

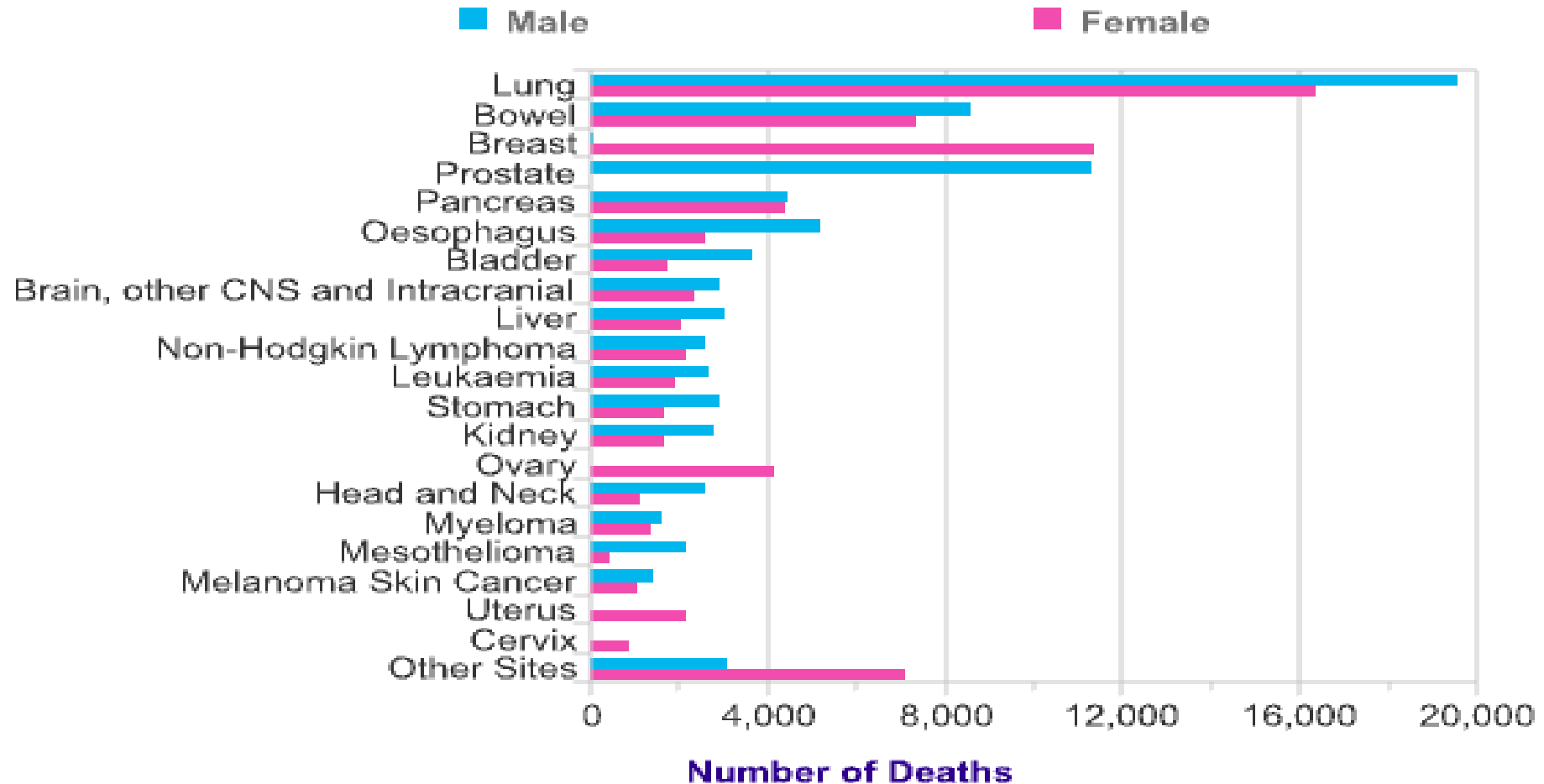
Recent advances in the management of Lung Cancer

David R Baldwin
Nottingham University Hospitals
Honorary Professor of Medicine, University of Nottingham
Chair, Lung Cancer Clinical Expert Group, NHSE

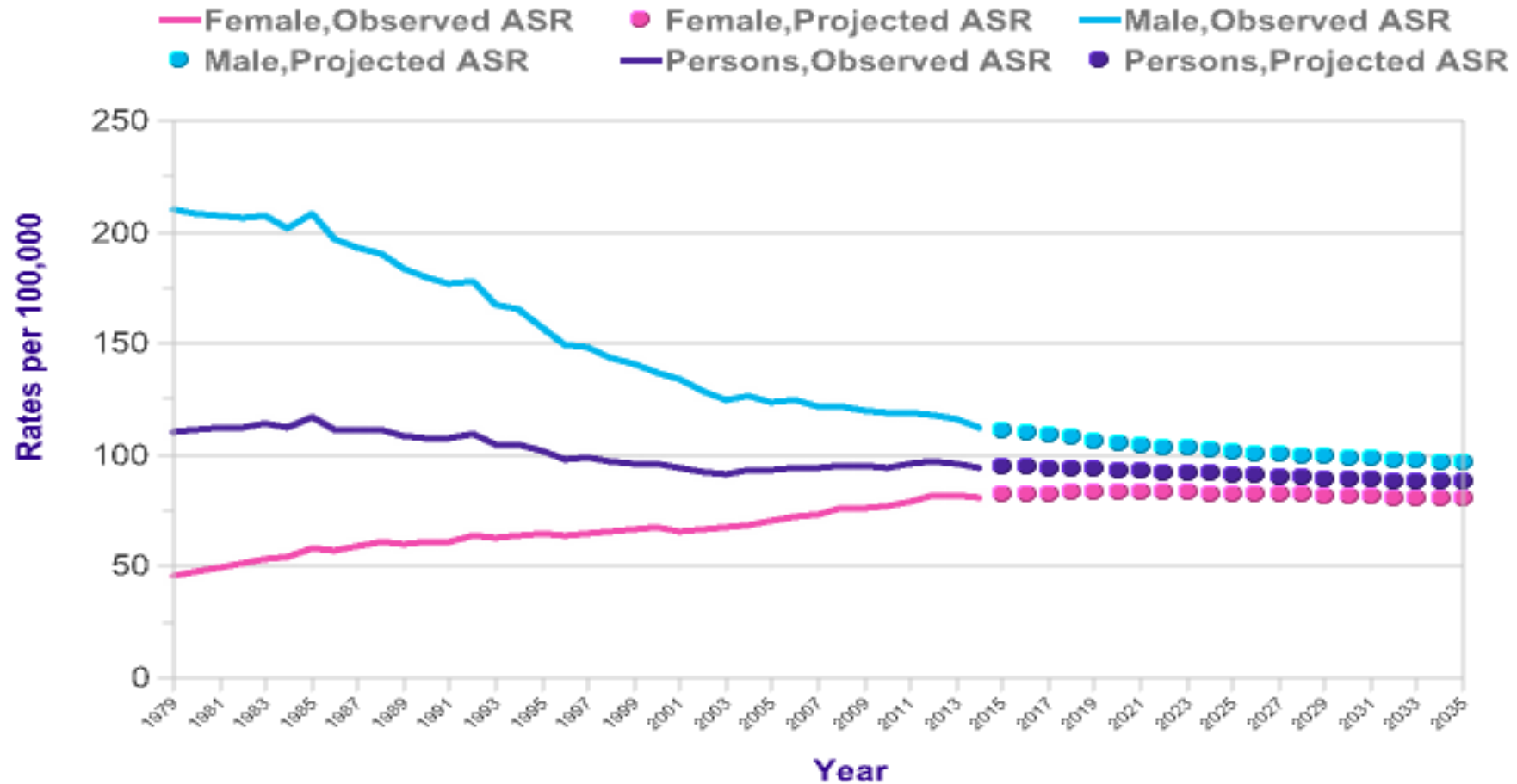
Conflicts of interest

- Educational grant to support Cambridge Chest Meeting from Agfa, Boehringer Ingelheim, Irwin Mitchell and Roche
- Travel support from Oncimmune Ltd

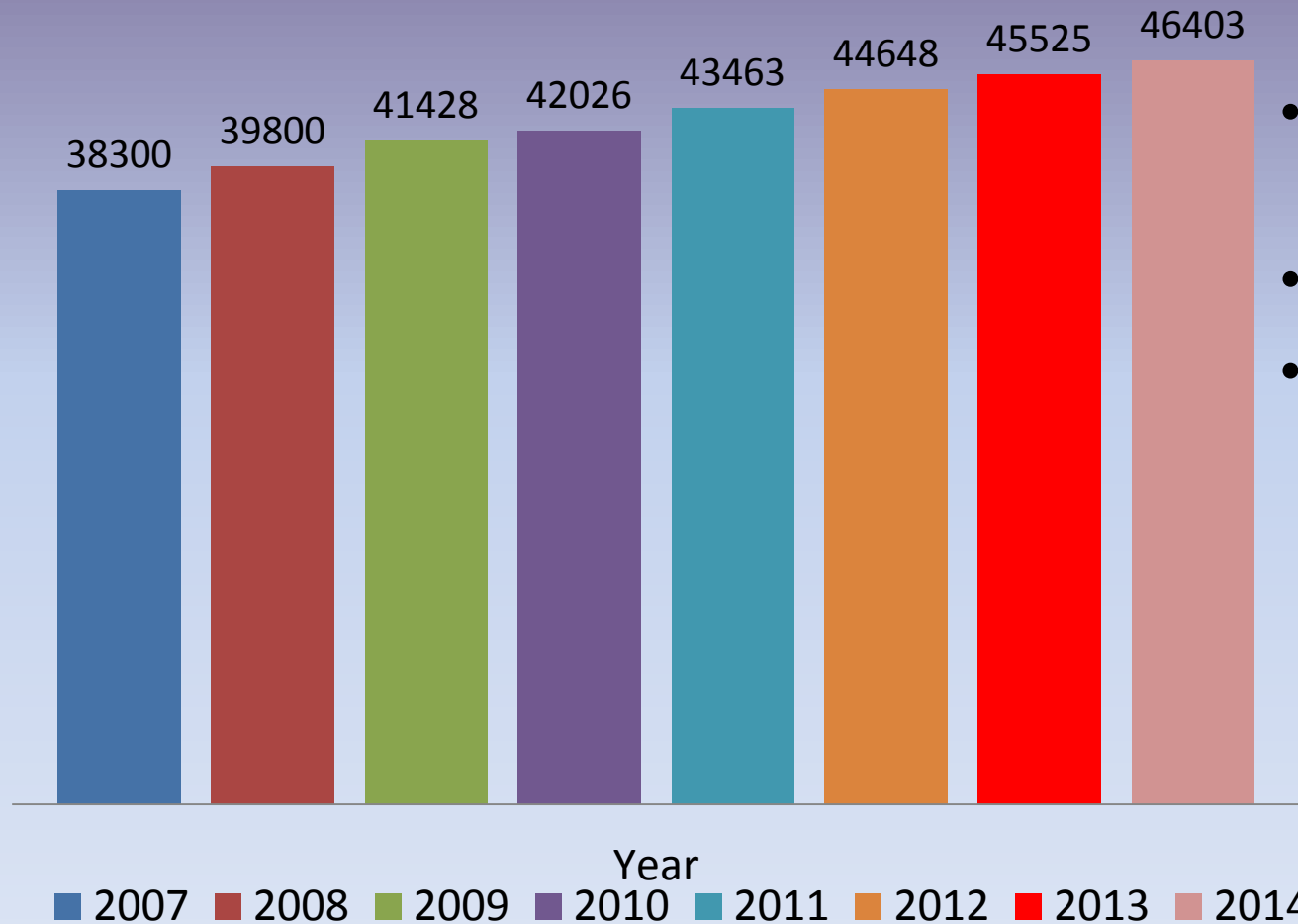
Cancer Mortality



Age Standardised Incidence Rates



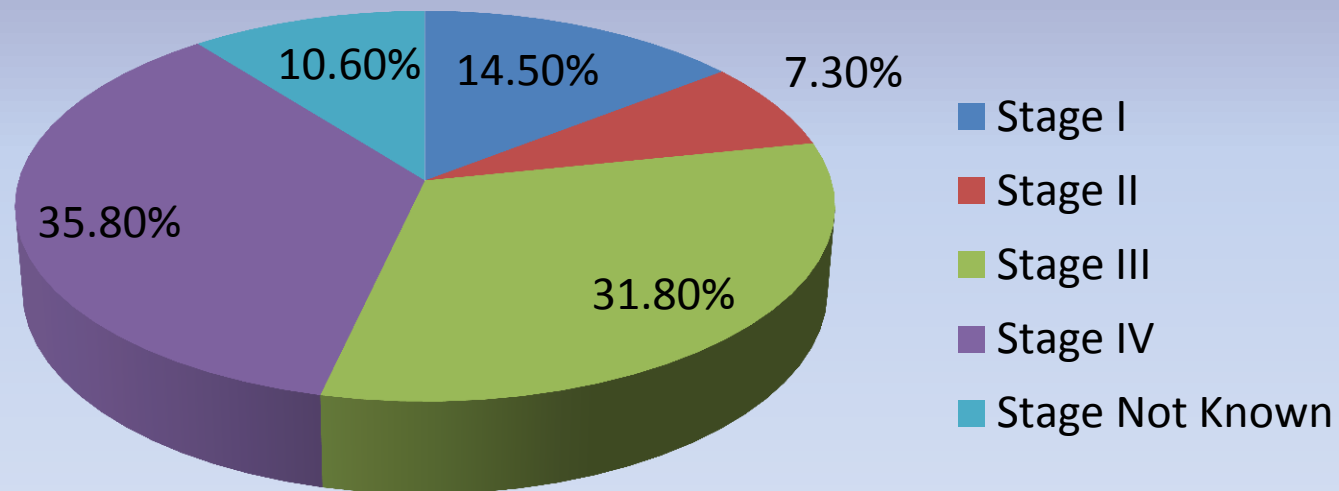
Annual incidence in the UK



- Male to female ratio 11.5:10
- In 1975 was 39:10
- ≈ 1000 extra diagnoses per year

Data from National Registries from the 4 UK countries

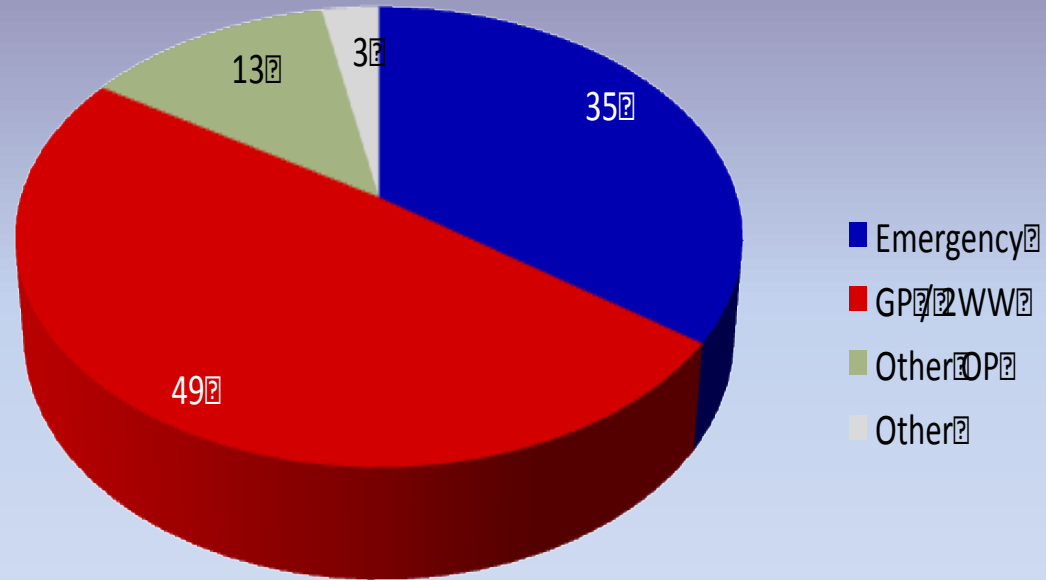
Stage at Presentation



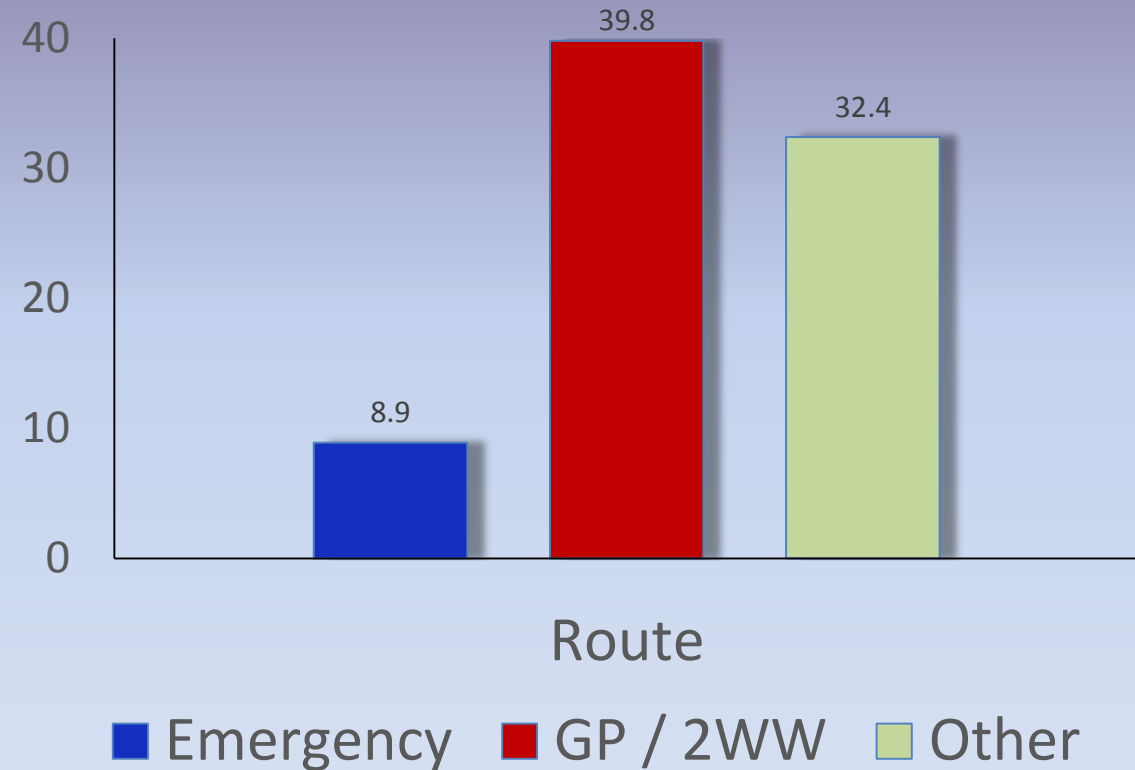
Data from National Lung Cancer Audit

NCIN Routes to Diagnosis

Route of presentation (%)



1 year survival (%)



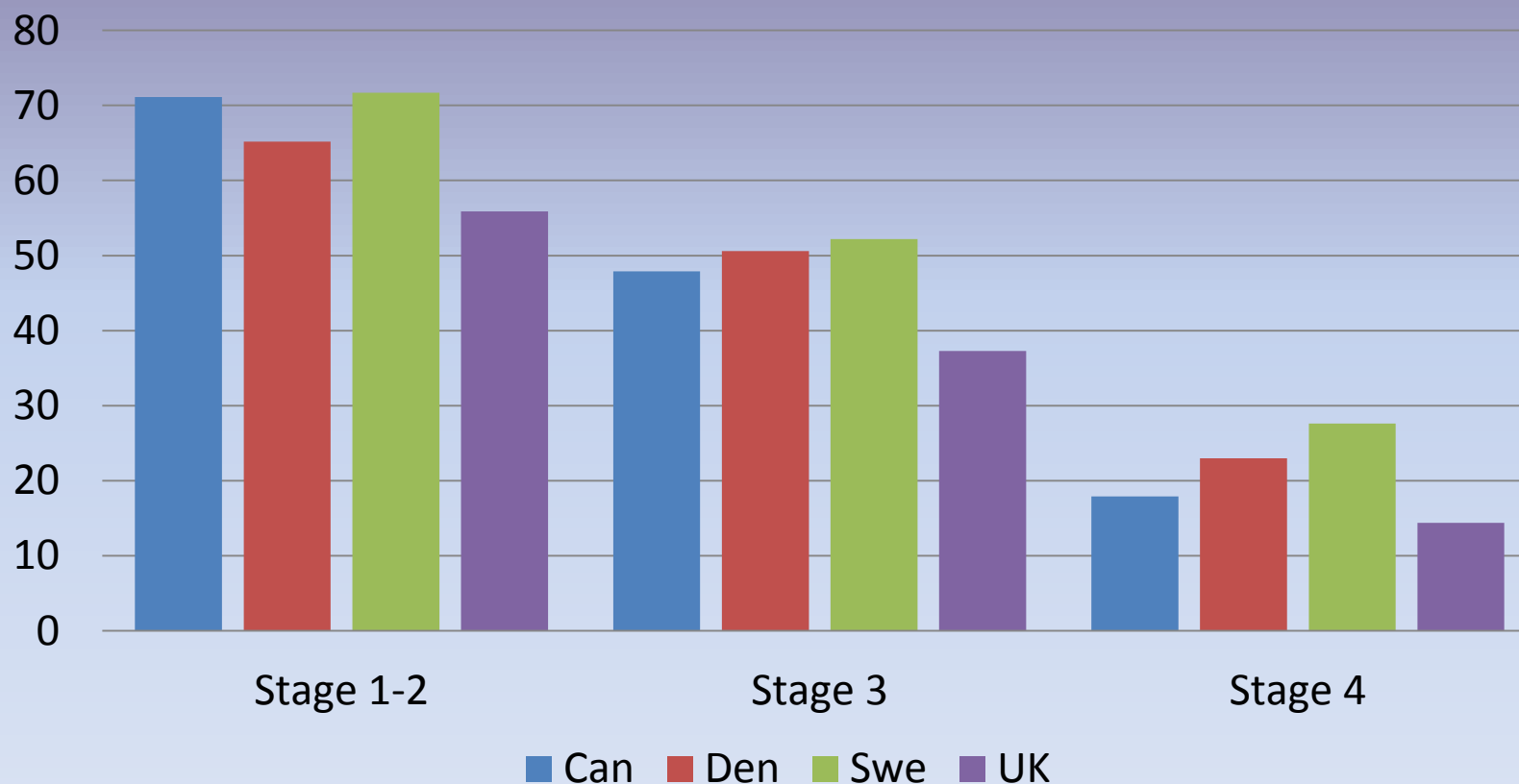
PS and overall survival

NLCA linked to HES

PS	Total	Died	%	HR	Adj HR*
0	5839	3804	64	1.0	
1	9267	7226	78	1.49 (1.43 to 1.55)	1.28 (1.22 to 1.33)
2	5300	4737	89	2.50 (2.40 to 2.61)	1.87 (1.76 to 1.99)
3	3230	3103	96	4.51 (4.30 to 4.74)	3.12 (2.91 to 3.35)
4	737	722	98	7.62 (7.03 to 8.25)	5.21 (4.39 to 6.17)
Missing	9992	8168	82	1.82 (1.75 to 1.89)	1.54 (1.45 to 1.62)

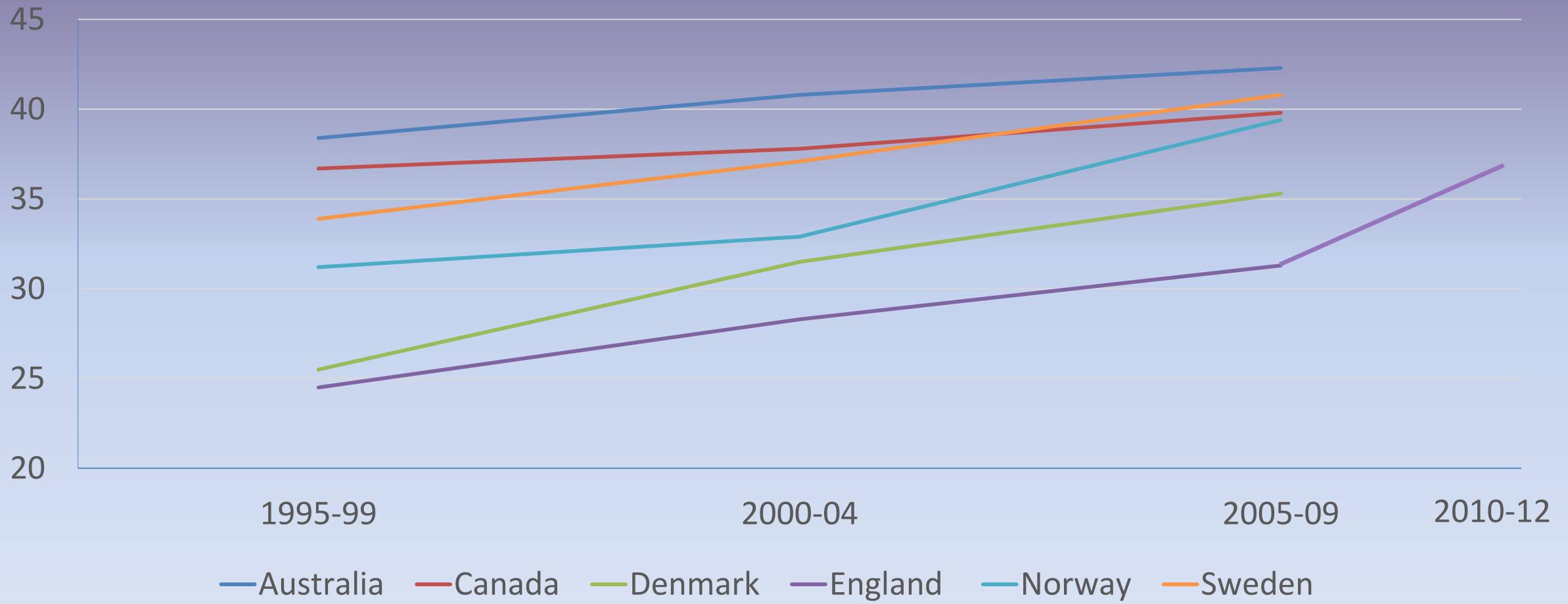
* Adjusted for age, sex, ethnicity, deprivation, comorbidity, stage, surgical centre, radiotherapy centre and trial entry centre

Age-standardised 1-year net survival from non-small cell lung cancer by stage at diagnosis

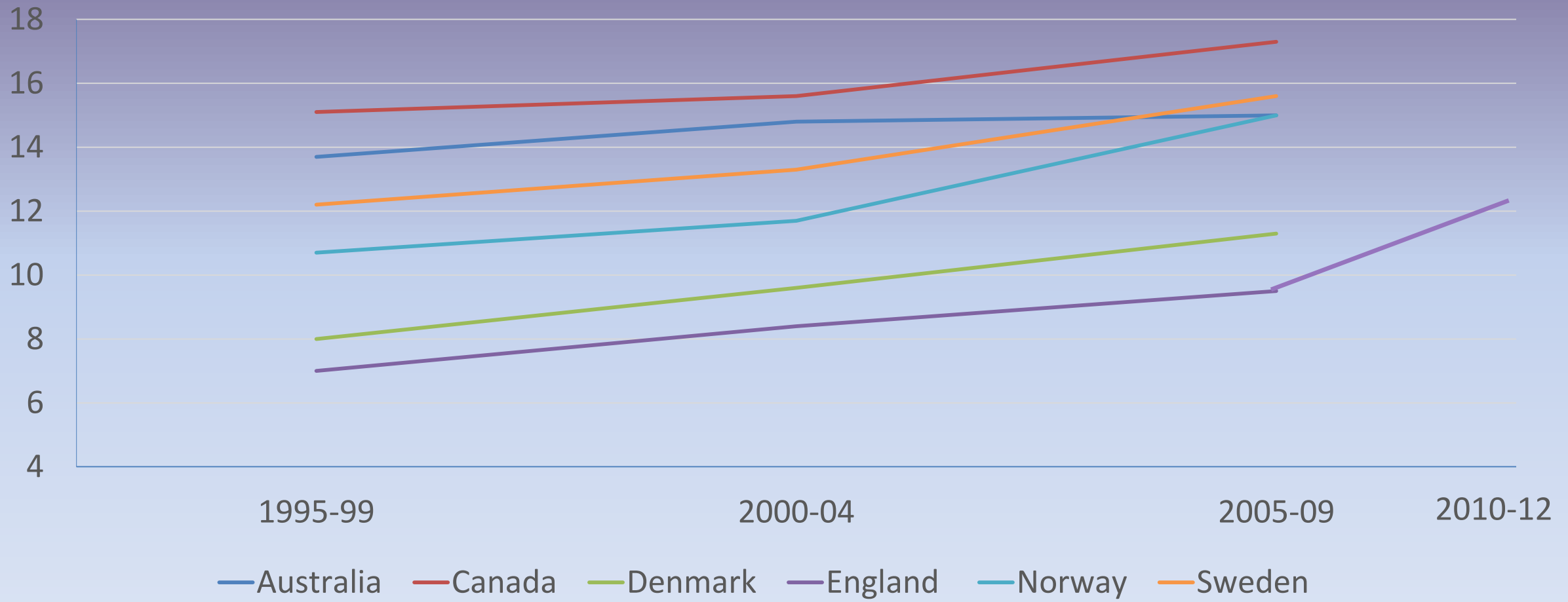


Advances – Treatment with Curative Intent

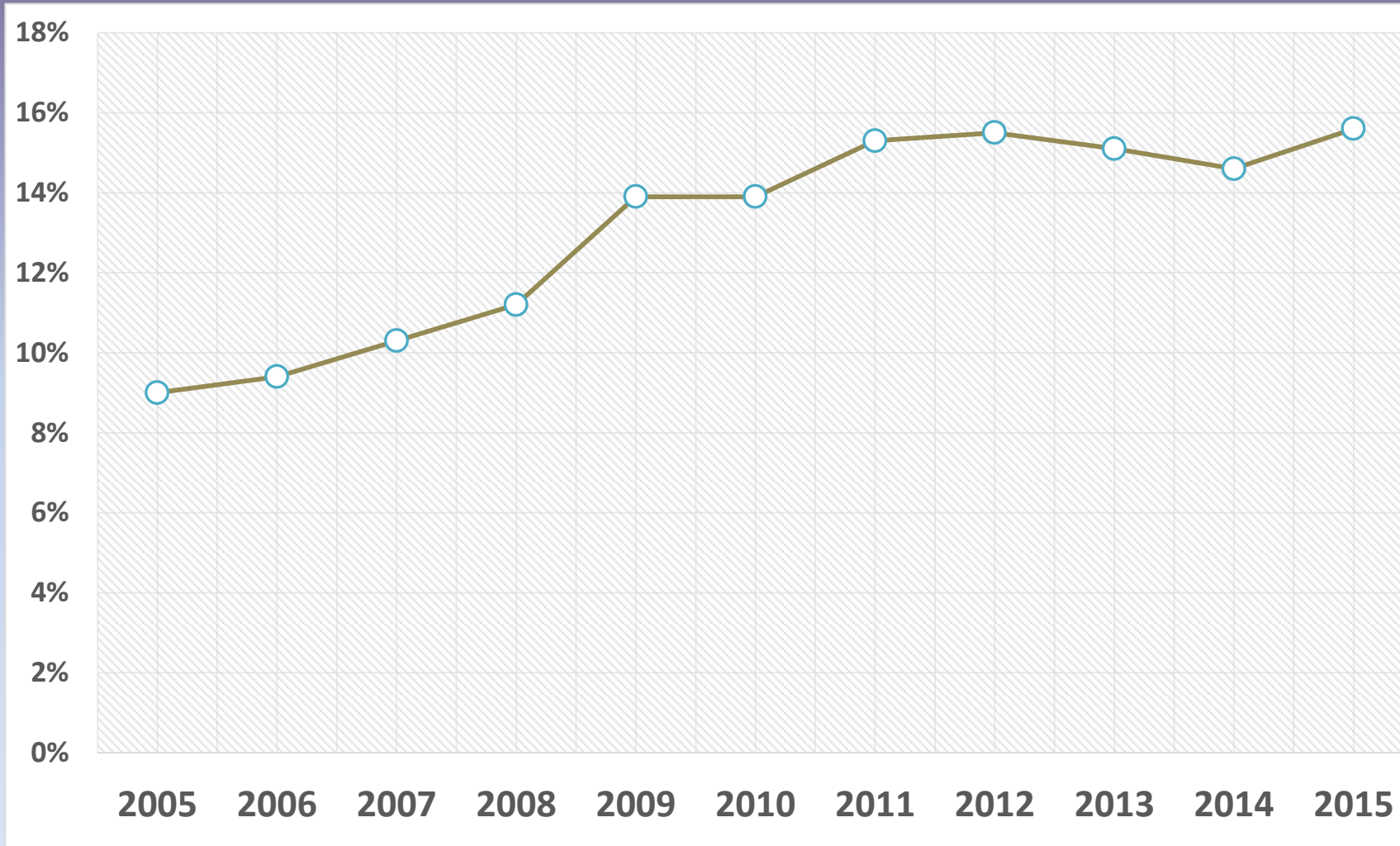
1 year Relative Survival



5 year Relative Survival

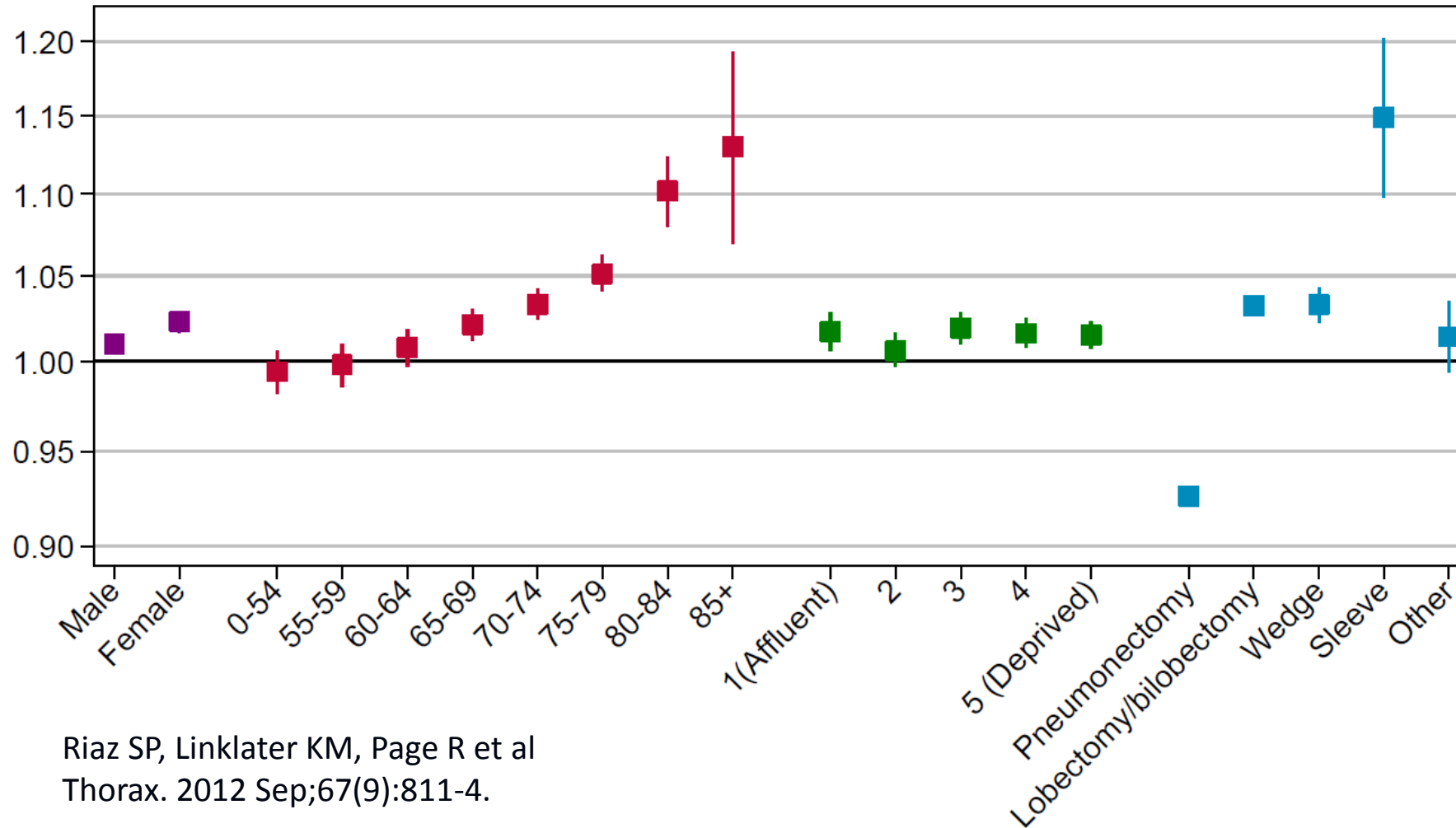


Surgical resection rate over time (England & Wales)



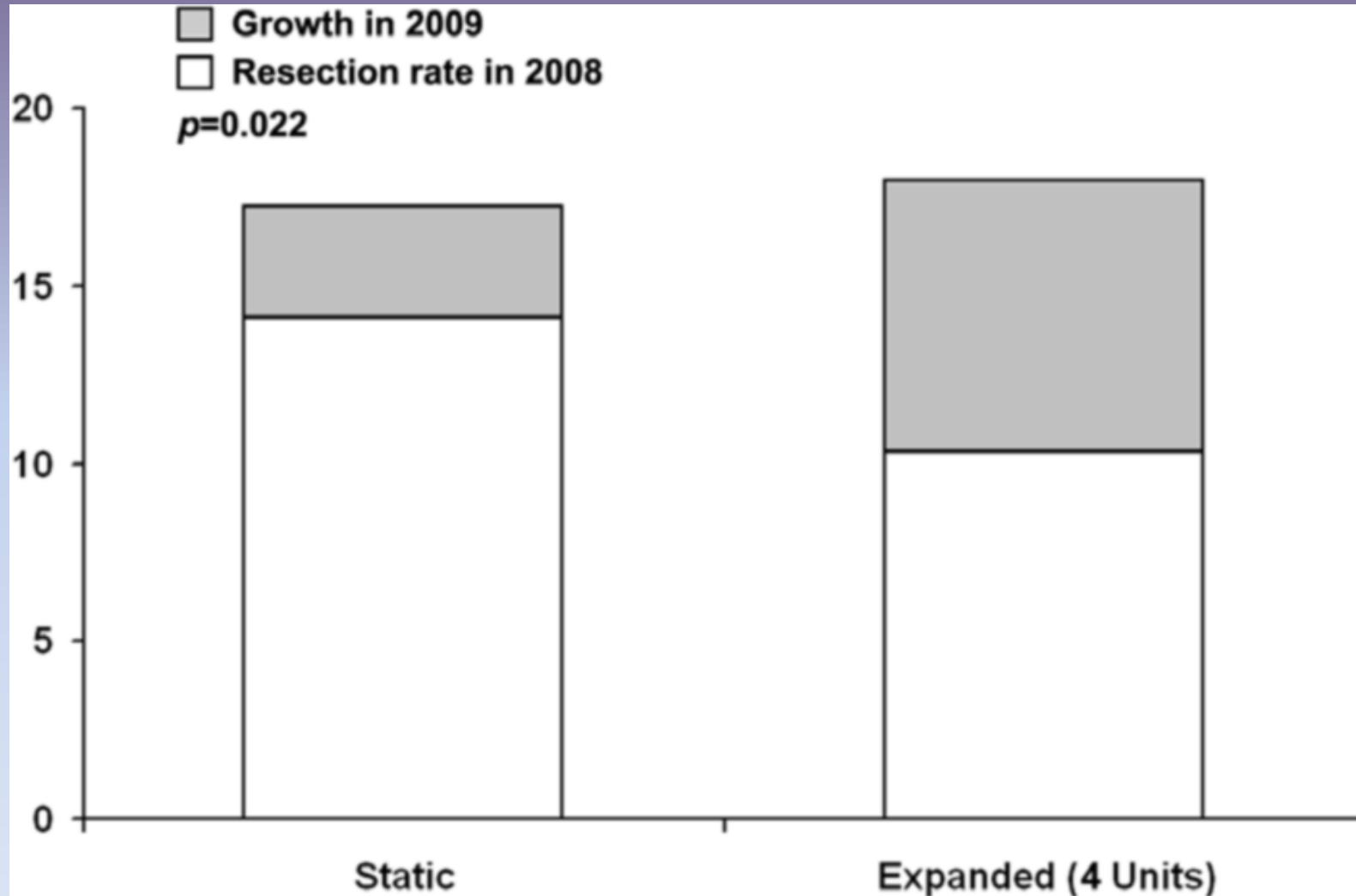
Source: National Lung Cancer Audit, slide curtesy of Mick Peake

Changes in surgical resection 1998-2008

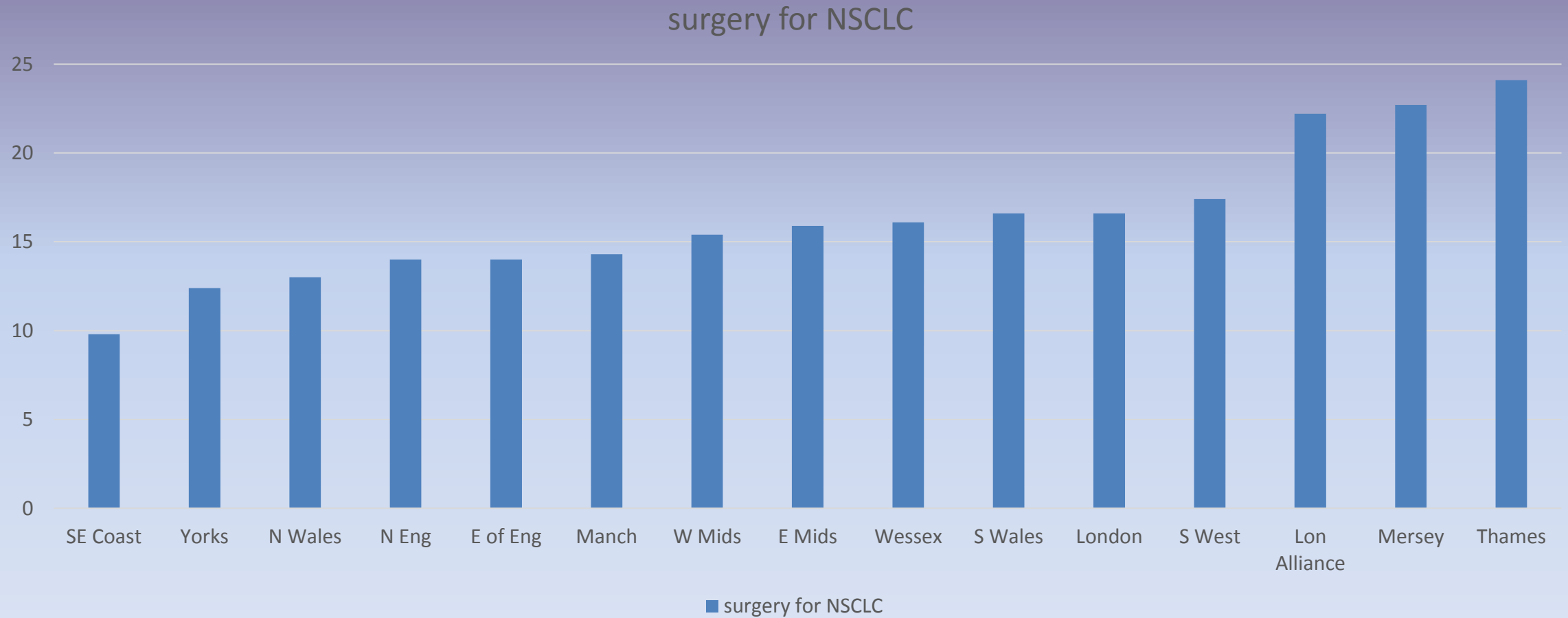


Riaz SP, Linklater KM, Page R et al
Thorax. 2012 Sep;67(9):811-4.

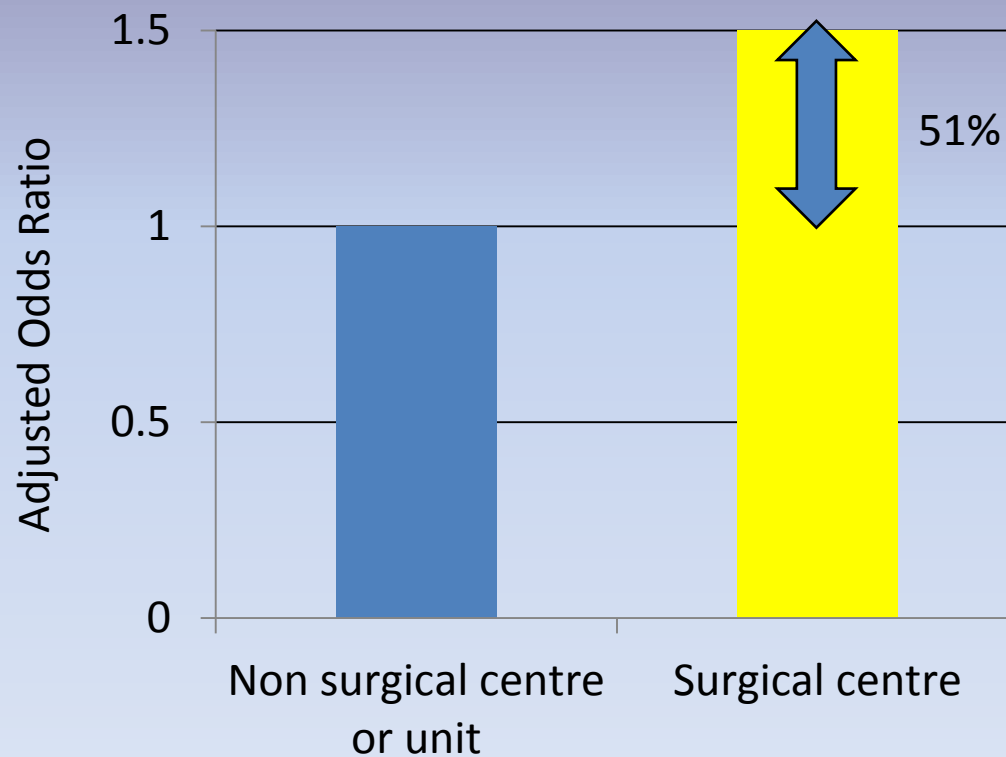
More thoracic surgeons



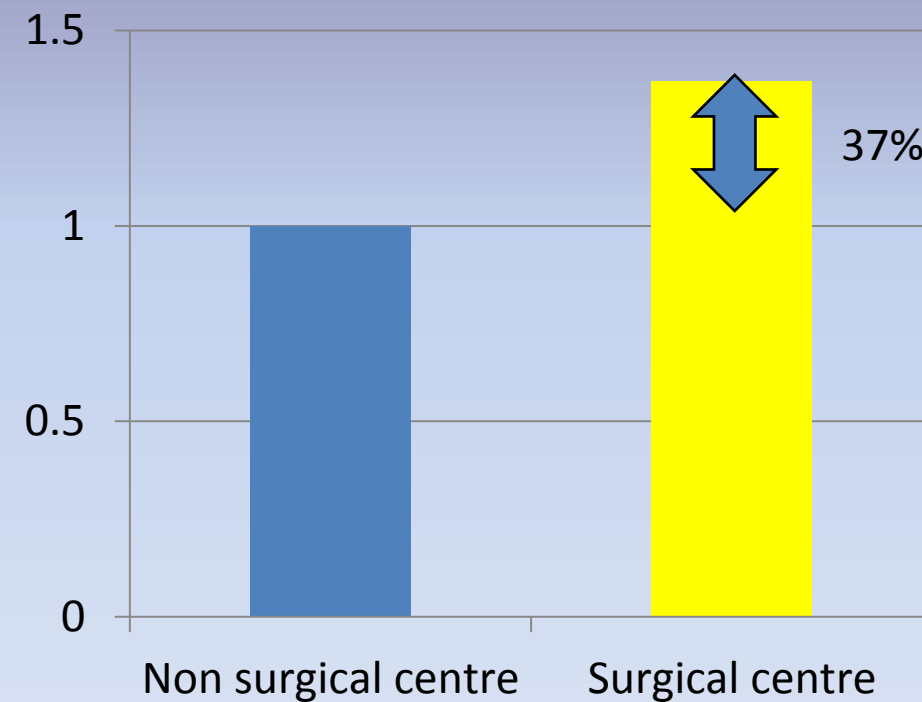
Variation in Treatment – Surgery for NSCLC



NHS Trust of First Contact and Chance of Having Surgery for Lung Cancer

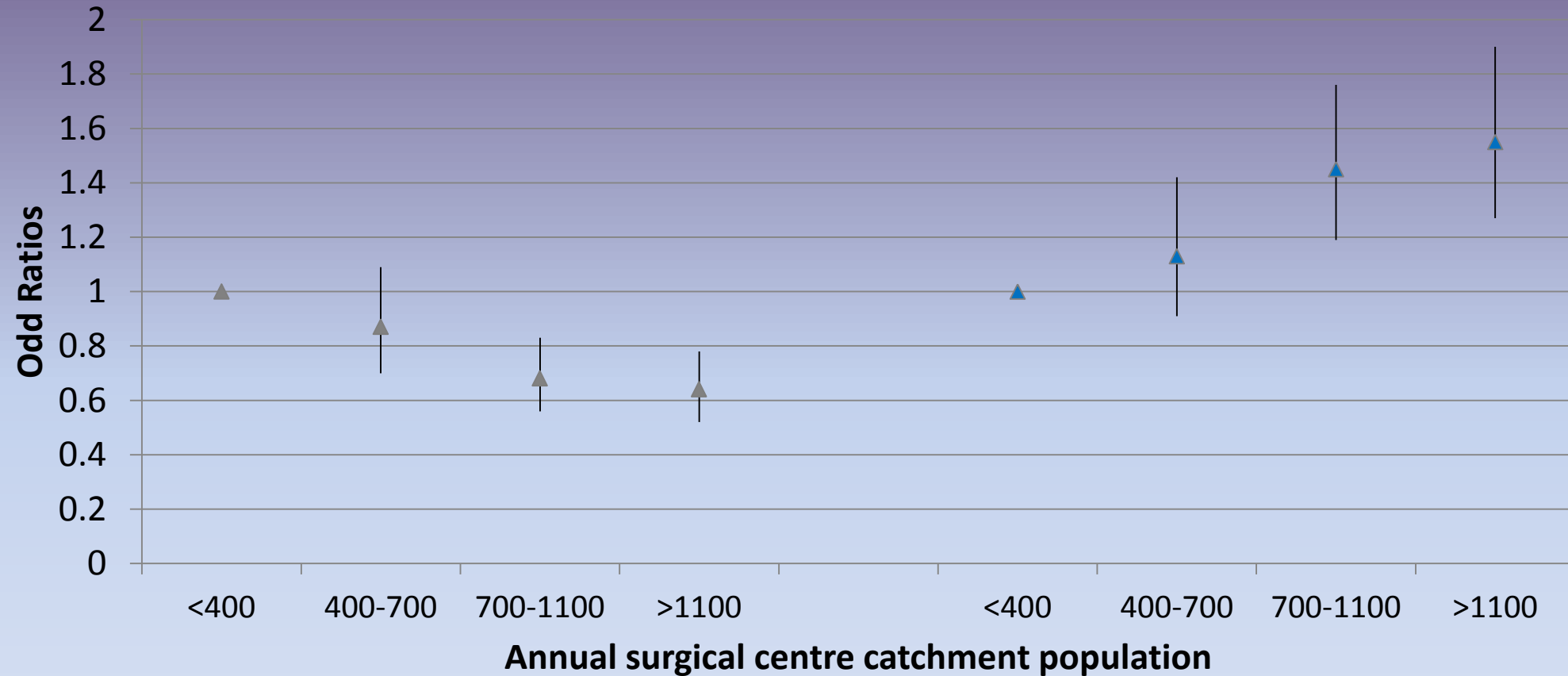


Rich A L et al Thorax. 2011;66(12):1078-84



Aamir Khakwani, et al. PLOS ONE 2014;9(2)e89426

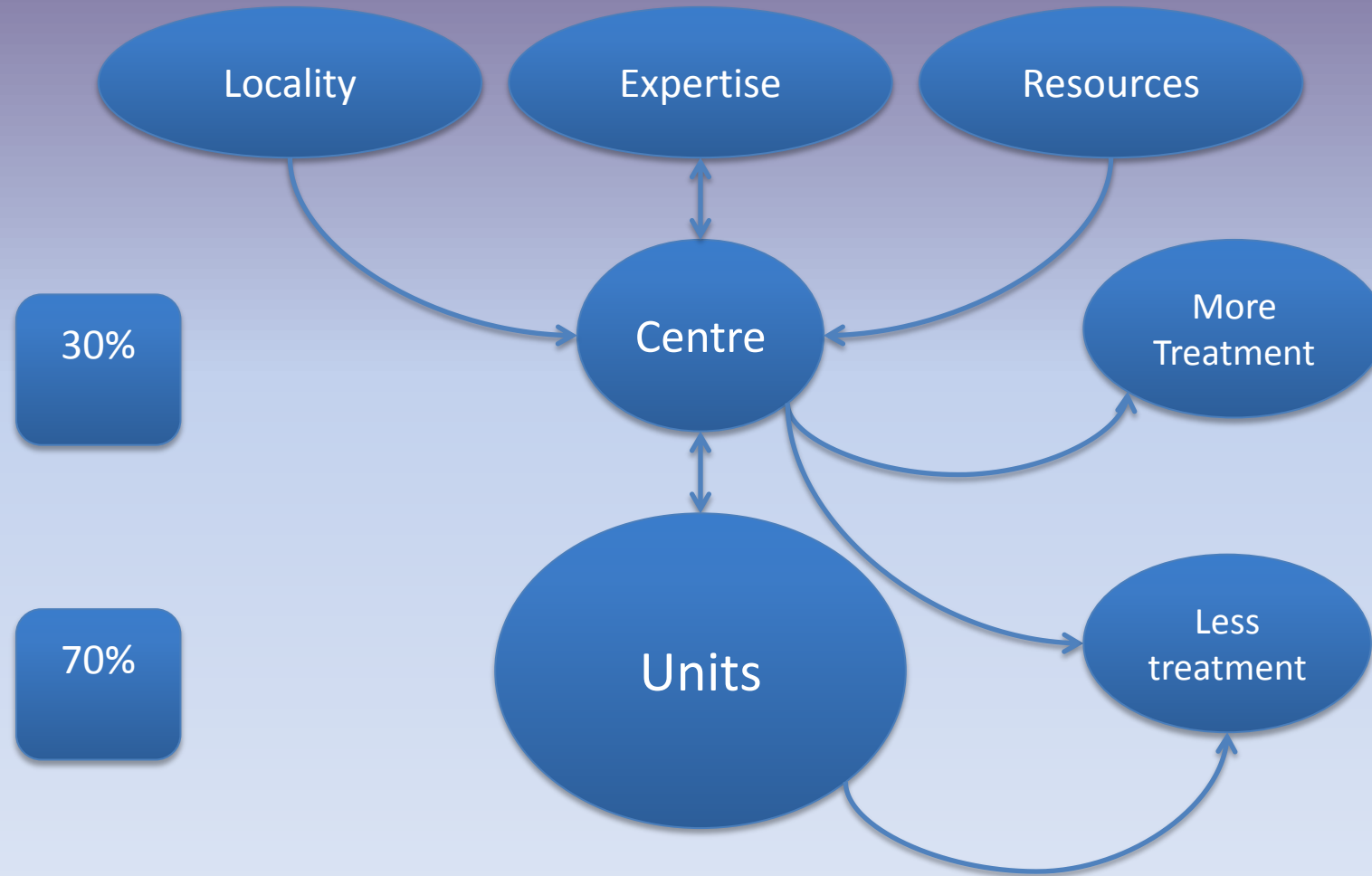
Interaction between surgical centre catchment population and likelihood of having surgery



Odds of resection when
First referred to a
Non-surgical hospital

Odds of resection when
First referred to a
Surgical centre

Hub and spoke





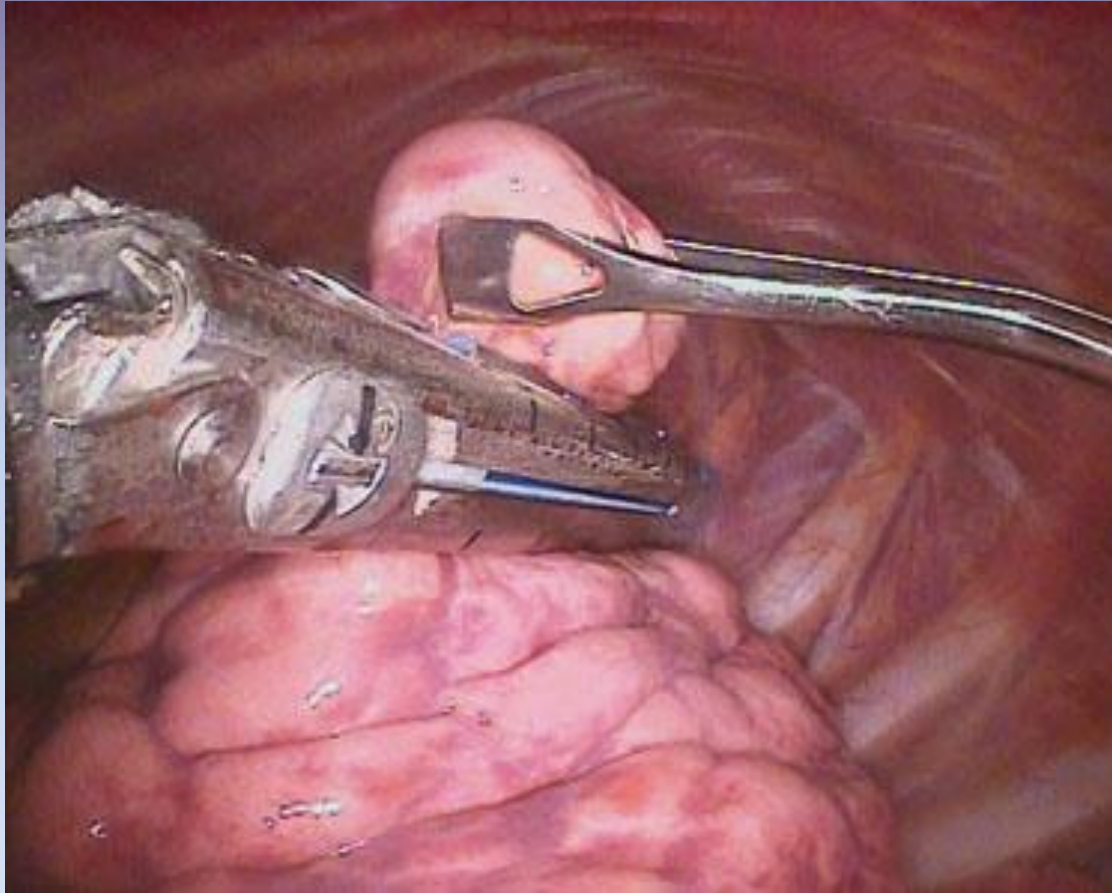
Mortality after Surgery for Lung Cancer

	<i>% of patients who died after surgery</i>		
	<i>≤30 days n=334</i>	<i>31-90 days n=313</i>	<i>≤90 days n=647</i>
<i>N=10,991</i>	3.0	2.9	5.9
Lobectomy	2.3	2.3	4.6
Pneumonectomy	7.0	4.5	11.5

90 day mortality by age and PS

	Performance status						
Age	0	1	2		0	1	2
<70	2% (1-2) 2534	3% (2-4) 1467	7% (3-10) 222		7% (5-10) 436	12% (8-16) 289	
70-80	4% (3-6) 1361	6% (5-7) 1420	8% (5-12) 219		18% (12-25) 143	12% (7-18) 154	
>80	6% (3-9) 263	7% (5-10) 377	17% (8-25) 72				
	LOBECTOMY				PNEUMONECTOMY		

Improving radical treatment



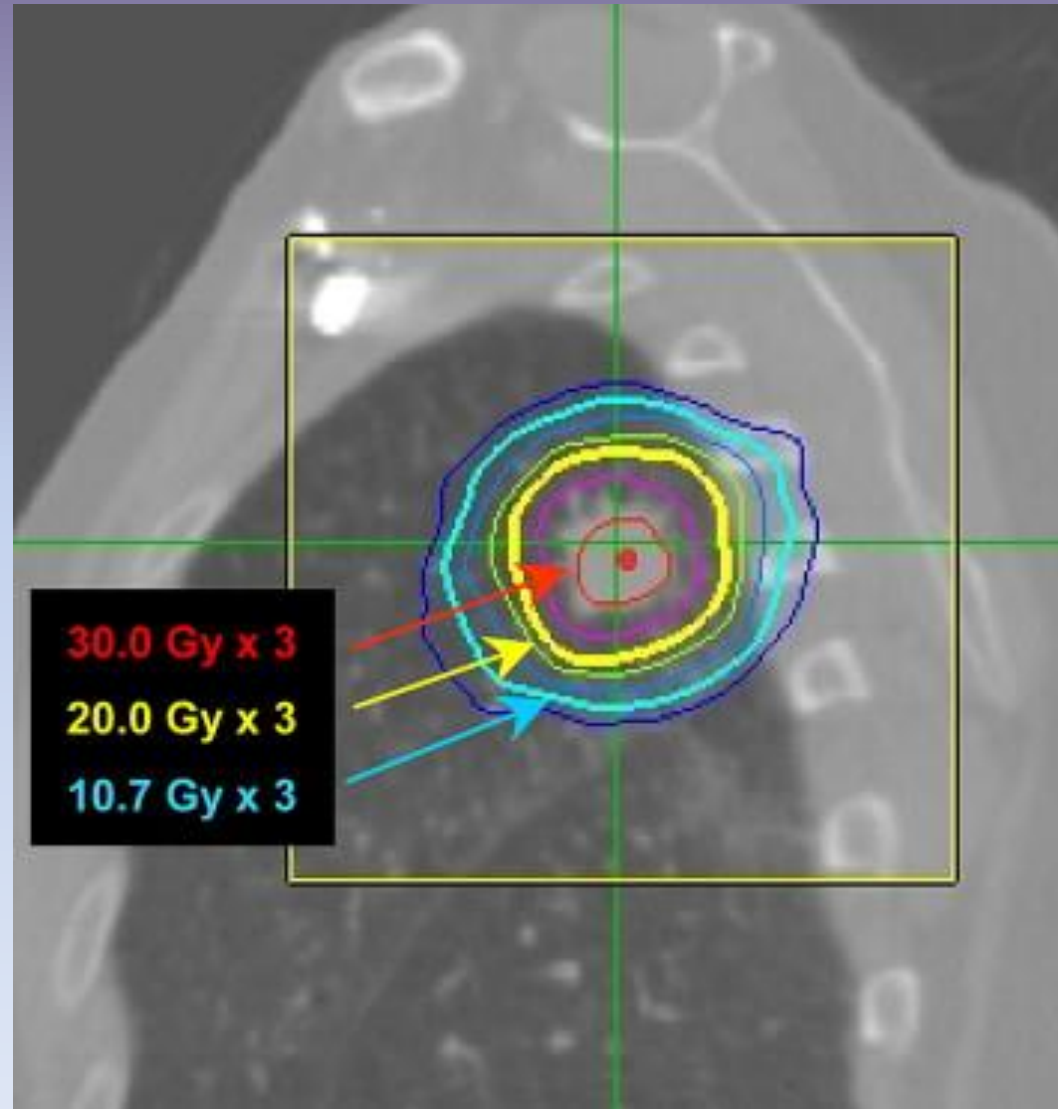
Outcome	Open n =2721	VATS n = 2721	P value
Complication	863 (31.7)	792 (29.1)	0.0357
Major C/P	435 (19.6)	316 (15.9)	0.0094
Atelectasis	150 (5.5)	65 (2.4)	<0.0001
LOS (median)	8	6	0.0003
Death (discharge)	52 (1.9)	27 (1.0)	0.0201

Video-assisted Thoracic Surgery

Treatment with Curative Intent

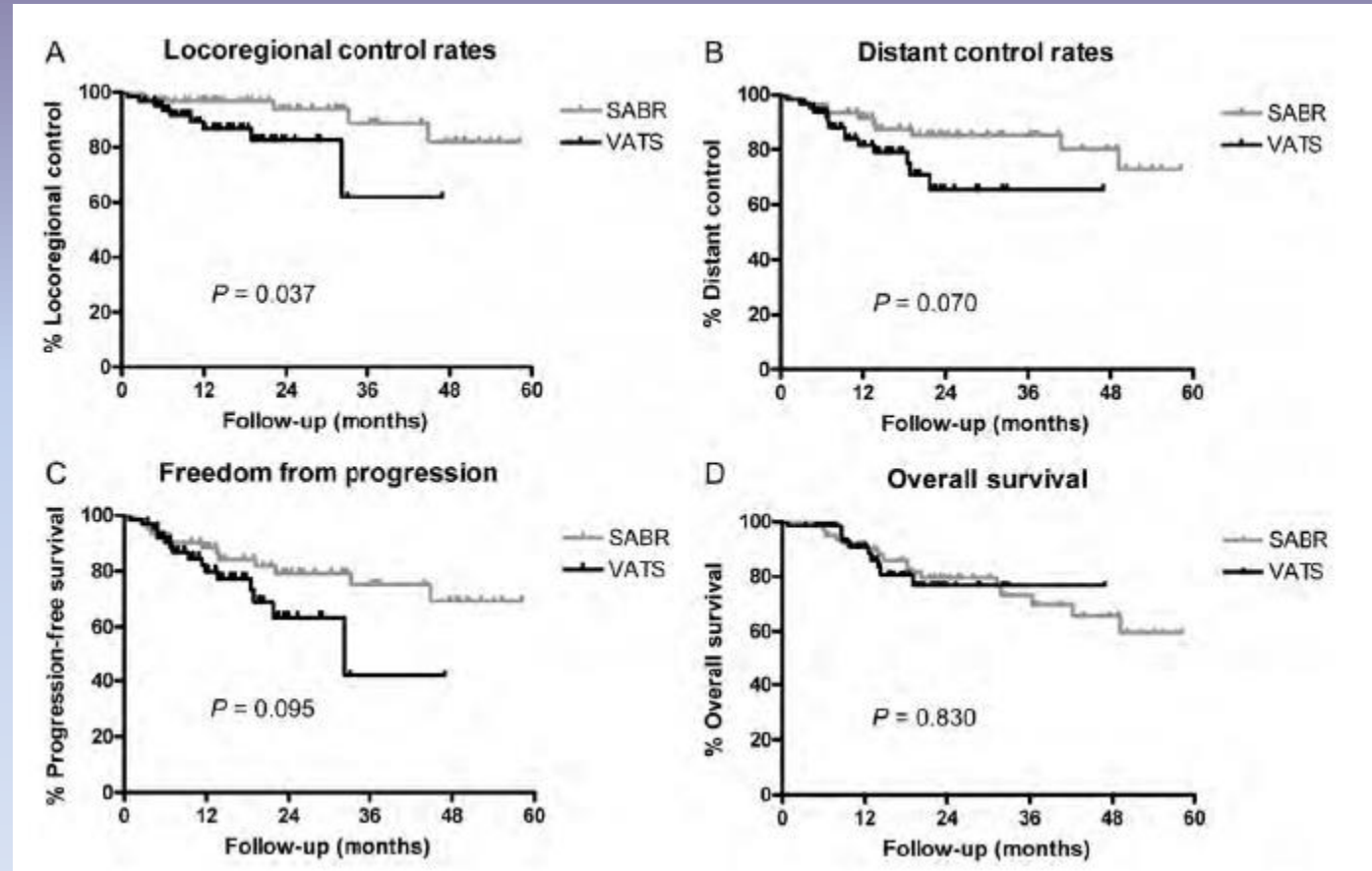
- Surgery
- Radical radiotherapy / chemoradiotherapy
- Radiofrequency Ablation (RFA)

Stereotactic Ablative Radiotherapy (SABR)



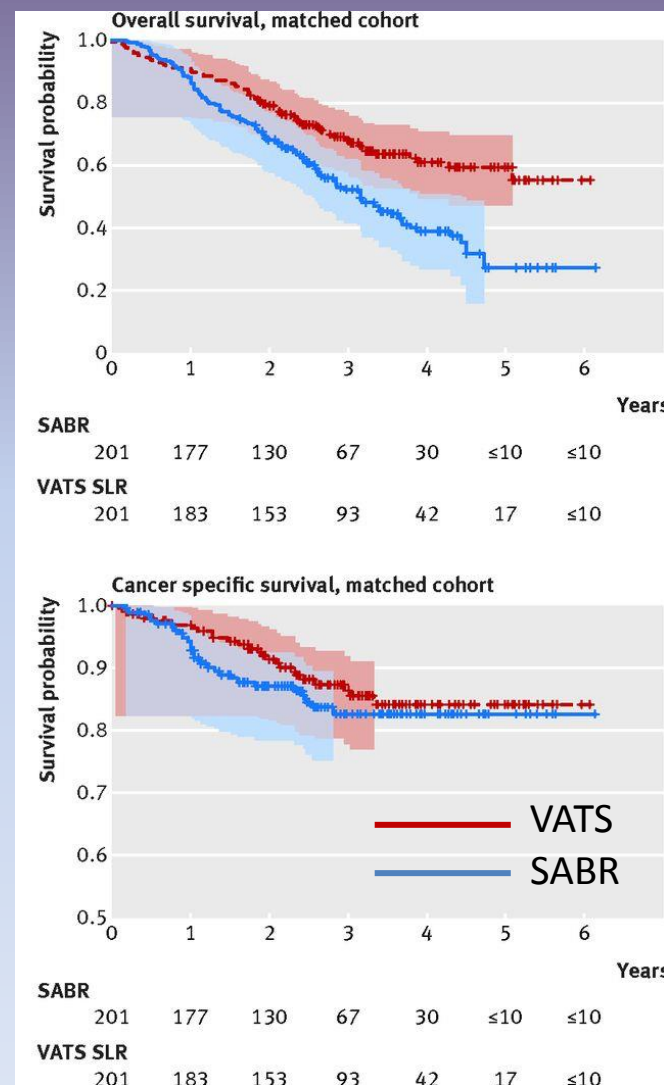
SABR vs. Surgery

- Retrospective
- Propensity matched
- 64 SABR
- 64 VATS
- RCT to start 2015

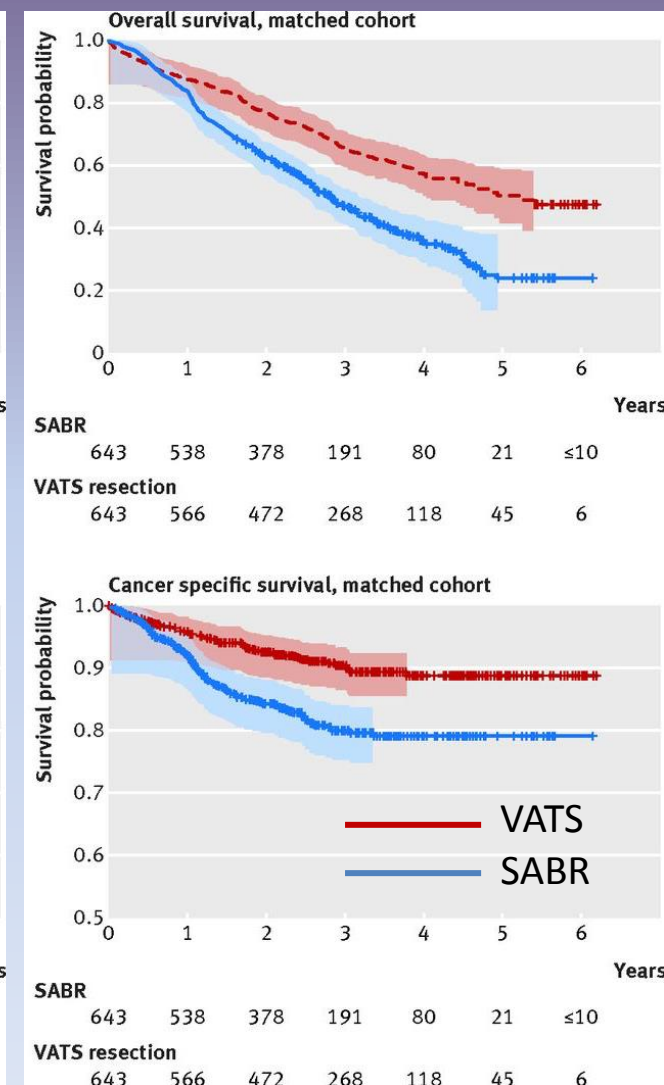


SABR vs. Surgery

- Medicare data linked to SEER
- Matched incl. comorbidity
- SABR vs VATS sub-lobar resection, tumour $\leq 2\text{cm}$
- SABR vs VATS lobectomy, tumour $\leq 5\text{cm}$
- No direct measure of PS



tumour $\leq 2\text{cm}$



tumour $\leq 5\text{cm}$

SABR vs. Surgery

Study	Design	Comparison	No randomised	Target	Status
STARS (US)	RCT phase 2/3	SABR vs lobectomy	36	80	Closed
ROSEL (NL)	RCT phase 3	SABR vs lobectomy	22	960	Closed
SABRTooth (UK)	RCT Feasibility	SABR vs lobectomy is higher risk	24	54	Closed
POSTILV (China)	RCT phase 2	SABR vs surgery		76	Recruiting
Stablemates (US)	RCT phase 2	SABR vs sub lobar resection		96	Recruiting
Valor (US)	RCT phase 3	SABR vs surgery		670	Start Mar 2017

Radiofrequency / microwave ablation



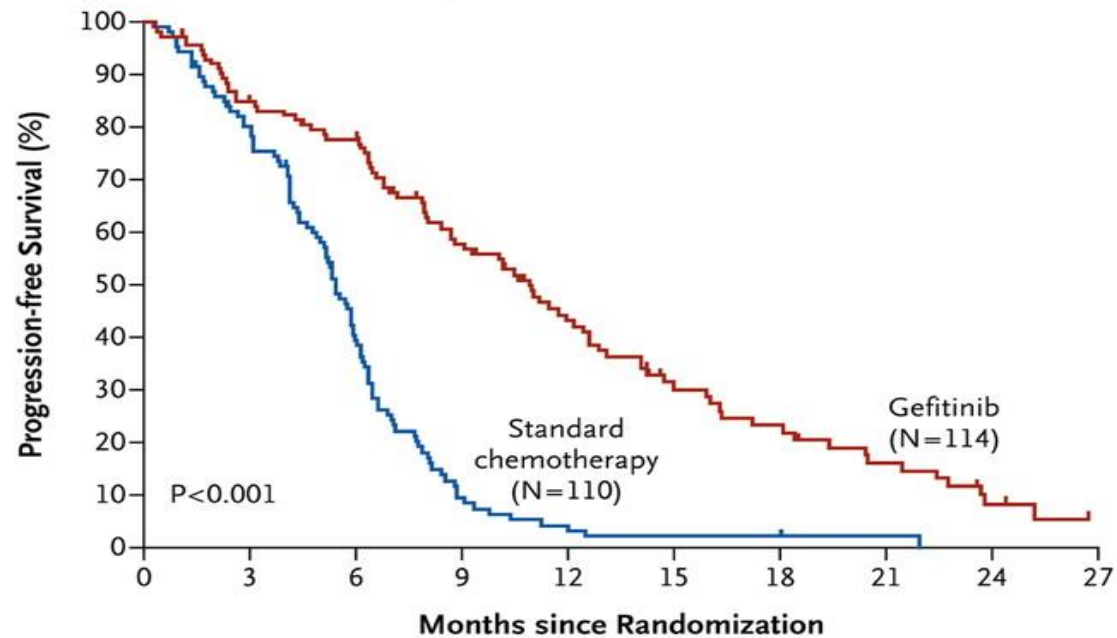
Advances – Systemic Treatment

Targeted drugs available or being assessed by NICE

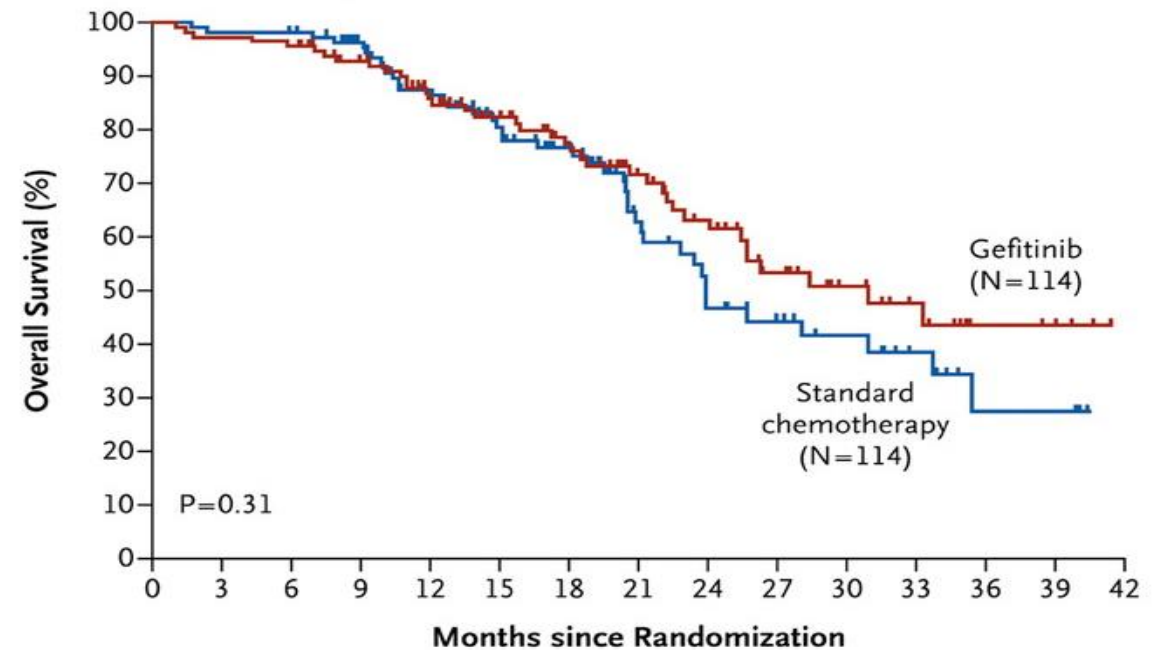
- EGFR – erlotinib, gefitinib, afatinib
- EGFR T790M – osimertinib, rocelestinib
- Anaplastic lymphoma kinase (ALK) – crizotinib, ceritinib, alectinib
- ROS-1 – crizotinib
- PD-1 – nivolumab, pembrolizumab, atezolizumab
- Angiogenesis inhibition – nintedanib
- Non-squamous - pemetrexed

Targeted Systemic Therapy

A Progression-free-Survival Population

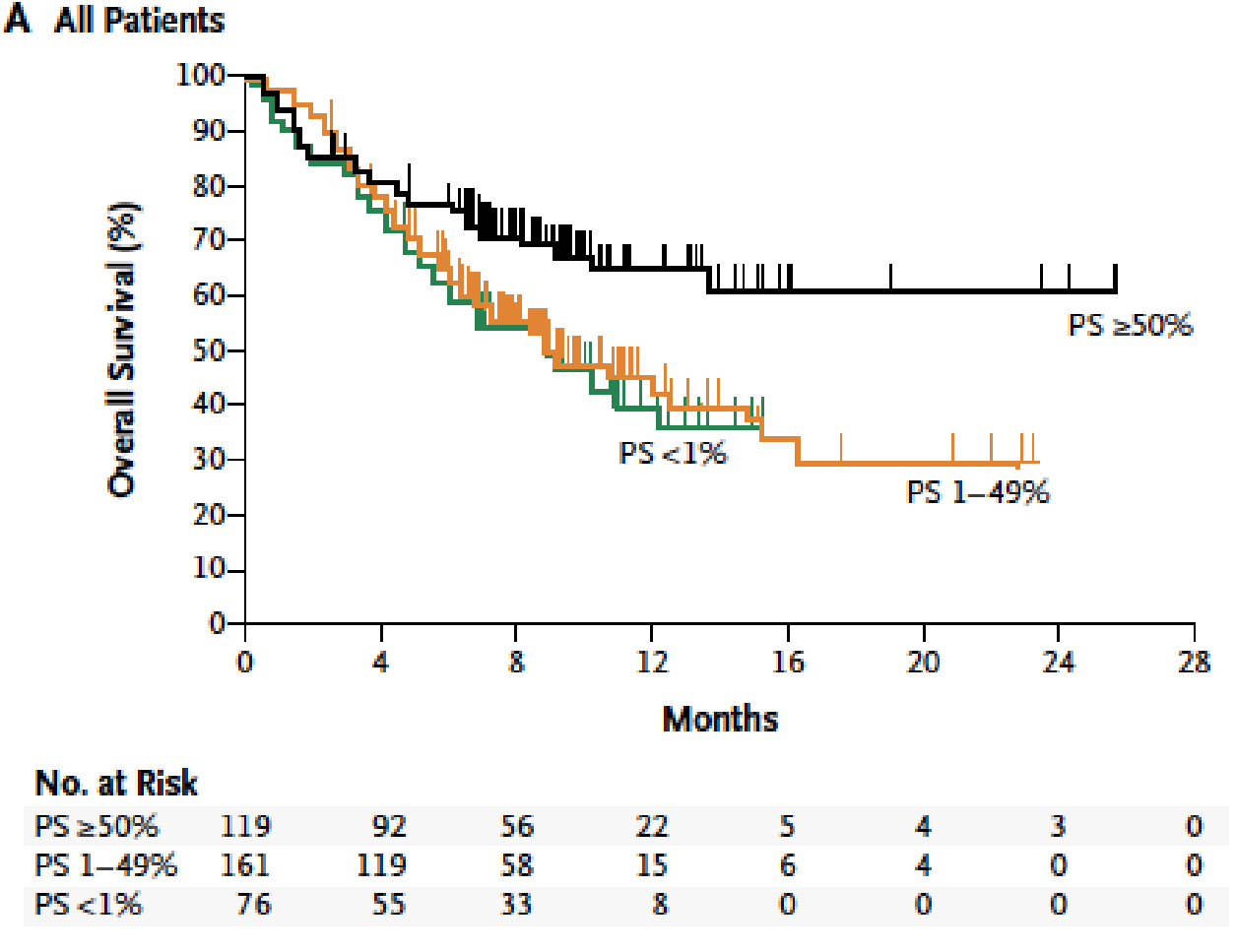


C Intention-to-Treat Population

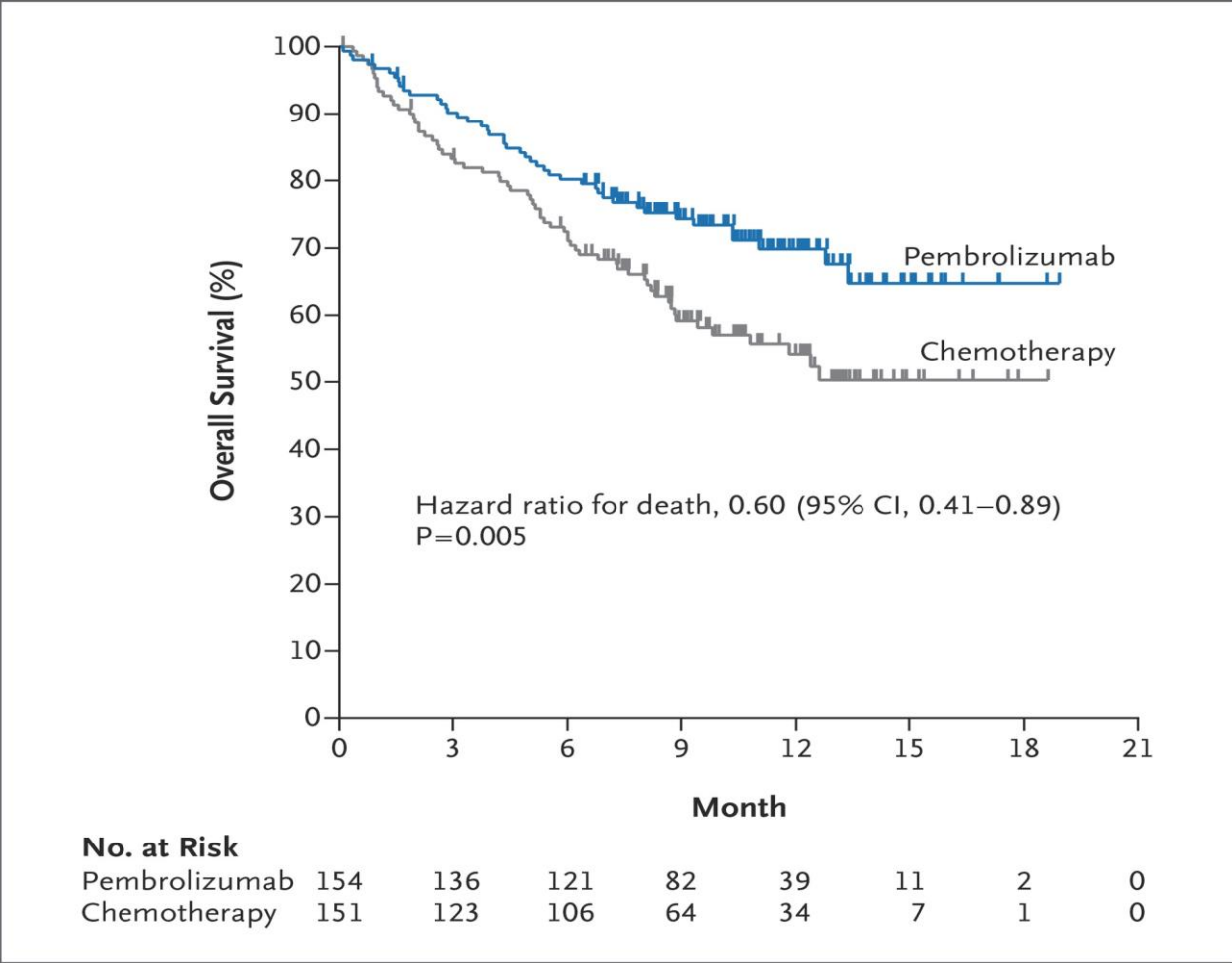


Overall Survival Pembrolizumab

A All Patients

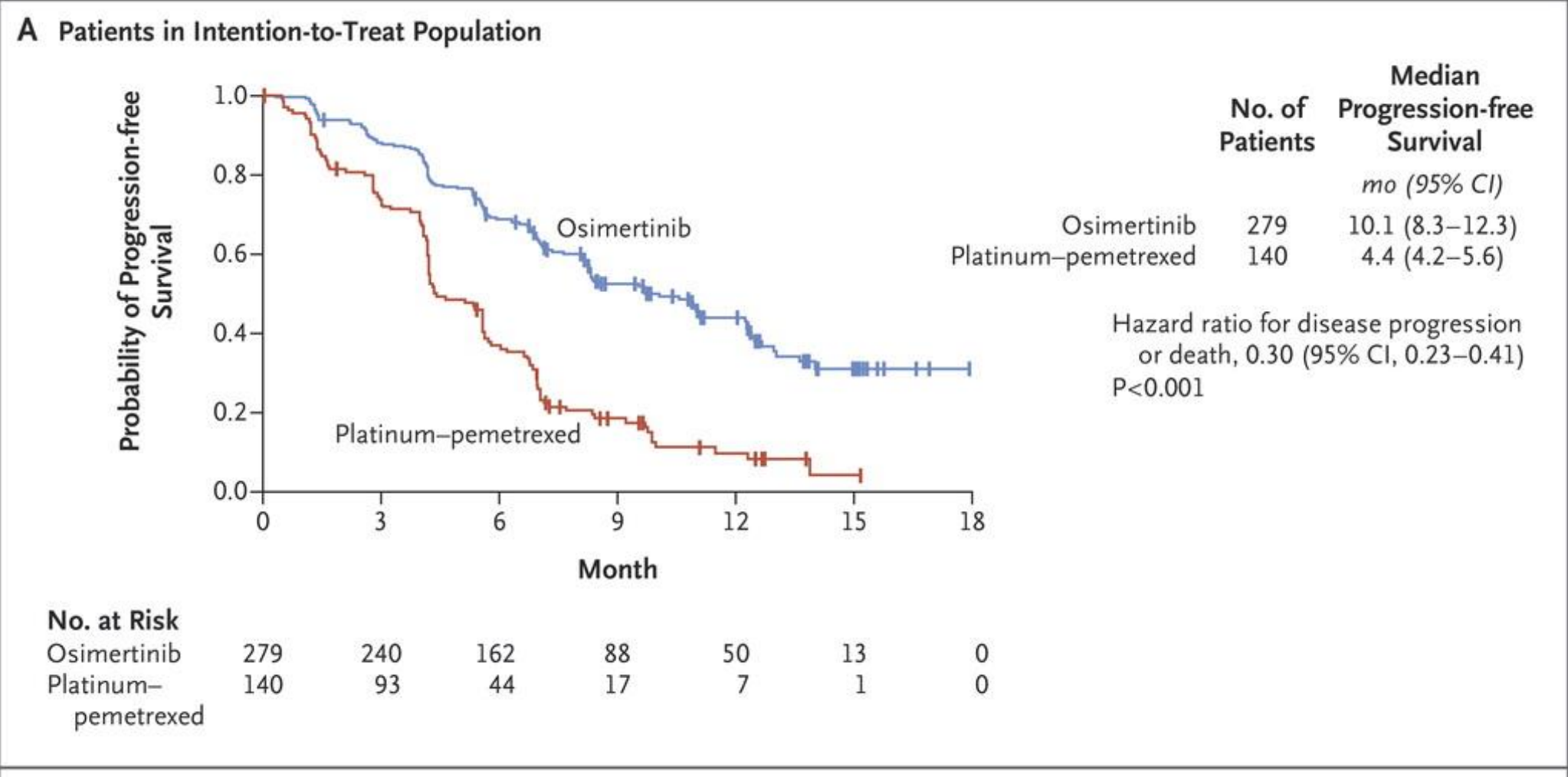


Garon EP et al NEJM 2015;372(21): 2018-2028.



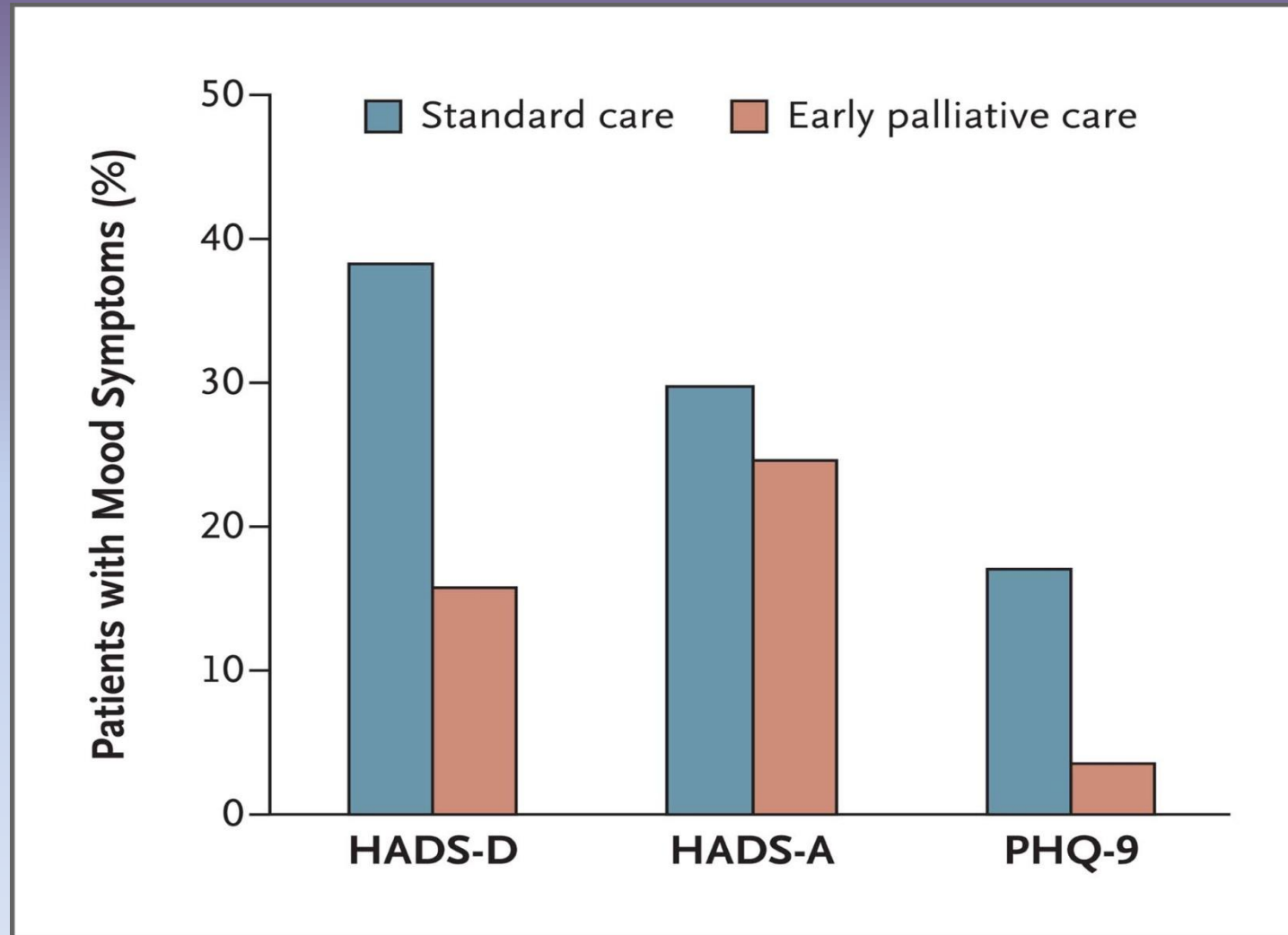
Reck M et al. NEJM 2016;375:1823-1833

Osimertinib for EGFR T790 mutation positive adenocarcnoma.



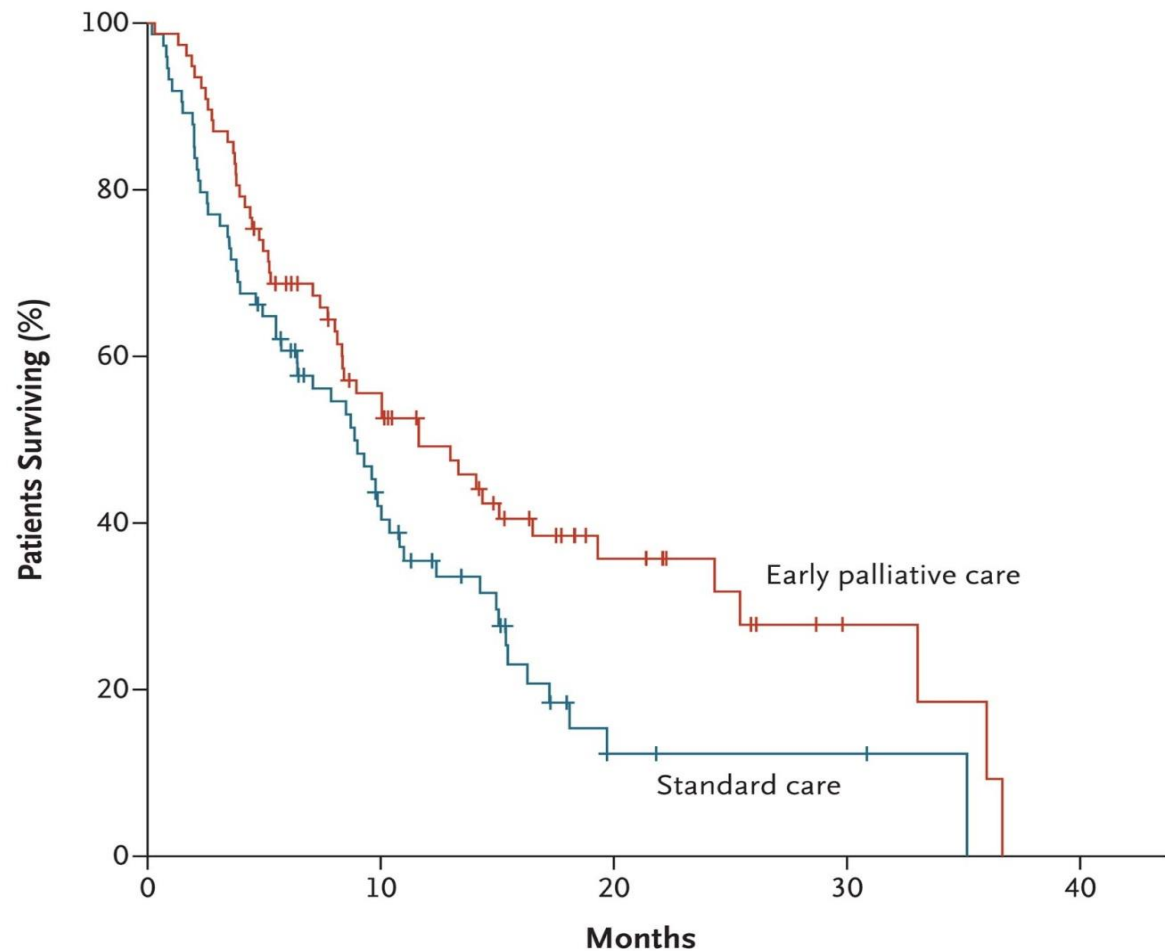
Advances – Supportive and Palliative Care

Twelve-Week Outcomes of Assessments of Mood

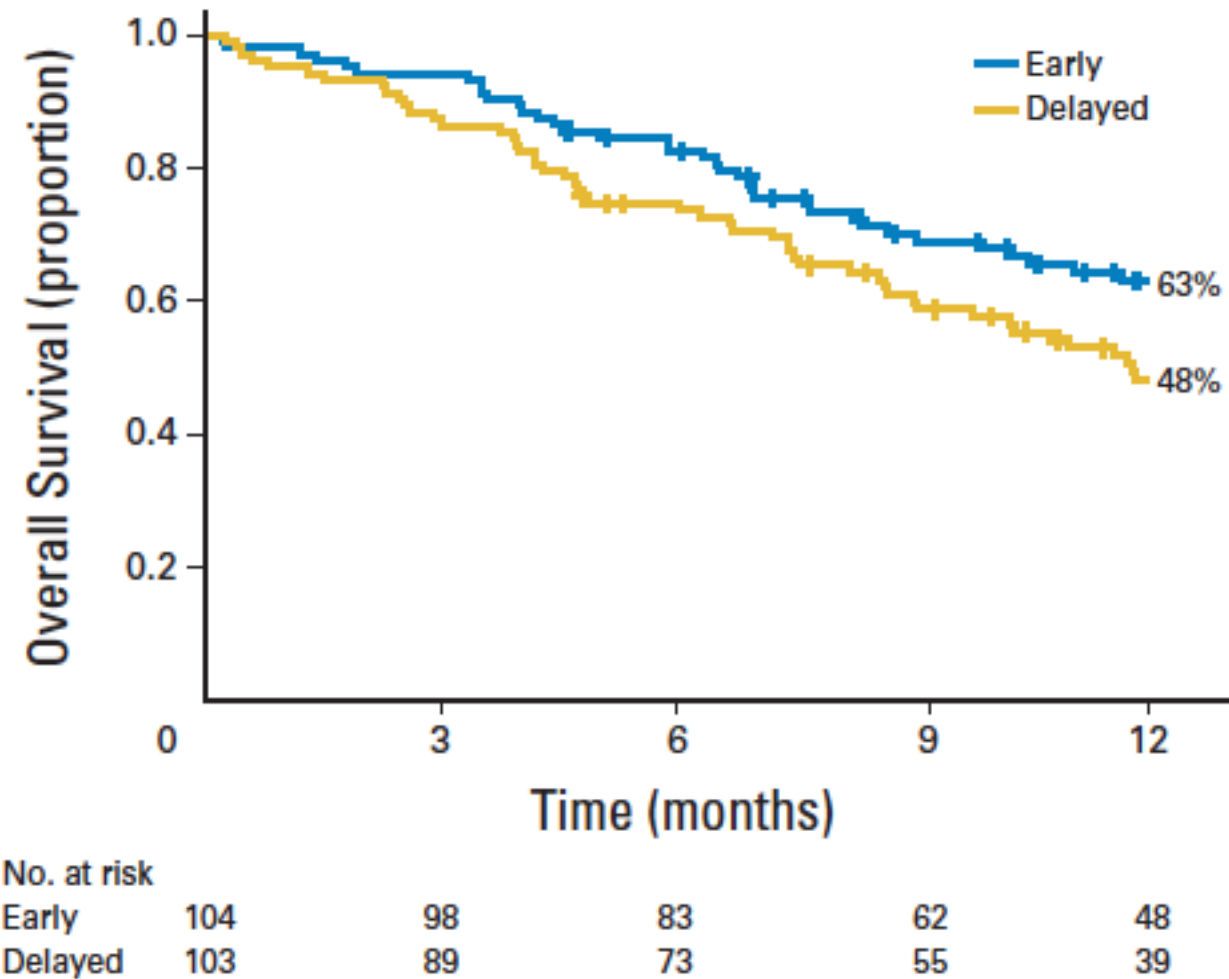


Temel JS et al. N Engl J Med 2010;363:733-742

Kaplan–Meier Estimates of Survival According to Study Group



Temel JS et al. N Engl J Med 2010;363:733-742



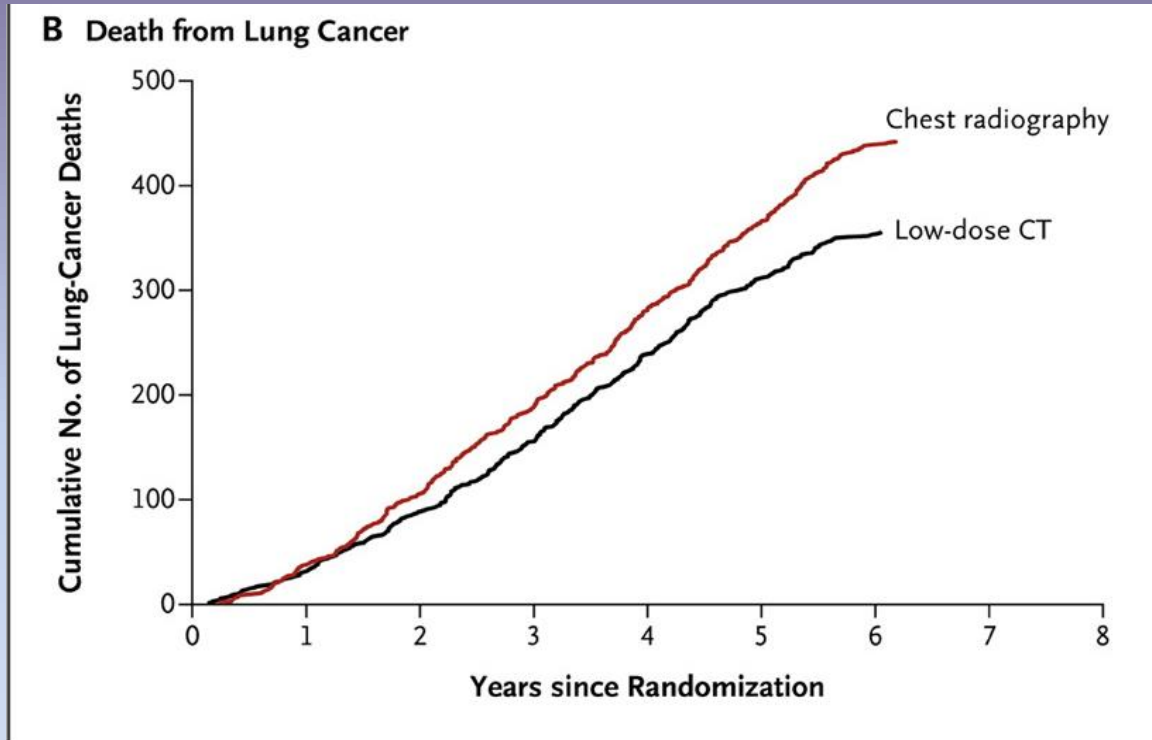
Bakitas MT et al. J Clin Oncol. 2015 May 1;33(13):1438-45.

Advances – Early Diagnosis

Early Diagnosis

- Screening
- Awareness
- Presentation
- Recognition
- Referral

National Lung Cancer Screening Trial (US)



Arm	Lung cancer deaths	Lung cancer mortality per 100,000 py	Reduction in lung cancer mortality (%)
CT	346	247	20.0 (6.8-26.7)
CXR	425	309	

$p = 0.004$ NNT = 320

All Cause Mortality

Arm	Deaths	Reduction in all cause mortality (%)
CT	1877	6.7 (1.2 to 13.6)
CXR	2000	

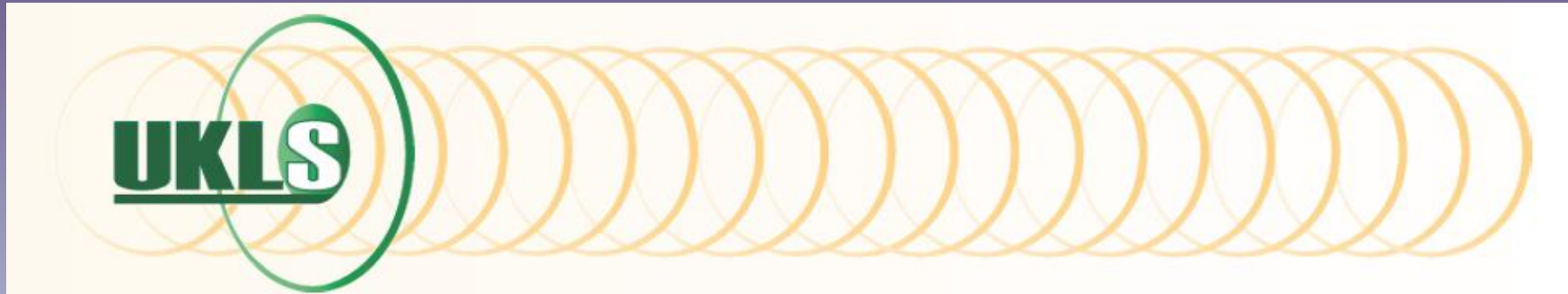
p = 0.02

- Cochrane systematic reviews:
 - Breast cancer 13 year FU HR 0.99 (0.97-1.01)
 - Colorectal cancer 13 year FU HR 1.00 (0.99-1.02)

The National Lung Screening Trial Research Team . N Engl J Med 2011;365:395-409.

Peter C Gøtzsche*, Karsten Juhl Jørgensen Cochrane Systematic Review 2013 DOI: 10.1002/14651858.CD001877.pub5

Hewitson P, Glasziou P, Les Irwig L, Towler B, Watson E. Cochrane Systematic review 2007 DOI: 10.1002/14651858.CD001216.pub2



UK Lung Cancer Screening trial

Funded by the NIHR HTA



Baldwin DR et al Thorax 2011;66:308-313

UKLS – Headline results

- 2.1% lung cancer detection rate
- 86% stage 1 and 2 (67% stage 1)
- 83% resection rate
- 10% benign resection rate
- ICER £8466 (5542 to 12 569)

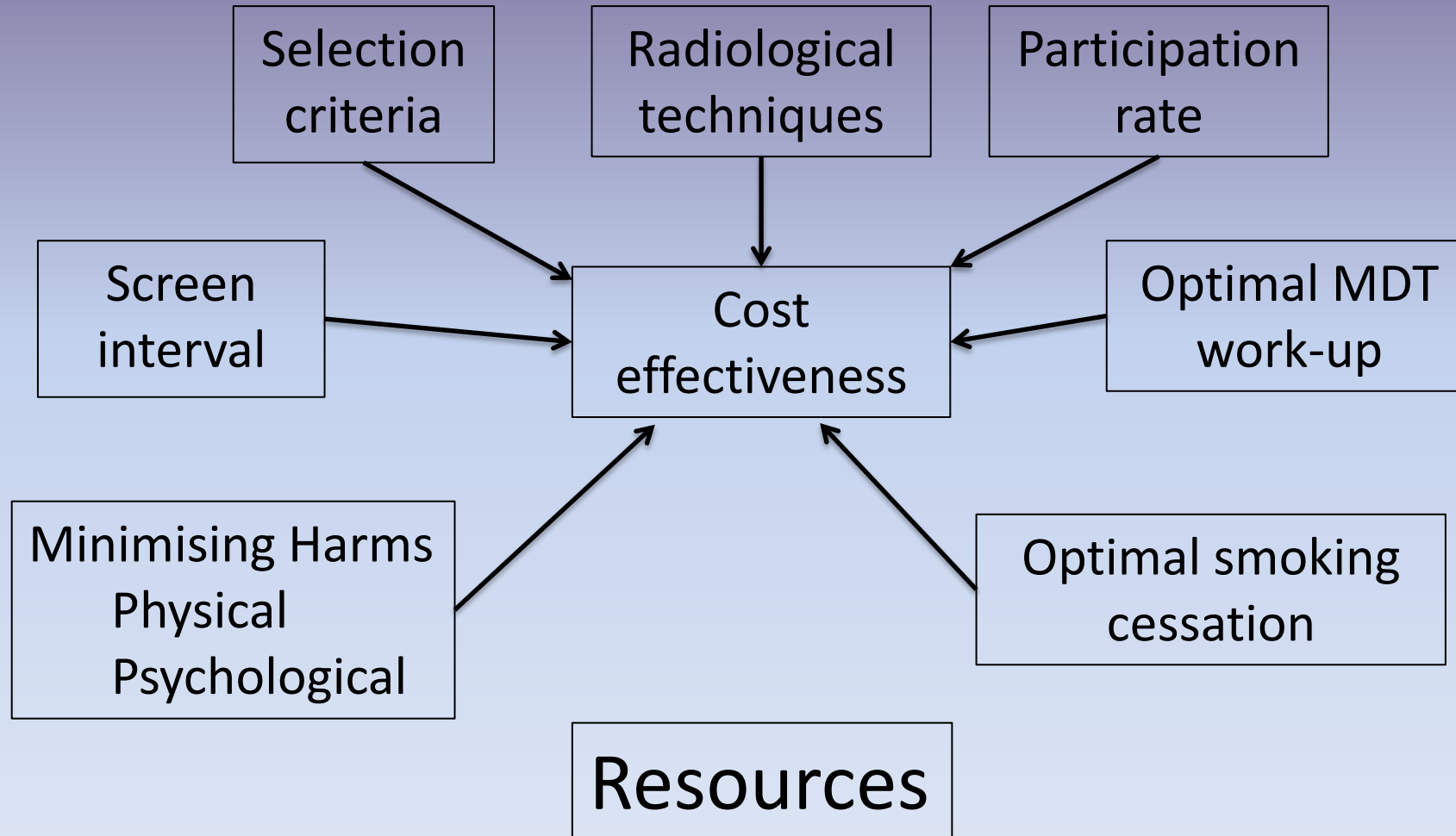
Time to Implement?

CT screening for lung cancer: countdown to implementation

John K Field, David M Hansell, Stephen W Duffy, David R Baldwin

Implementation of lung cancer CT screening is currently the subject of a major policy decision within the USA. Findings of the US National Lung Screening Trial showed a 20% reduction in lung cancer mortality and a 6·7% decrease in all-cause mortality; subsequently, five US professional and clinical organisations and the US Preventive Services Task Force recommended that screening should be implemented. Should national health services in Europe follow suit? The European community awaits mortality and cost-effectiveness data from the NELSON trial in 2015–16 and pooled findings of European trials. In the intervening years, a recommendation is proposed that a demonstration trial is done in the UK. In this Review, we summarise the existing evidence and identify questions that remain to be answered before the implementation of international lung cancer screening programmes.

Issues for implementation



What is happening Nationally?

- Detailed proposal to UK Screening Committee - 2014
- Submission to Science and Technology Committee - 2014
- Publications recommending implementation
- Local pilots (6) as part of Accelerate, Coordinate, Evaluate project
- HTA review started January 2017, due to report July 2017

Be Clear on Cancer National Campaign

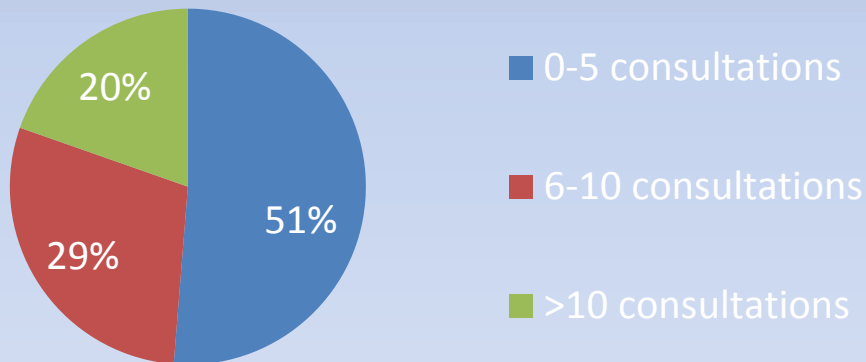
May to July 2012



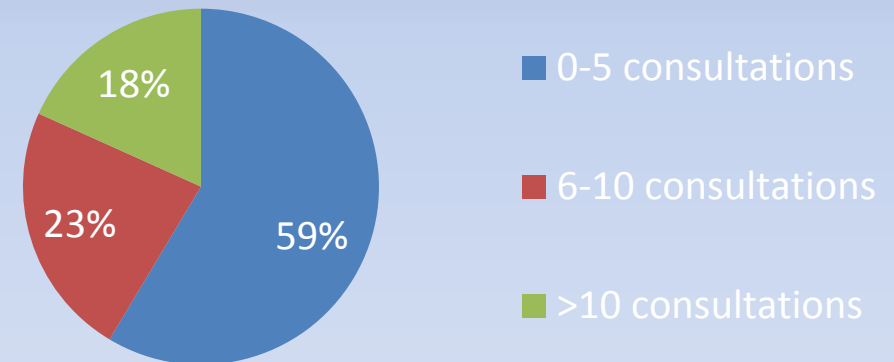
- Estimated 700 additional cancers diagnosed, compared to the same period in the previous year.
- Approximately 400 more people diagnosed at an earlier stage (23.4% to 26.1%)
- Around 300 additional patients had surgery (13.6% to 16%)

Patients who die early and interaction with Primary Care

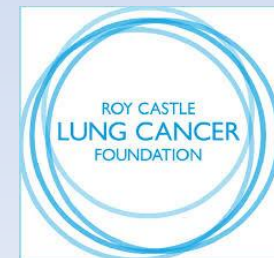
Early death



"Controls"



O'Dowd EL, McKeever TM, Baldwin DR et al. Thorax. 2015 Feb;70(2):161-8.



Lung Cancer symptoms at referral

	No malignant	Percent	No benign	Percent
No patients	650		392	
Cough	266	41	255	65
Dyspnoea	355	55	153	39
Weight loss	308	47	100	26
Haemoptysis	140	22	119	30
Chest pain	256	39	80	20

Lewis NR, Le Jeune I, Baldwin DR. British Journal of Cancer (2005) 93, 905–908.

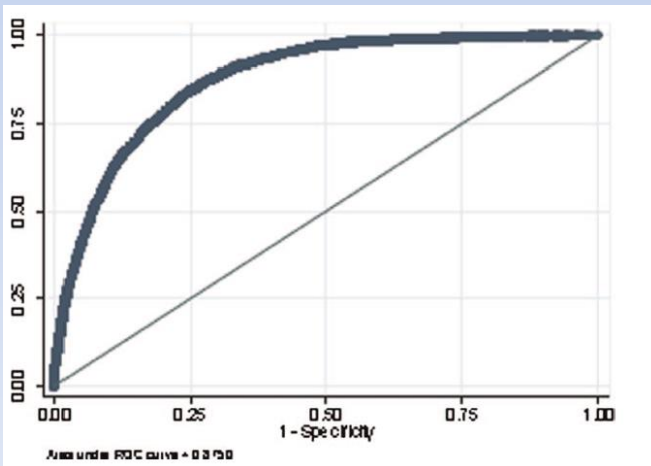
Suspected Cancer: Recognition and Referral (NICE NG12, 2015)

- 1.1.2 Offer an urgent chest X-ray in people aged ≥ 40 if they:
 - have 2 or more of the following unexplained symptoms,
 - have ever smoked and have 1 or more of the following unexplained symptoms:
- cough
- fatigue
- shortness of breath
- chest pain
- weight loss
- appetite loss. [new 2015]

Can we do better?

Quantifying risk

First author	Database	Cases	Dates	Setting
Hamilton 2005	Notes review	247	1998-2002	Exeter practices
Jones 2007	GPRD	(224)	1994-2000	National
Hippisley-Cox 2011	EMIS /Qresearch	3785	2000-2010	National
Iyen-Omofoman 2013	THIN	12074	2000-2009	National

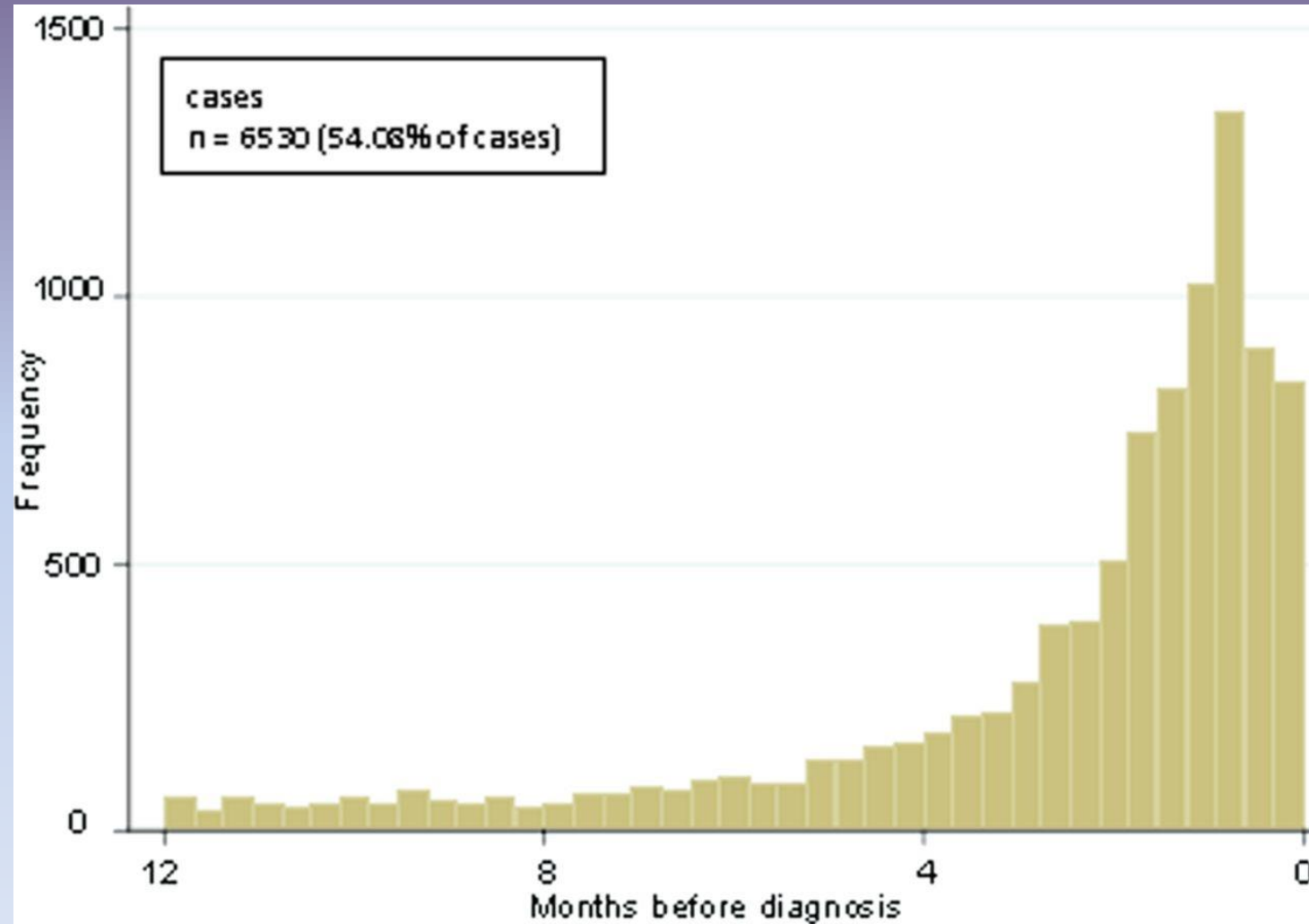


- $AUC = 0.88$
- Using NICE referral criteria need 421 CXR per lung cancer diagnosis
- Using this score: 119 CXRs per diagnosis

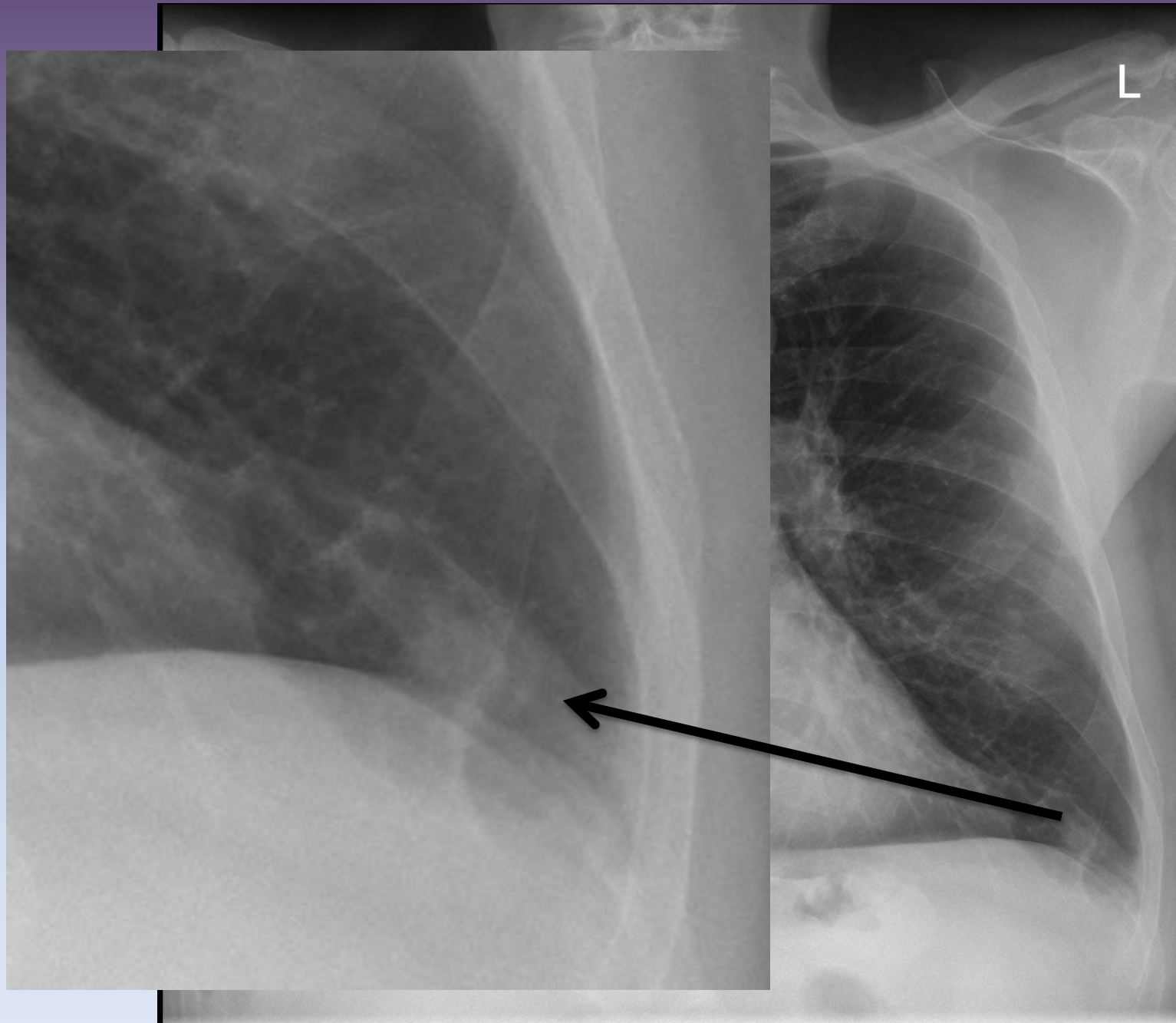
Role of Commissioning

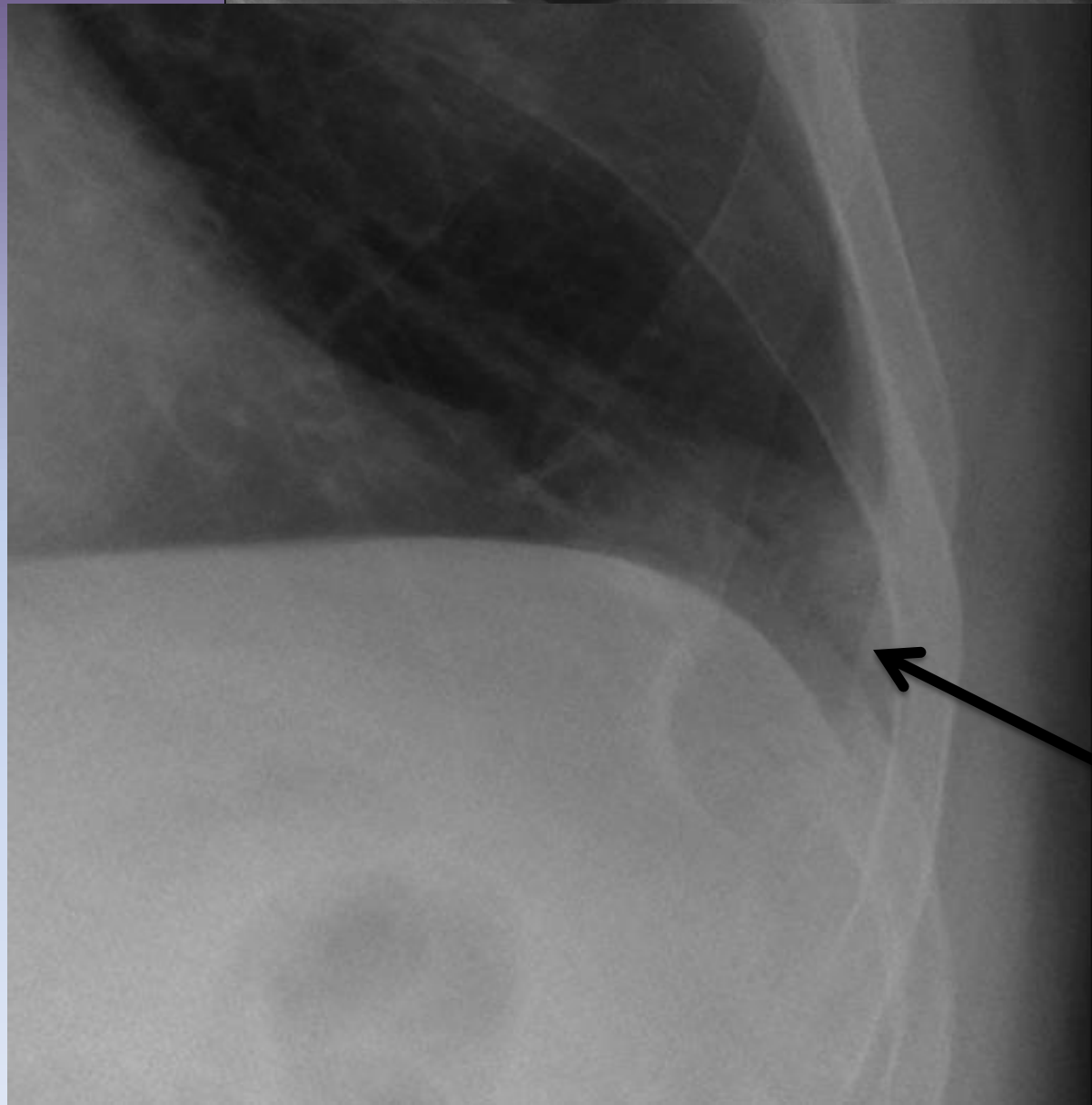
- Lung Cancer CRG (now CEG) has produced Service Guidance
 - Commissioning expertise to balance hub and spoke effect
 - National Optimum Lung Cancer Pathway

Chest x-rays prior to a diagnosis of lung cancer in general practice



8 Dec
2016

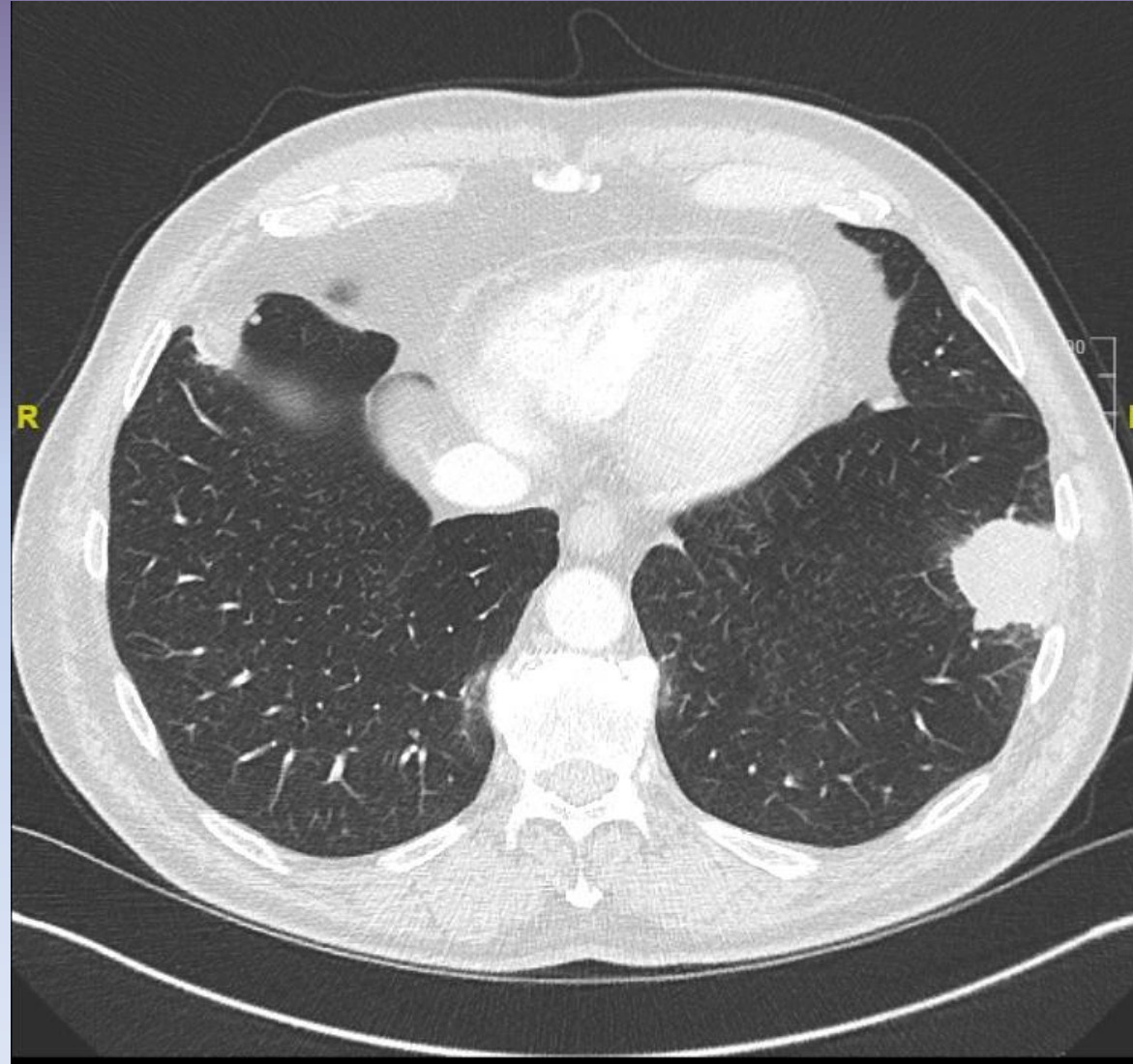




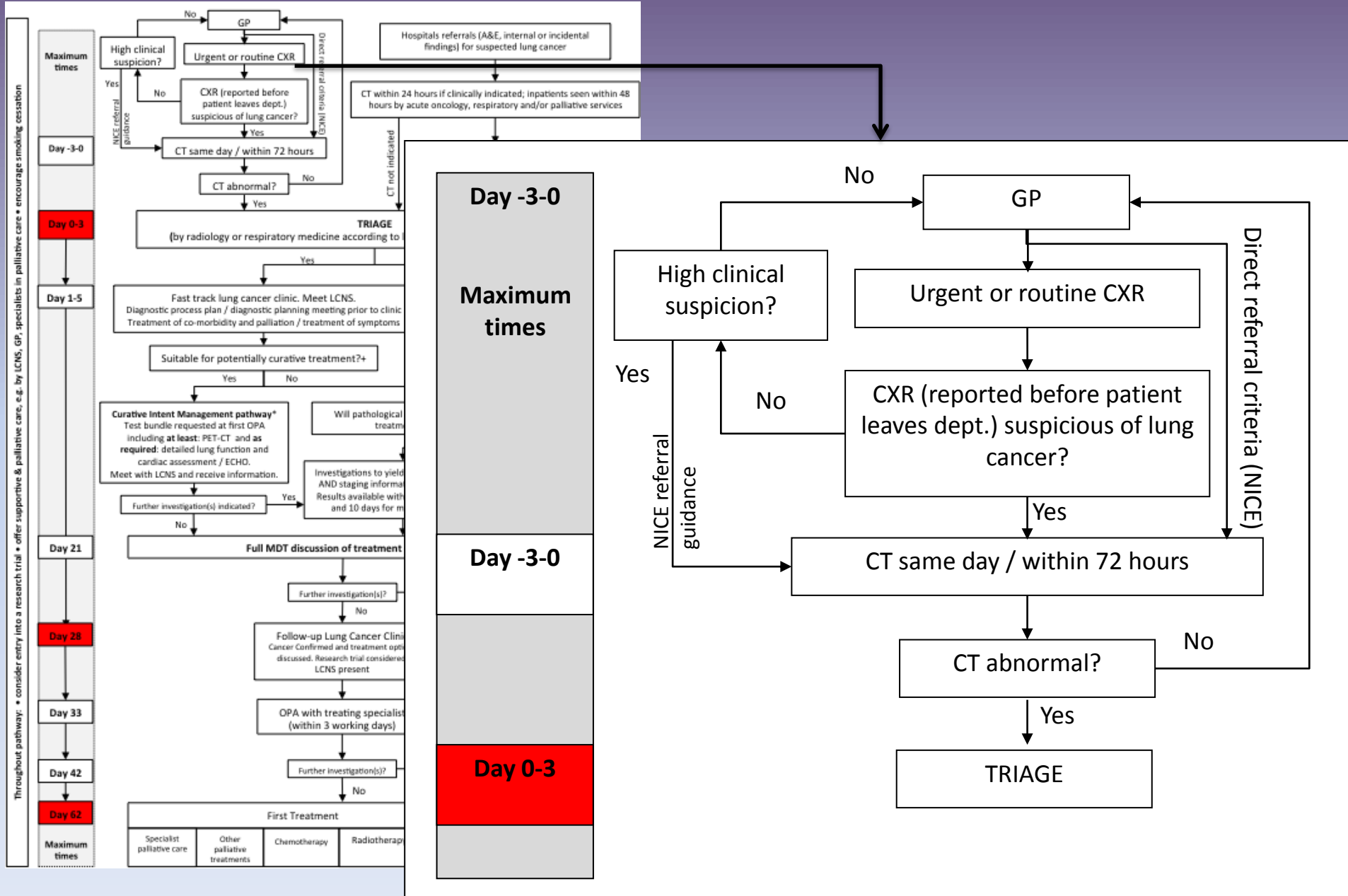
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24 Feb
2016

12 March 2016



National Optimum Lung Cancer Pathway



Lung Cancer Progress and Challenges

- Best curative treatment to the right patient
 - Surgery or SABR or ?
- Best palliative treatment
 - New targeted agents
 - ?Early palliative care
- Reduce variation – commissioning guidance
- Early diagnosis
 - Awareness initiatives – how effective?
 - New pathways
 - Screening in the UK?

Thank you