho, 2016; Lee, 2020  $\geq 2\text{mm}$

Lung-RADS, 2022  $\geq 4\text{mm}$

Lung window

Mediastinal window



Revel et al. *Radiology* vol. 286,1 (2018): 316-325

DO NO  
HARM

AVOID  
unnecessary  
exposure to  
healthcare settings  
Over-medicalisation

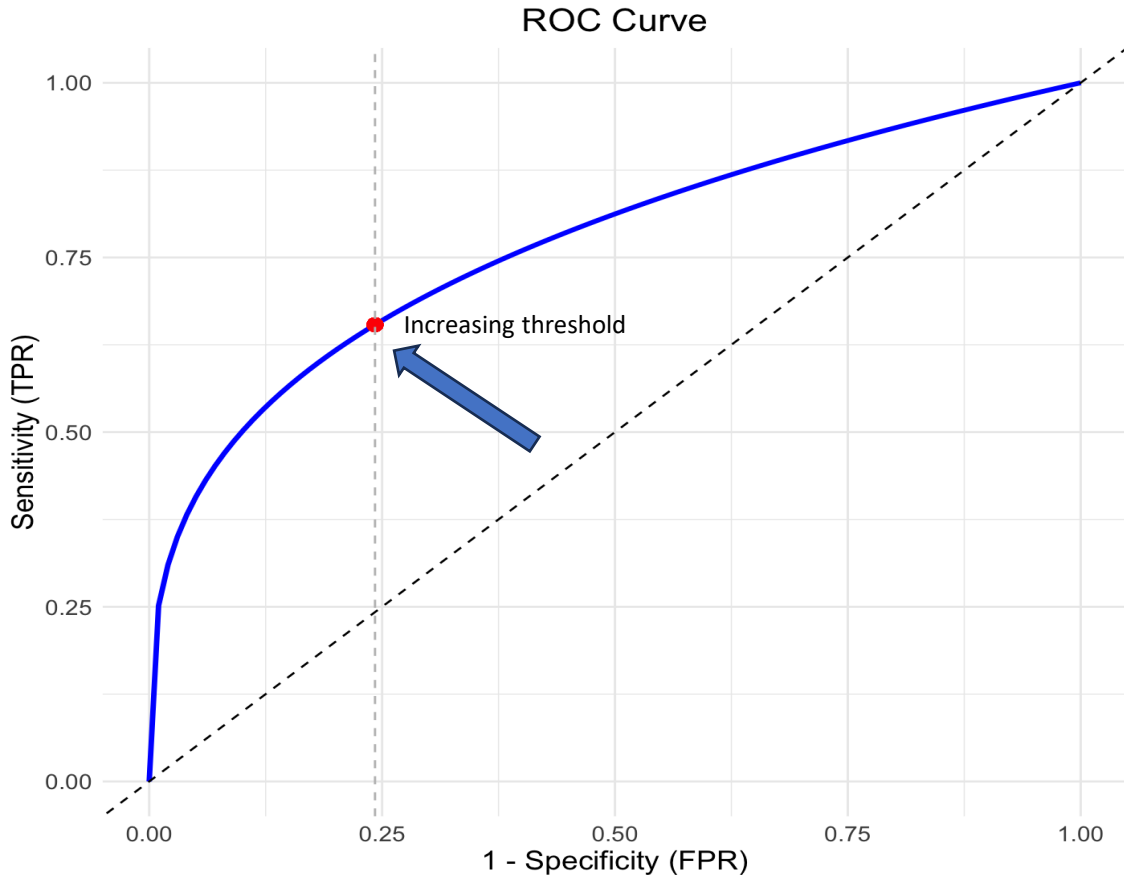
MINIMISE  
HARMS  
Delayed diagnosis  
False positives



DO GOOD

EARLY  
DETECTION  
→ Diagnosis at a curative  
stage...

→ ...BUT referral for  
treatment only at a point  
where a meaningful  
intervention can be  
performed



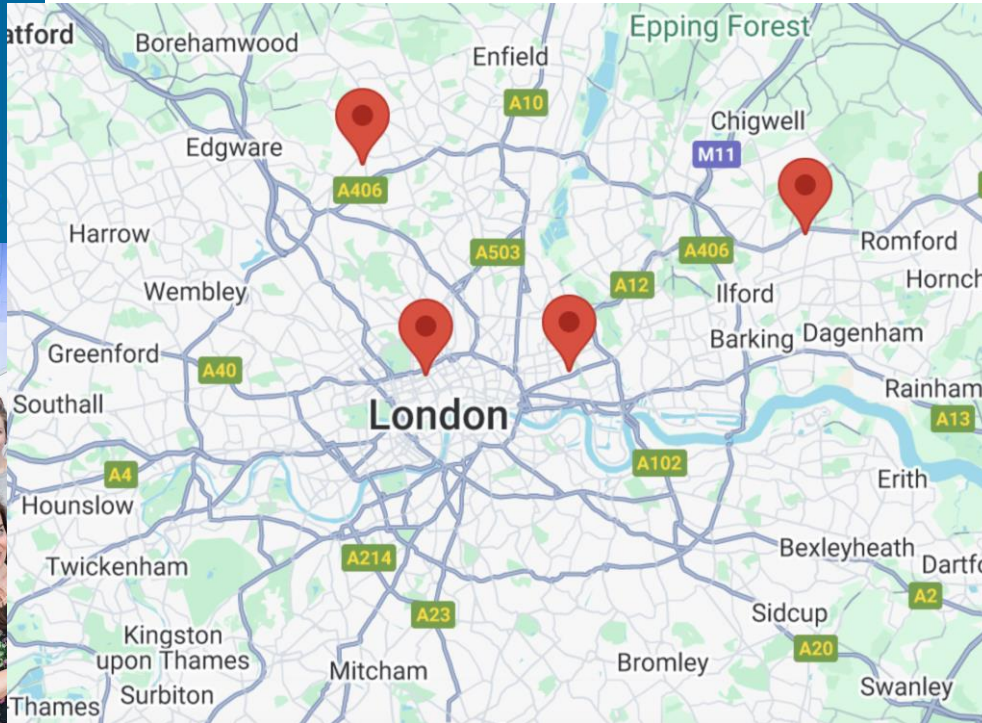
Assess the accuracy of recommended thresholds:-

- absolute size,
- change in metrics, and
- combinations of these

to achieve optimum performance for detecting **invasive** adenocarcinoma at the point at which unequivocal treatment will be recommended in sub-solid pulmonary nodules.

# Methods

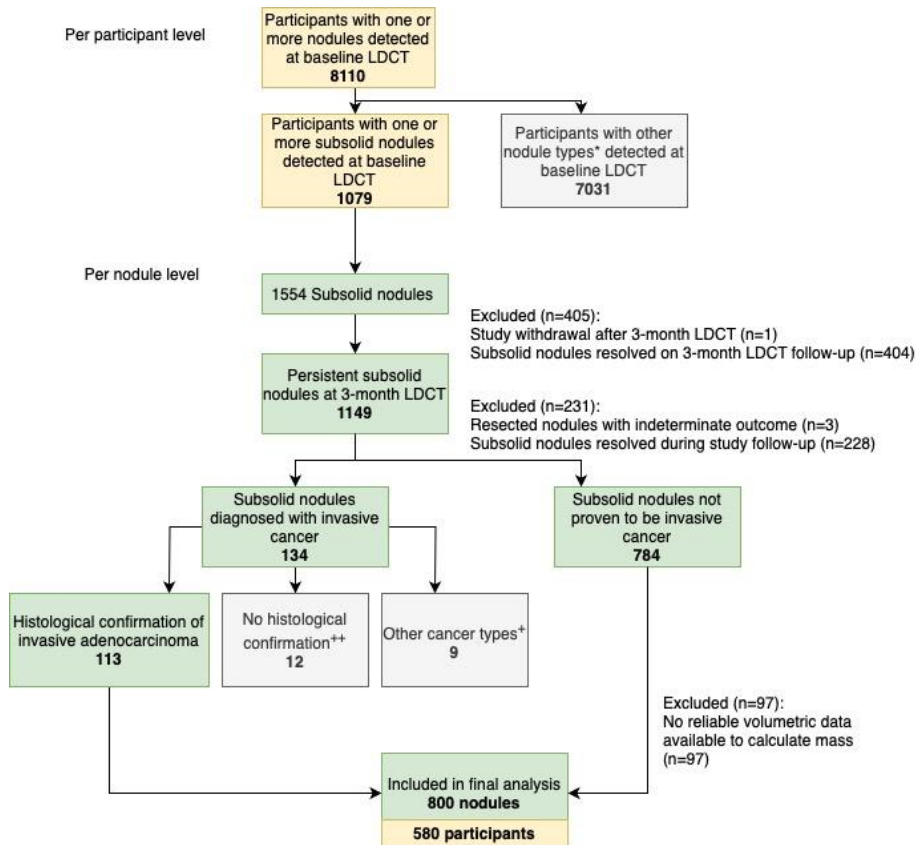
## SUMMIT study population



- 4 scanning sites
- 12 referral hospitals
- > 13,000 participants consented 2019 - 2023



More information on the SUMMIT study is available at: [www.summitstudy.co.uk](http://www.summitstudy.co.uk)



**13.3% had at least one subsolid nodules at baseline**

**40% resolved on follow-up scans (excluded)**

**Final group: 580 participants (800 nodules)**

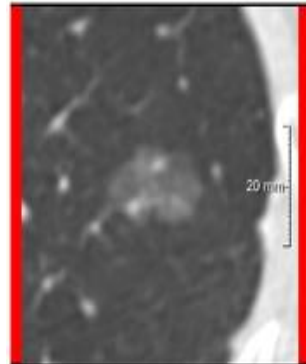
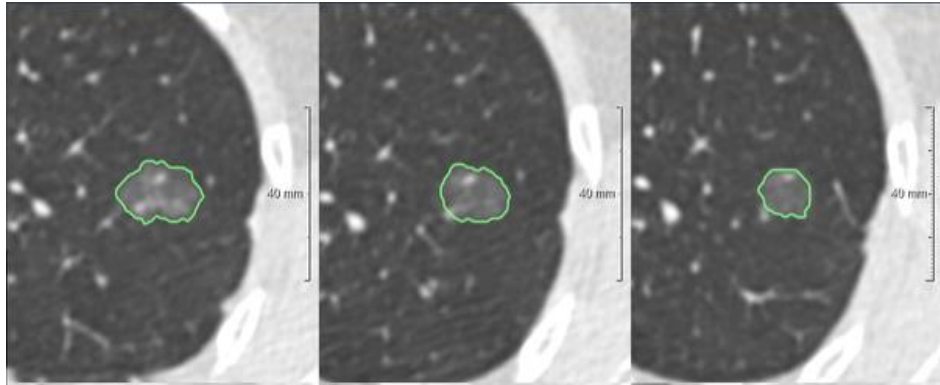
\*Other nodule types reported in SUMMIT include solid, endobronchial, perifissural and consolidation.

<sup>+</sup>Other cancer types include non-adenocarcinoma lung cancer or non-lung cancers.

Cancer outcome linked to nodule ID.

- Cancer diagnosed during study: Study outcome completed by the treating hospital following referral from the study.
- Cancer diagnosed after study concluded: National Cancer Registration and Analysis Service (NCRAS).
- Nodules not proven to be invasive cancer.
  - Definitive investigation after referral to local lung cancer MDT
  - Persistent nodules with no lung cancer diagnosis on NCRAS

Median follow up for all nodules:  
4.44 years (IQR: 3.70–4.70 years)



Finding	24 Oct 2019	23 Jan 2020	30 Oct 2020	08 Nov 2021
Segment/Lobe	Right Lower Lobe	Right Lower Lobe	Right Lower Lobe	Right Lower Lobe
Location	Slice 281 (HTF)	Slice -1 (HTF)	Slice 284 (HTF)	Slice 290 (HTF)
Status	Baseline	Stable	Stable	Stable
Type	Non-solid	Non-solid	Non-solid	Non-solid
Altered Morphology	-	-	-	-
Spiculated	No	No	No	No
Long Axis	13.7 mm	13.4 mm	13.9 mm	15.5 mm
Short Axis	13.1 mm	10.5 mm	12.9 mm	12.5 mm
Average Diameter	13.4 mm	12.0 mm	13.4 mm	14.0 mm
Equivalent Diameter	11.4 mm	10.6 mm	11.4 mm	12.2 mm
Volume	769 mm <sup>3</sup>	629 mm <sup>3</sup>	769 mm <sup>3</sup>	938 mm <sup>3</sup>
Mass	358 mg	281 mg	362 mg	455 mg
Volume Change (prior)	-	-18%	+22%	+22%
VDT (prior)	-	-	969 d	1305 d
MDT (prior)	-	-	769 d	1134 d
Volume Change (1st)	-	-18%	+0%	+22%
VDT (1st)	-	-	-	2603 d
MDT (1st)	-	-	23206 d	2157 d
Malignancy Risk Estimation	8.1%	5.9%	6.5%	8.4%

Nodule type

Location

Diameter

Solid component diameter (in part-solid)

Volume

Mass

Volume doubling time

Mass doubling time

<b>Absolute solid component diameter (SCD)</b>	
Lung-RADS, 2022; Fleischner Society, 2017	$\geq 8\text{mm}$
<b>Solid component diameter change (SCD change)</b>	
BTS, 2015; Cho, 2016; Lee, 2020	$\geq 2\text{mm}$
Lung-RADS, 2022	$\geq 4\text{mm}$
<b>Mass</b>	
Scholten, 2015	Mass percentage change $\geq 30\%$
BTS, 2015 (adapted); Scholten, 2015	Mass doubling time $\leq 400$ days

- Sensitivity, specificity were calculated for each threshold
- Area under the Receiver Operating Curve (AUROC)
- Decision curve analysis<sup>1</sup>
  - Net benefit =  $(\text{True positives}/n) - (\text{False positives}/n) \times (P_t/(1 - P_t))$   
where  $n$  is the number of patients, and  $P_t$  is the threshold probability (set at 30% in our analysis)



<sup>1</sup> Vickers AJ, Elkin EB. Decision curve analysis: a novel method for evaluating prediction models. *Med Decis Making* 2006; 26: 565–574.

Per Participant level	Diagnosis confirmation of invasive adenocarcinoma		p-value
	Yes (n=100)	No (n=480)	
<b>Age (years)</b>			
Median (IQR)	67.0 (60.8 – 72.0)	67.0 (62.0 – 72.0)	0.496
<b>Sex, n(%)</b>			
Female	59 (59.0%)	260 (54.2%)	
Male	41 (41.0%)	220 (45.8%)	0.439
<b>Smoking status, n(%)</b>			
Current	38 (38.0%)	252 (52.5%)	<b>0.011</b>
Former	62 (62.0%)	228 (47.5%)	
<b>Pack years smoking</b>			
Median (IQR)	39.2 (31.5 – 48.5)	40.0 (31.4 – 52.5)	0.451

Per nodule level	Nodules with confirmed invasive adenocarcinoma (n=104)
<b>Diagnosis, n(%)</b>	
Invasive adenocarcinoma	97 (93.3)
Minimally invasive adenocarcinoma	7 (6.7)
<b>Pathology stage, n(%)</b>	
IA1	31 (29.8)
IA2	52 (50.0)
IA3	9 (8.7)
IB	8 (7.7)
II	1 (1.0)
III	1 (1.0)
IV	2 (1.9)

# Results

## Sensitivity/ specificity/ AUC

Study/ Guideline	Thresholds	TP/TP+FN	Sensitivity	TN/TN+FP	Specificity	AUC
<b>Absolute solid component diameter (absolute SCD)</b>	≥ 8mm	66/104	63.0% (53.0-73.0) 	665/696	96.0% (94.0-97.0) 	0.80 (0.75-0.84)
<b>Solid component diameter change (SCD change)</b>	≥ 2mm	59/104	57.0% (47.0-66.0)	655/696	94.0% (92.0-96.0)	0.75 (0.71-0.80)
	≥ 4mm	39/104	38.0% (28.0-48.0)	670/696	96.0% (95.0-98.0)	0.67 (0.62-0.72)
<b>Mass</b>	Mass doubling time (MDT) ≤ 400 days	23/104	22.0% (15.0-31.0)	675/696	97.0% (95.0-98.0)	0.60 (0.55-0.64)
	Mass ≥ 30%	64/104	62.0% (51.0-71.0)	532/696	76.0% (73.0-80.0)	0.69 (0.64-0.74)

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Unpublished data

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# Results

## Combination thresholds

Criteria	TP/TP+FN	Sensitivity	TN/TN+FP	Specificity	AUC
<ul style="list-style-type: none"> <li>Absolute SCD <math>\geq</math> 8mm OR</li> <li>SCD change <math>\geq</math> 2mm</li> </ul>	81/104	78.0% (69.0-85.0) ↑	636/696	91.0% (89.0-93.0)	0.85 (0.80-0.89)
<ul style="list-style-type: none"> <li>Absolute SCD <math>\geq</math> 8mm OR</li> <li>Mass <math>\geq</math> 30%</li> </ul>	93/104	89.0% (82.0-95.0) ↑↑	508/696	73.0% (70.0-76.0)	0.81 (0.78-0.85)
<ul style="list-style-type: none"> <li>Absolute SCD <math>\geq</math> 8mm OR</li> <li>MDT <math>\leq</math> 400 days</li> </ul>	74/104	71.0% (61.0-80.0) ↑	646/696	93.0% (91.0-95.0)	0.82 (0.78-0.86)

# Results

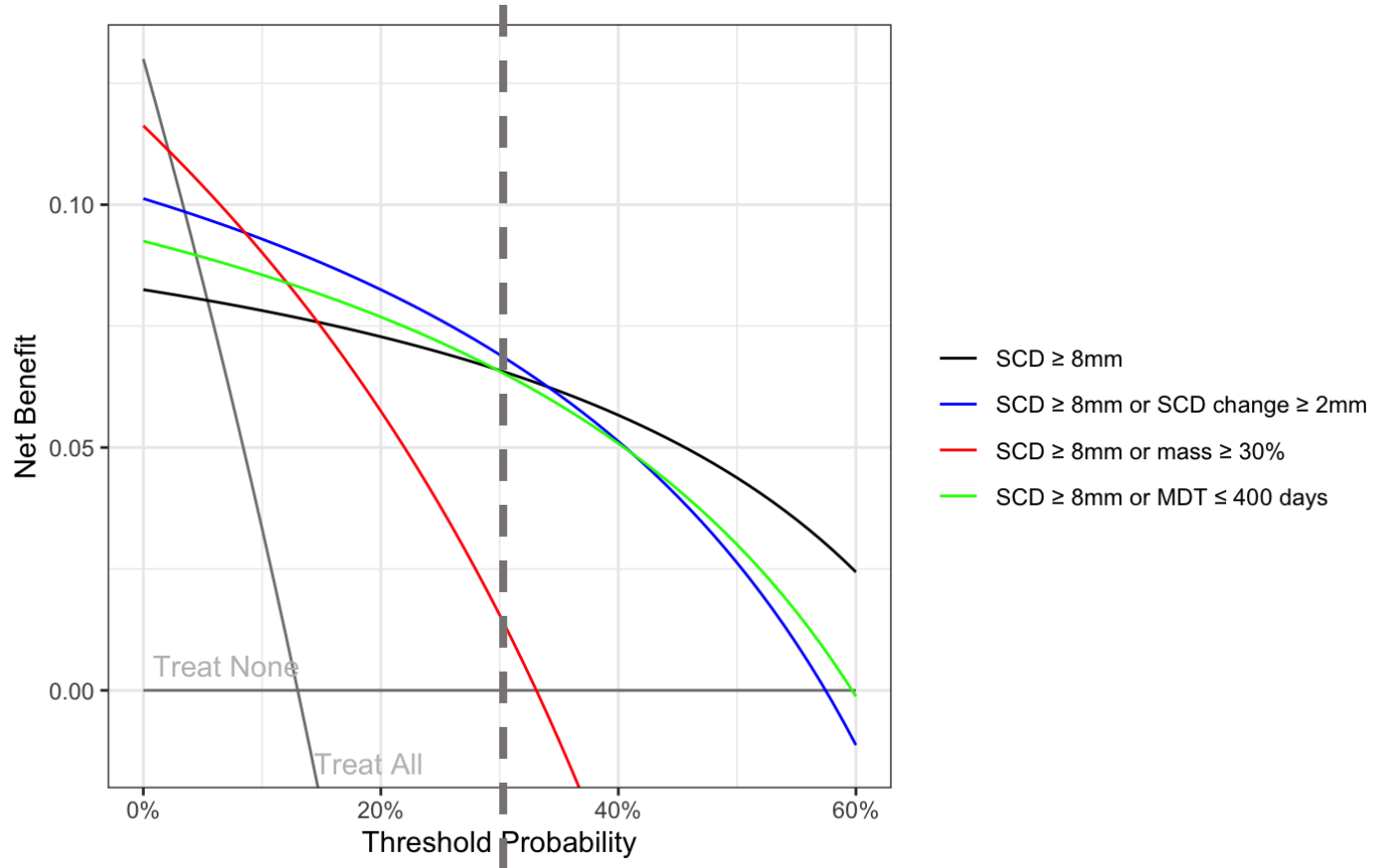
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# Results

## Decision curve analysis

Criteria	Net benefit (%)
SCD $\geq$ 8mm	6.59
SCD $\geq$ 8mm OR SCD change $\geq$ 2mm	6.91
Absolute SCD $\geq$ 8mm OR MDT $\leq$ 400 days	6.57
Absolute SCD $\geq$ 8mm OR Mass $\geq$ 30%	1.55



- A combined strategy using absolute SCD  $\geq 8\text{mm}$  or SCD change  $\geq 2\text{mm}$  (for cases with SCD  $< 8\text{mm}$ ) provides the highest net benefit for diagnosing invasive adenocarcinoma in sub-solid nodules.
- Other thresholds and metrics may become more useful as treatments improve, we better understand tumour behaviour, and patient perspectives influence decision-making.

## **Validation**

Future analysis needed to validate findings on other datasets.

## **Genomic Profiles**

Investigate the molecular landscape of fast- vs. slow-growing tumours.

*ASCENT study (UCLH/Barts)*

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