Lung Cancer 2009-2019
A Decade of Progress

Peter Mazzone

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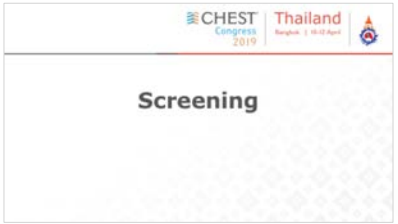
Tobacco and Environment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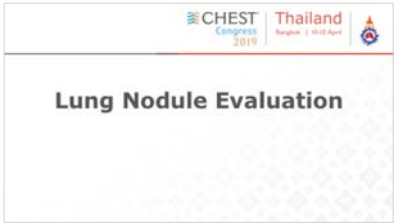
Screening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Lung Nodule Evaluation


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Surgical Advances


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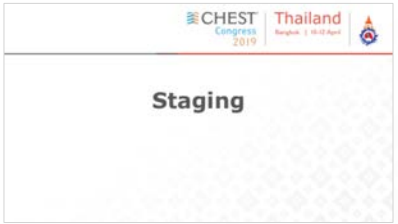
Stereotactic Radiotherapy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Staging


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Molecular Profiling


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Targeted Therapy


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Immune Checkpoint Inhibitors


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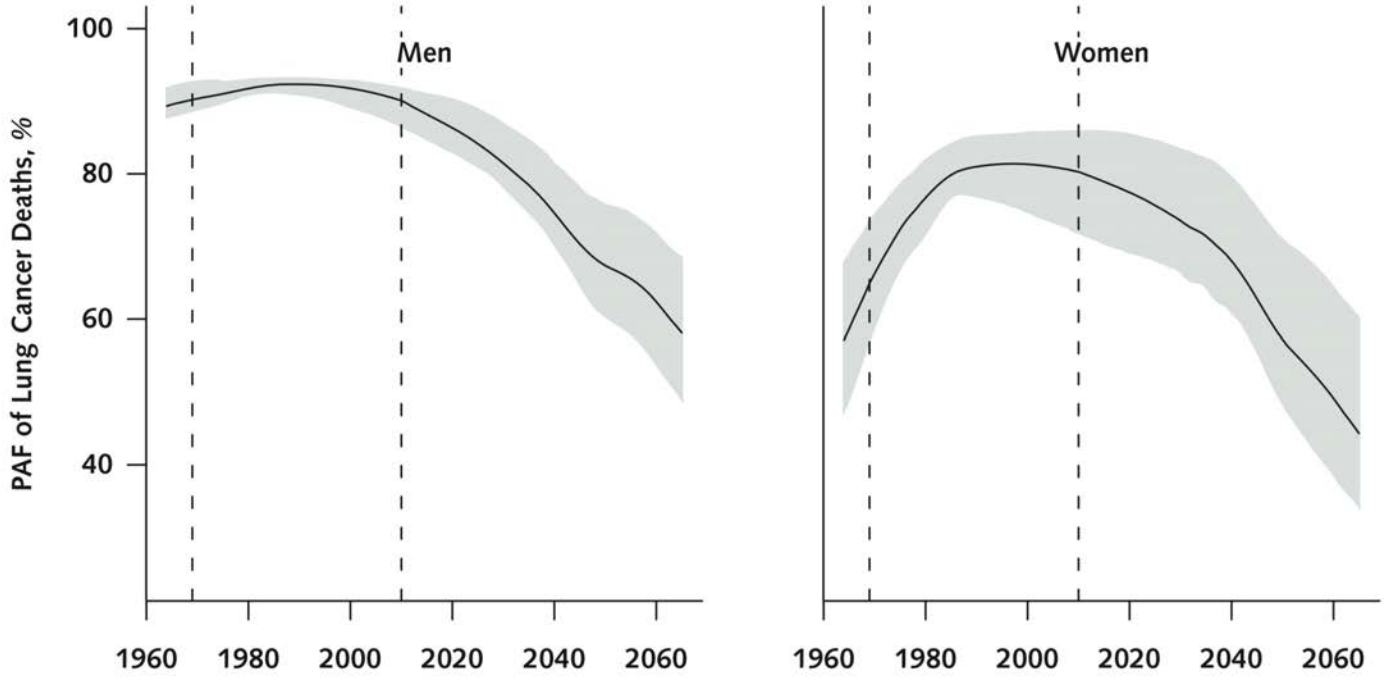
Supportive Care

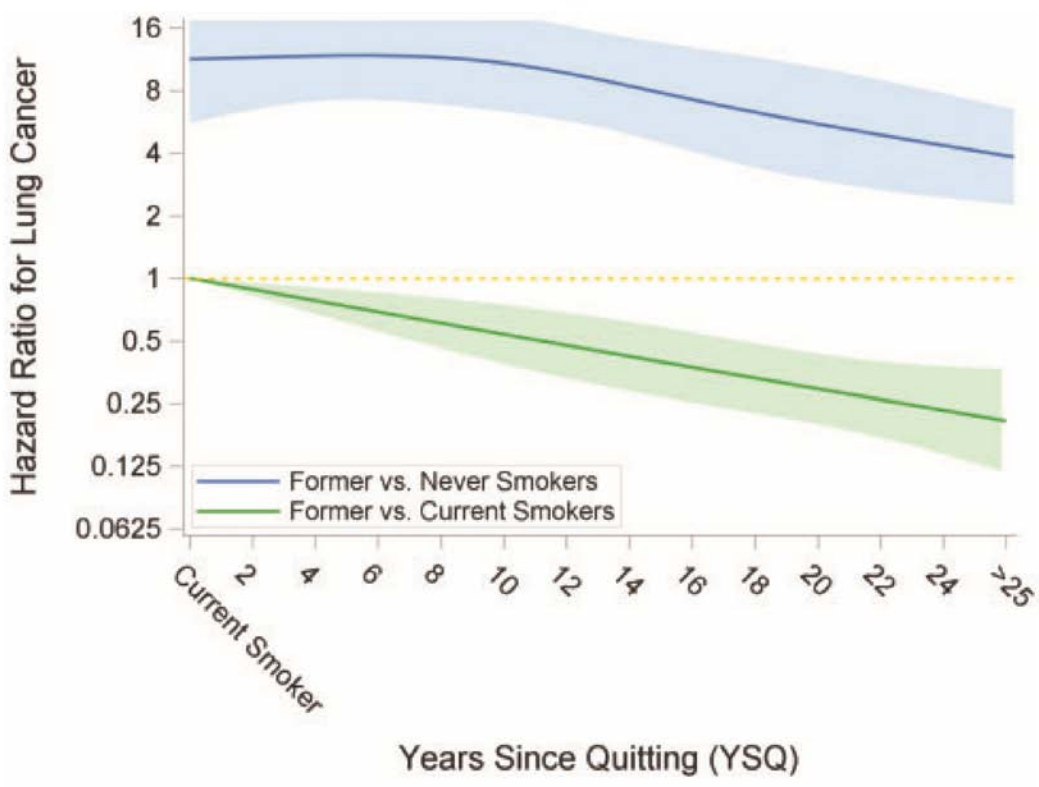
Tobacco and Environment

Lung Cancer Phenotype Changes



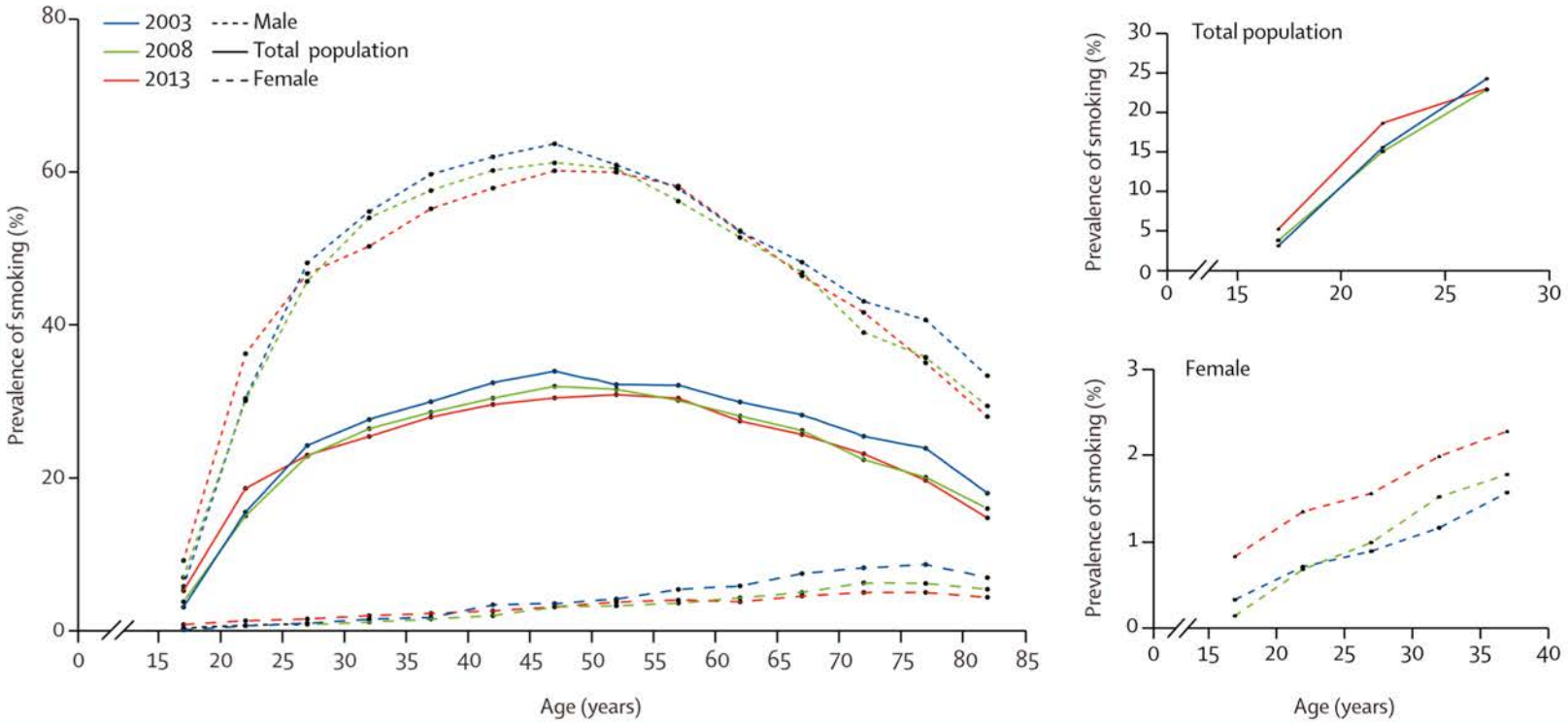
Jeon, Ann Int Med 2018.

Former Smokers Lung Cancer Risk



Tindle, JNCI 2018.

Smoking Rates in China



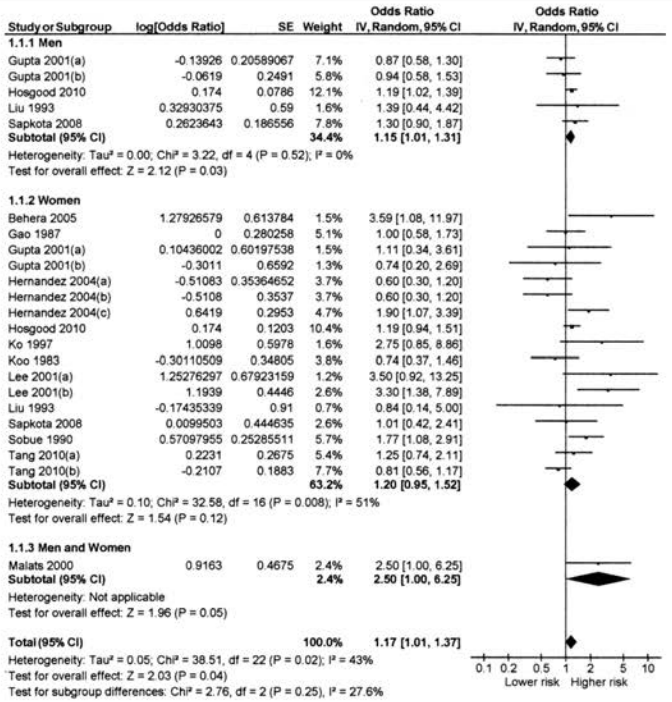
Wang, Lancet Respir Med 2019.

E-Cigarettes vs. Nicotine Replacement Therapy

Abstinence	E-Cigarettes	Nicotine Replacement	Adjusted RR
At 52 weeks	18.0	9.9	1.75
At 4 weeks	43.8	30.0	1.43
At 26 weeks	35.4	25.1	1.36
26-52 weeks	21.2	11.9	1.82

Hajek, N Engl J Med 2019.

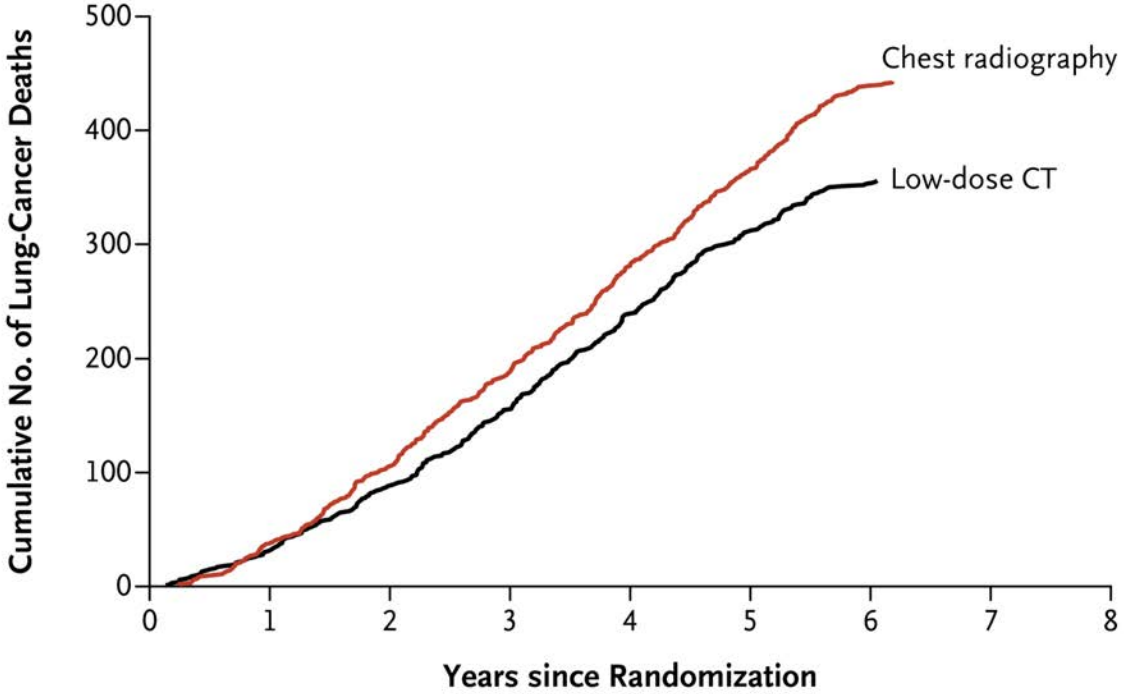
Biomass Fuels and Lung Cancer Risk



Bruce, Thorax 2015.

Screening

NLST Results



NLST Team. N Engl J Med 2011.

Cost-Effectiveness

Characteristic	Cost per QALY ($)
Overall	81,000
Male	147,000
Female	46,000
Former smoker	615,000
Current smoker	43,000

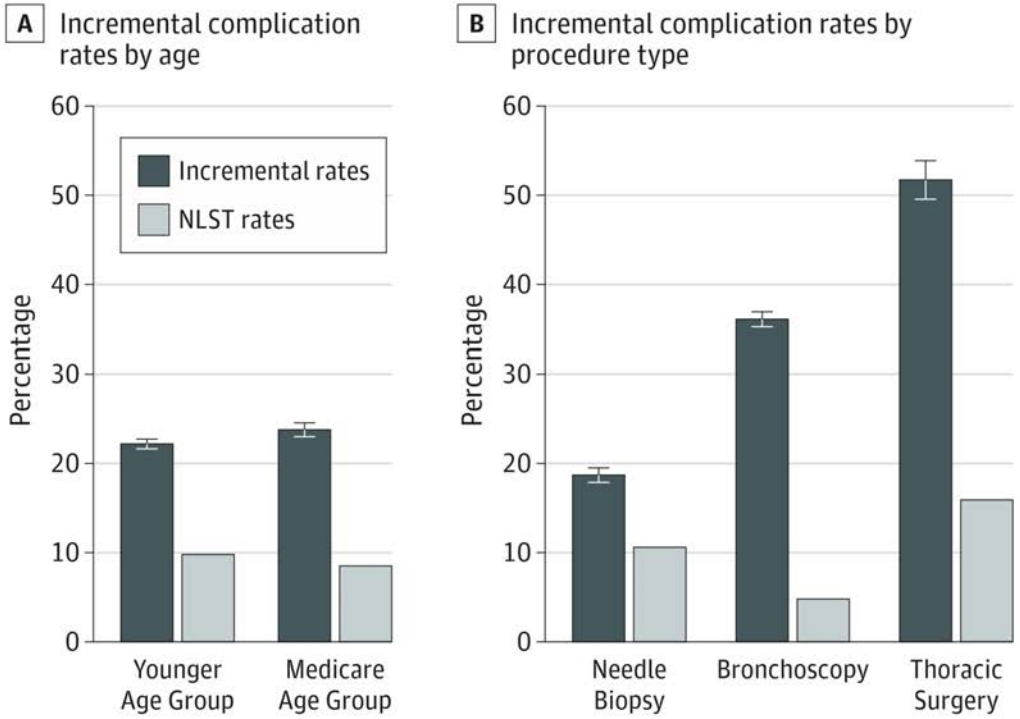
Black, N Engl J Med 2014.

VA Implementation Study

	%
Eligible and screened	49.6
Nodules (all)	59.7
Nodules > 8 mm	12.7
Suspicious – not cancer	2.0
Confirmed cancer	1.5
Incidental findings	40.7

Kinsinger, JAMA Int Med 2017.

Procedure Complication Rates



Huo, JAMA Int Med 2019.

Risk Calculation

PLCOm2012 Risk	USPSTF Negative	USPSTF Positive	Total
Negative	20,712 101	3,695 33	24,407 135
Positive	2,445 93	10,475 449	**12,920** **542**
Total	23,157 195	**14,170** **482**	37,327 677

Tammemagi, N Engl J Med 2013, PLoS One 2014.

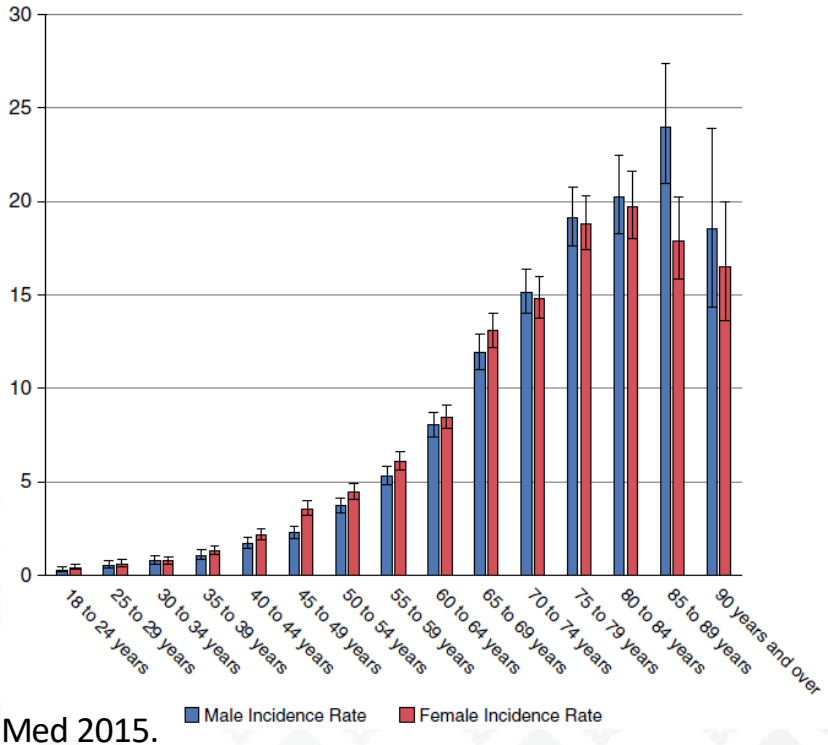
NELSON Final Round

	Round 2 (%)	Round 4 (%)
Stage I	75.8	60.8
Stage 4	3.4	13.0
Adenocarcinoma	60.3	50.0
Squamous cell	5.2	21.7
Interval cancers	5	28

Yousaf-Khan, Thorax 2017.

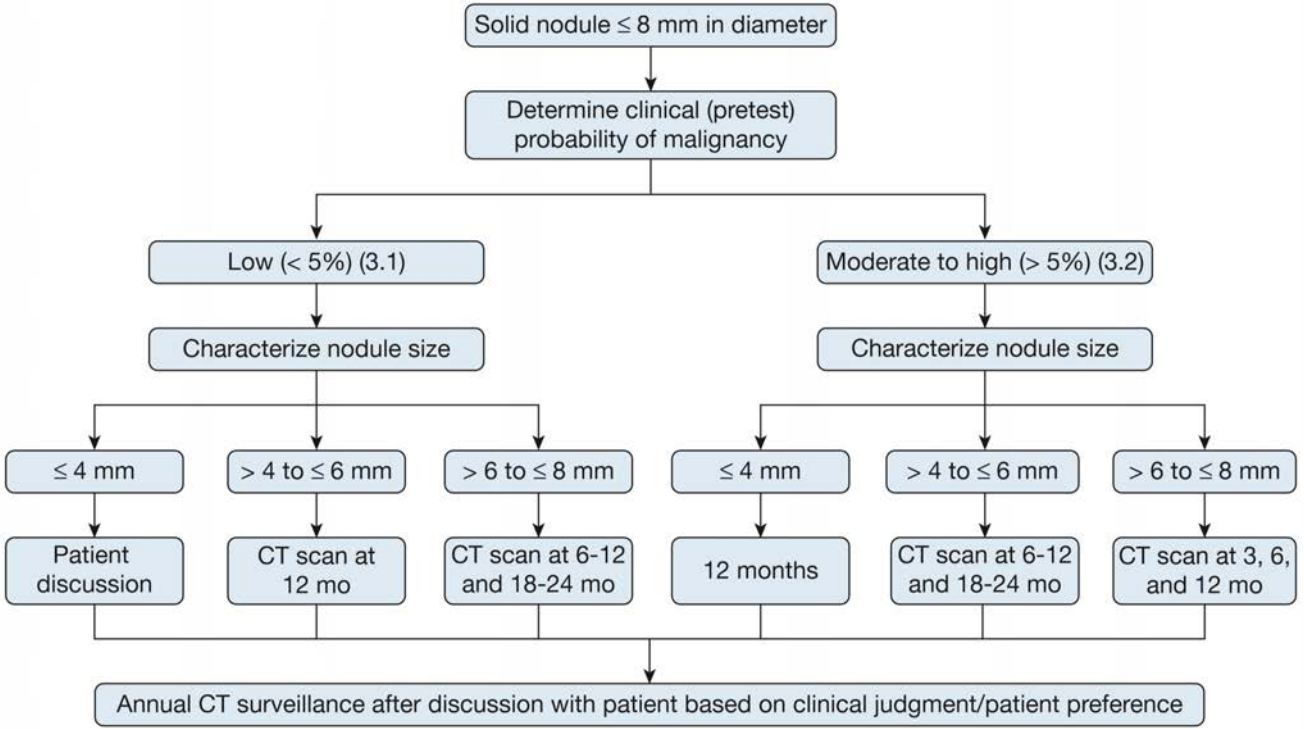
Lung Nodule Evaluation

Lung Nodule Incidence



Gould, Am J Resp Crit Care Med 2015.

Nodule Management Guidelines



Bai, Chest 2016.

Ultrathin Bronchoscope Yield

	Ultrathin (%)	Thin with GS (%)
Malignant		
≤ 20 mm	76	61
> 20 – 30 mm	87	79
All		
≤ 20 mm	65	49
> 20 – 30 mm	84	71

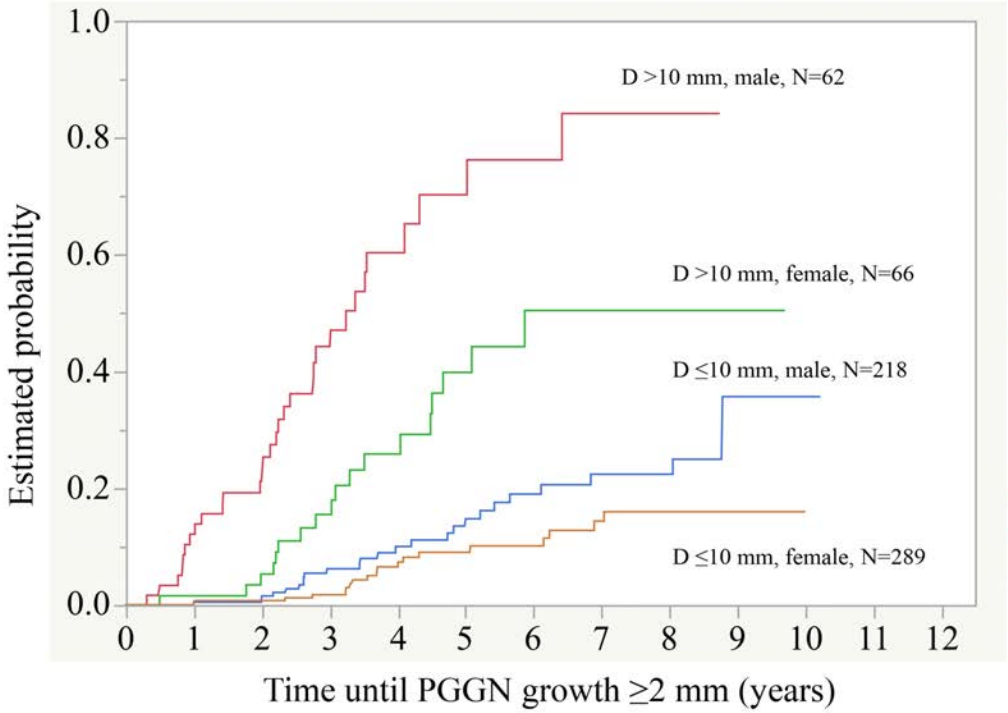
Oki, Am J Respir Crit Care Med 2015.

Bronchoscopy Yield

	Standard Bronch (%)	Thin Bronch – EBUS (%)
Malignant	45.8 - 49.1	60.0 - 64.3
Benign	29.4 - 37.1	28.6 - 38.5

Tanner, Chest 2018.

Sub-Solid Lung Nodules



Kakinuma, J Thorac Oncol 2016.

Surgical Advances

Open Thoractomy vs. VATS

	Open (%)	VATS (%)
Respiratory complications	32	27
Extended length of stay	16	8
Mortality	4	2

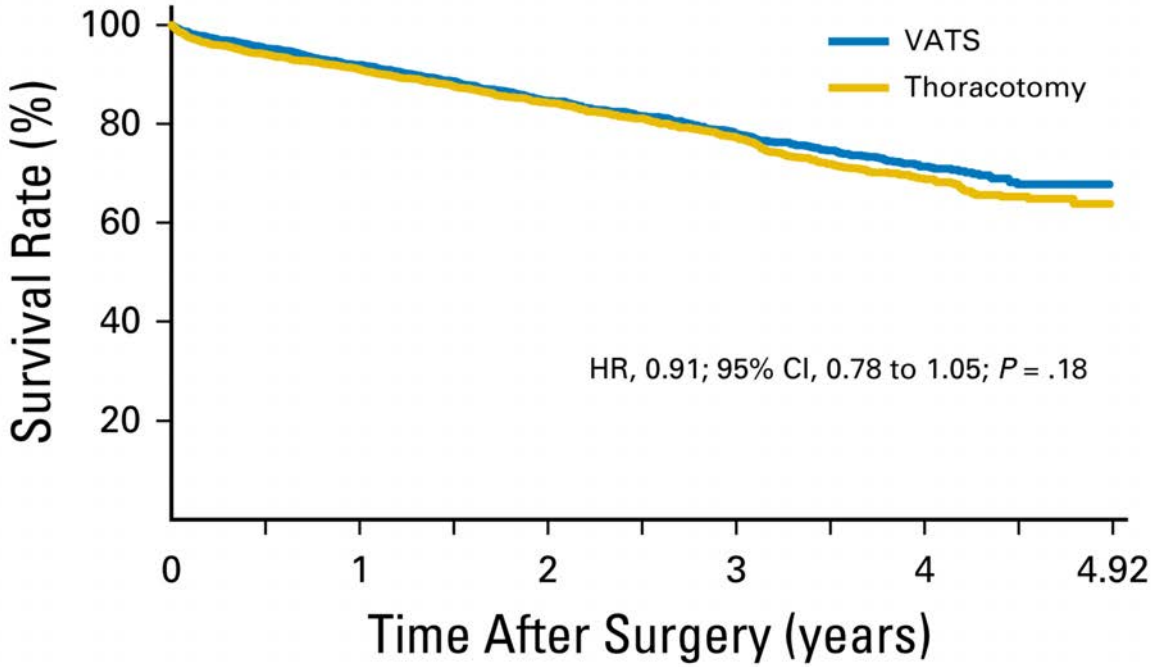
Ezer, Ann Am Thorac Soc 2018.

VATS in the Elderly

	VATS	Thoracotomy
Length of stay (days)	5	6
ICU admission (%)	2.5	14.8
Discharge to rehab (%)	5.0	22.5
30 day readmission (%)	0	8.6

Port, Ann Thorac Surg 2011.

VATS vs. Thoracotomy Survival



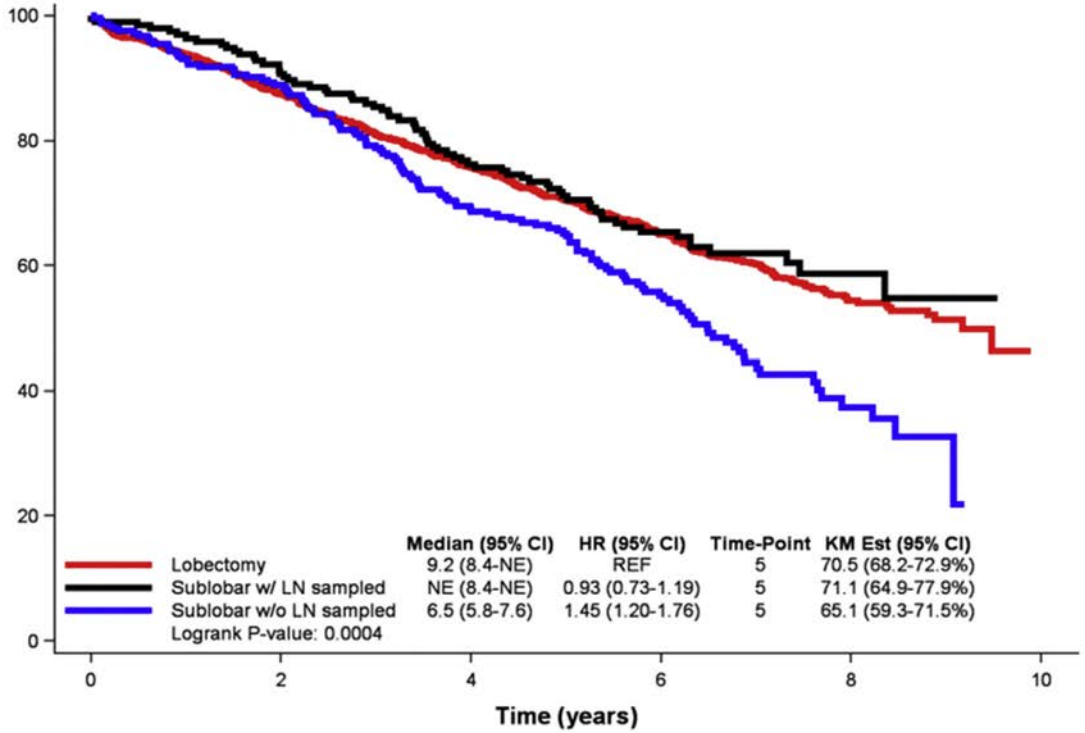
Boffa, J Clin Oncol 2018.

Robot Assisted Thoracoscopic Surgery

	Inexperienced	Experienced
30 day mortality (%)	2.0	1.1
LN examined (#)	8	10
Length of stay (days)	5	4
Conversion (%)	11.8	7.4

Arnold, J Am Coll Surg 2018.

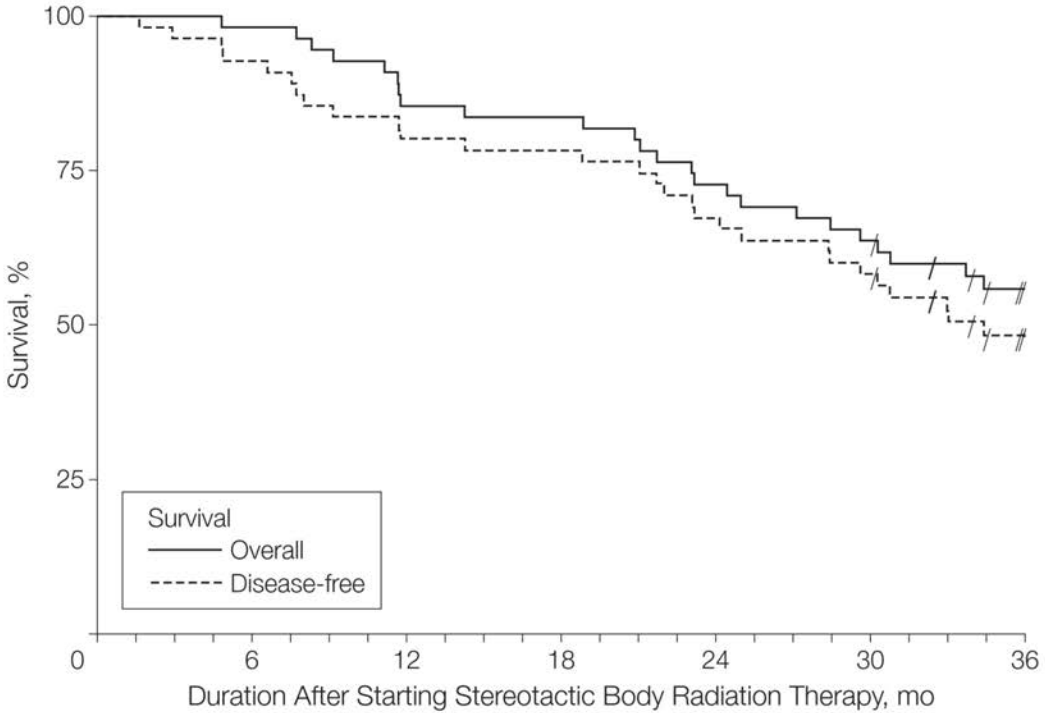
Sublobar Resection in LPA



Cox, J Thorac Oncol 2017.

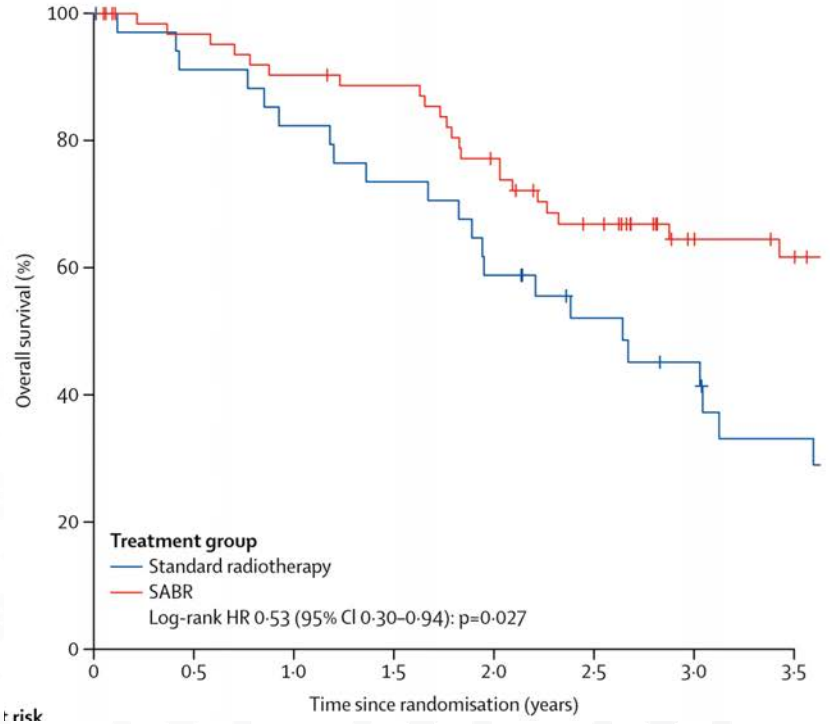
Stereotactic Radiotherapy

SBRT in Inoperable Stage I NSLCLC



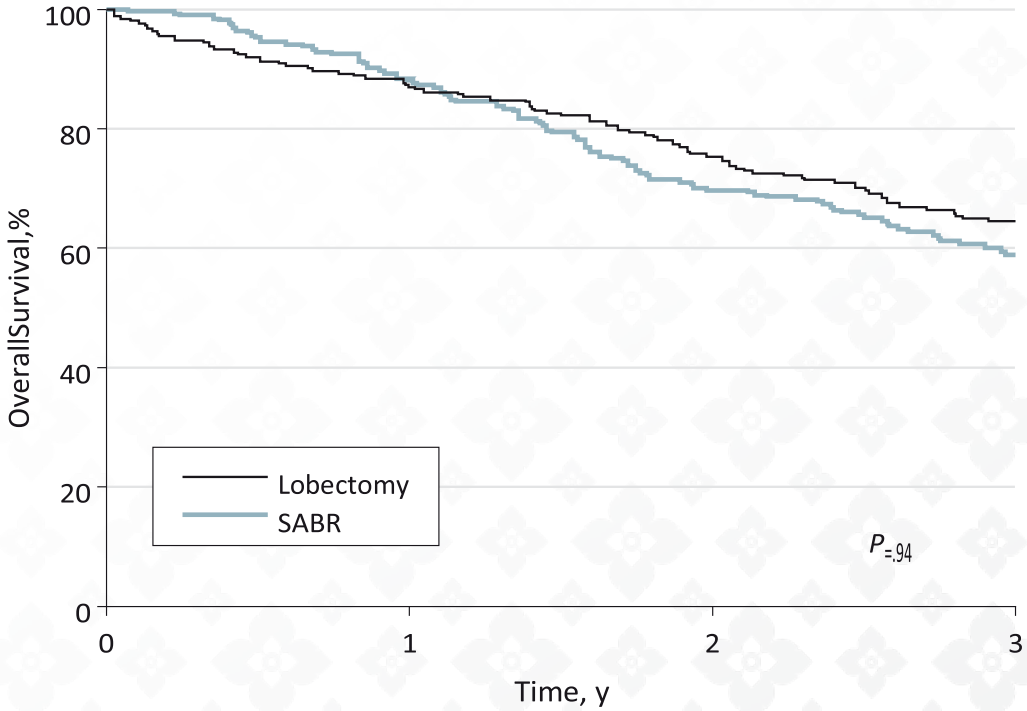
Timmerman, JAMA 2010.

SBRT vs. Conventional Radiotherapy



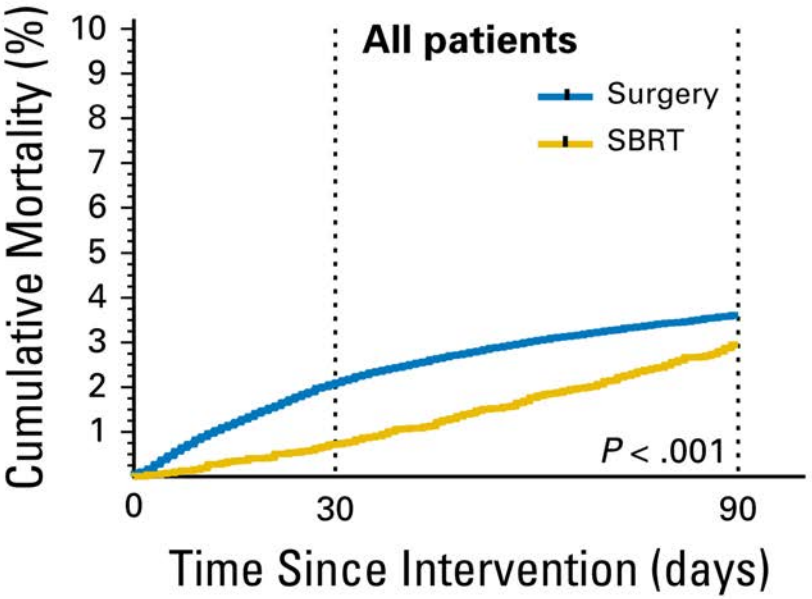
Ball, Lancet Oncol 2019.

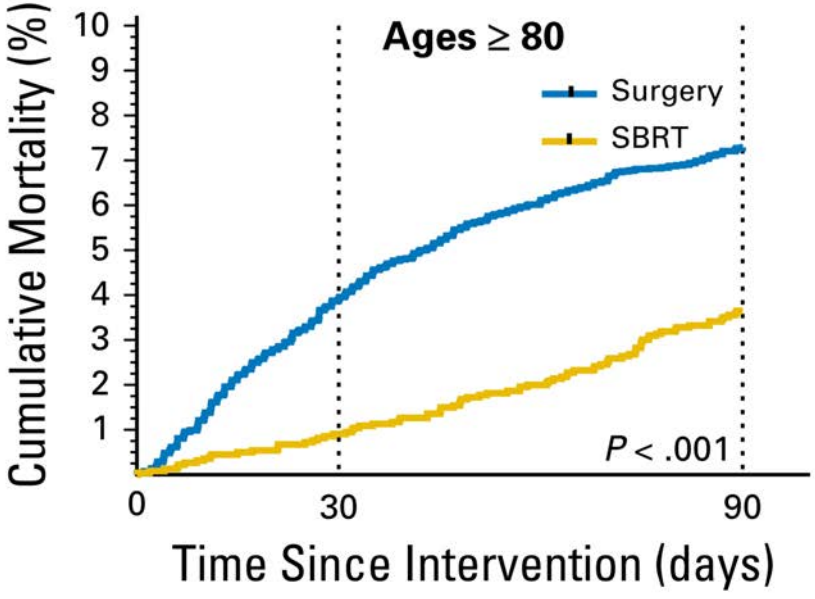
Lobe vs. SBRT - Propensity Matched



Shirvani, JAMA Surg 2014.

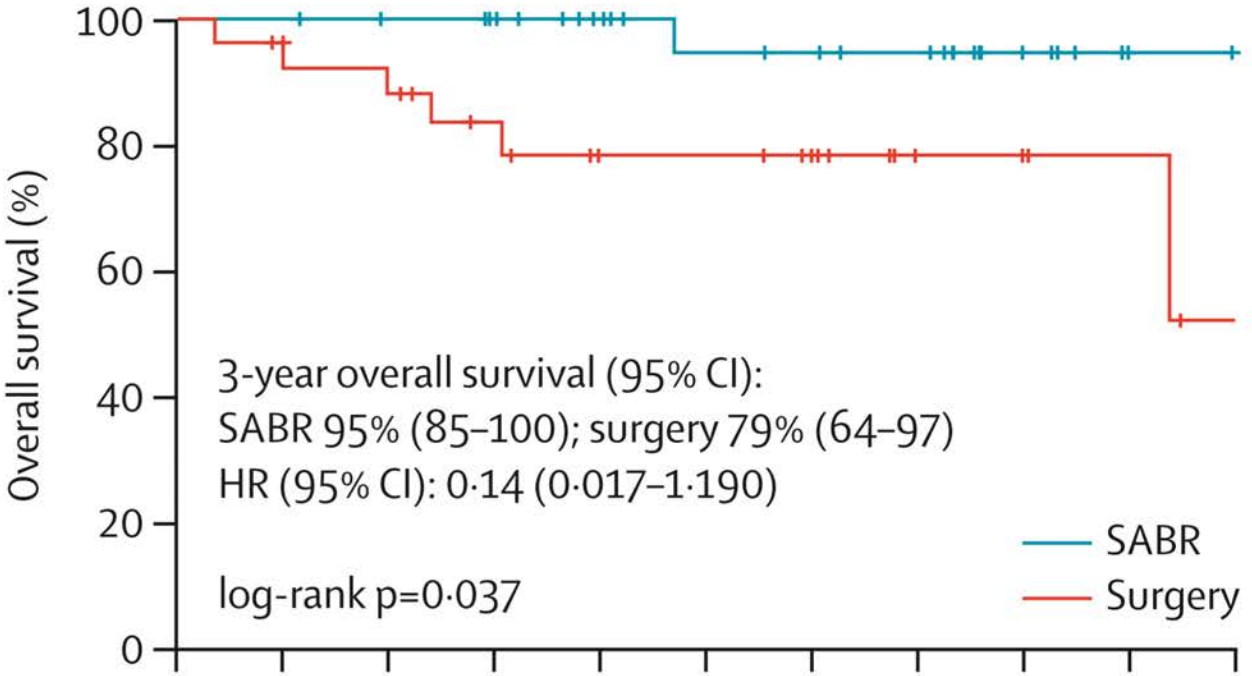
Early Mortality





Stokes, J Clin Oncol 2018.

SBRT vs. Surgery



Chang, Lancet Oncol 2015.

Staging

8th Edition Stage Classification

- The T category is broken down by size in 1 cm increments until 5 cm
- Tumors > 5-7 cm are considered T3 and those > 7 cm T4.
- Tumors involving the main bronchus or causing atelectasis are considered T2a, while those that invade the diaphragm are labeled T4.
- The M component now takes into account whether there is a solitary extra-thoracic metastasis or multiple metastases.
- Stages IA, III, and IV have subdivisions that were not previously present.

Goldstraw, J Thorac Oncol 2016.

8th Edition Stage Classification

	Second Primary Lung Cancer	Multifocal GG/L Nodules	Pneumonic-Type Adenocarcinoma	Separate Tumor Nodule
Imaging features	Two or more distinct masses with imaging characteristic of lung cancer (e.g., spiculated)	Multiple ground glass or part-solid nodules	Patchy areas of ground glass and consolidation	Typical lung cancer (e.g., solid, spiculated) with separate solid nodule
Pathologic features	Different histotype or different morphologic features by comprehensive histologic assessment	Adenocarcinomas with prominent lepidic component (typically varying degrees of AIS, MIA, LPA)	Same histologic features throughout (most often invasive mucinous adenocarcinoma)	Distinct masses with the same morphologic features by comprehensive histologic assessment
TNM classification	Separate cTNM and pTNM for each cancer	T based on highest T lesion with (#/m) indicating multiplicity; single N and M	T based on size or T3 if in single lobe, T4 or M1a if in different ipsilateral or contralateral lobes; single N and M	Location of separate nodule relative to primary site determines if T3, T4, or M1a; single N and M
Conceptual view	Unrelated tumors	Separate tumors, albeit with similarities	Single tumor, diffuse pulmonary involvement	Single tumor, with intrapulmonary metastasis

Detterbeck, J Thorac Oncol 2016.

PET-CT Staging

Futile Thoracotomy	PET-CT	Conventional
No (%)	65	48
Yes (%)	35	52

Fischer, N Engl J Med 2009.

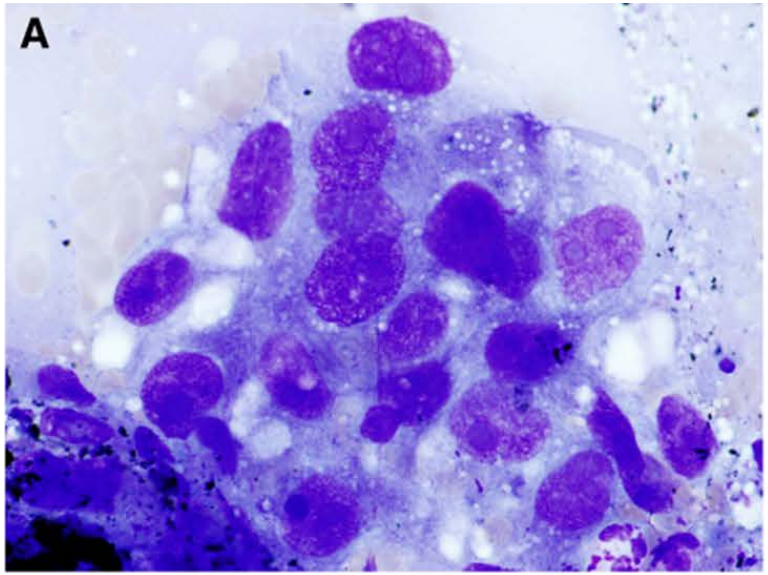
EBUS vs. Mediastinoscopy

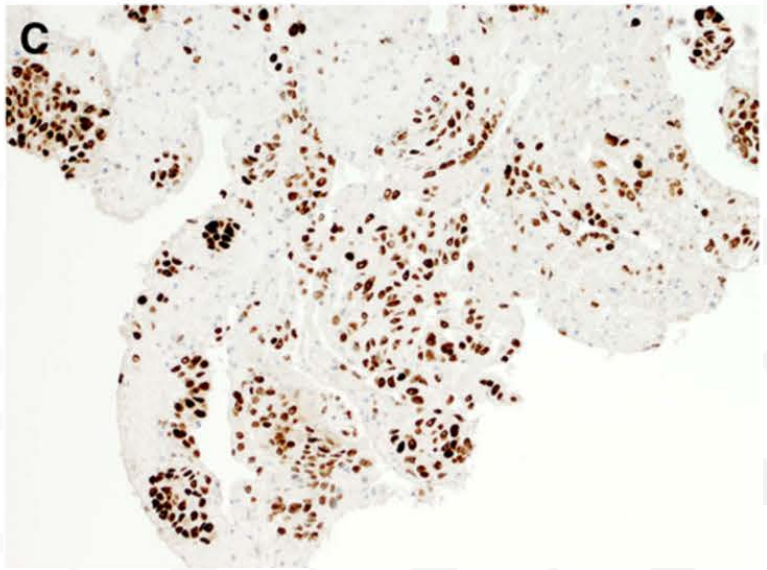
N2/N3	Surgical	Endosonography
Sensitivity	79%	94%
NPV	86%	93%

	Surgical	Endosonography
Avoidable Thoracotomies	21	9
Complications	7	6

Annema, JAMA 2010.

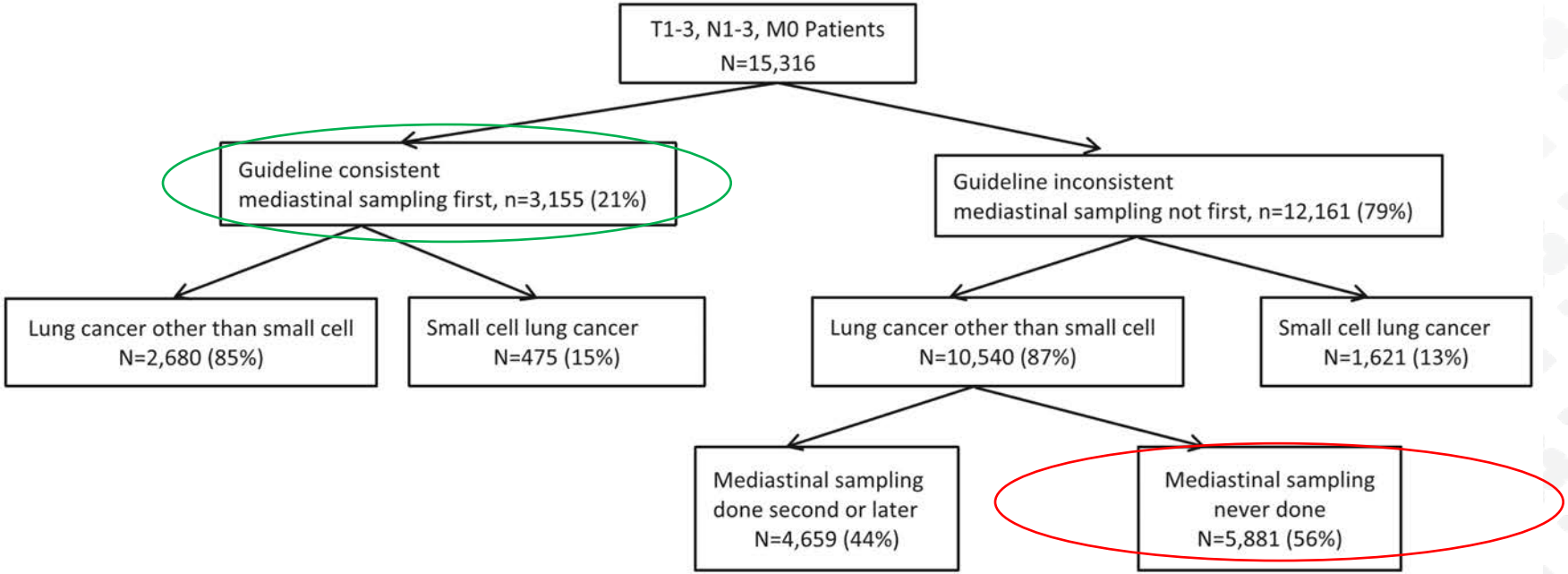
EBUS and Tumor Characterization





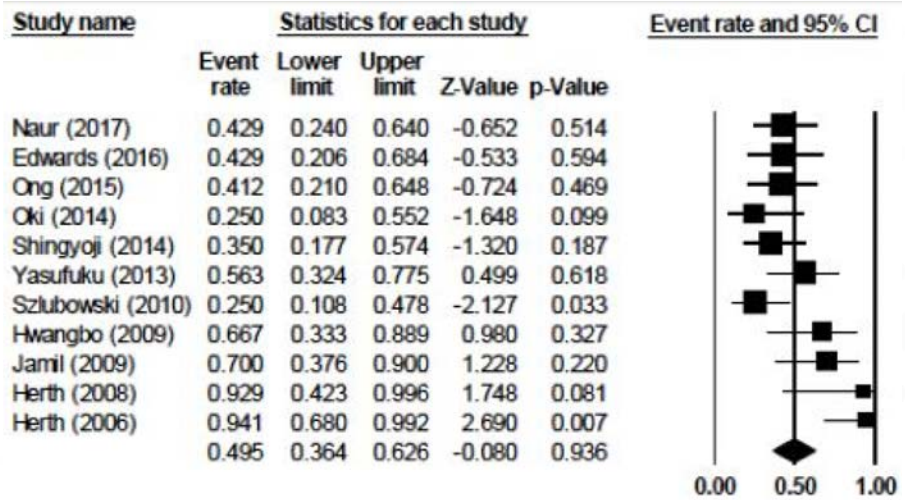
Navani, Am J Respir Crit Care Med 2012.

Staging Guideline Consistent Care



Ost, Chest 2014.

EBUS - Normal Mediastinum
EBUS – PD-L1



	PD-L1 ≥ 1%	PD-L1 ≥ 50%
Sensitivity	70	40
Specificity	100	97
PPV	100	80
NPV	79	84
Concordance	86	83

El-Osta Ann Am Thorac Soc 2018. Sakata, Chest 2018.

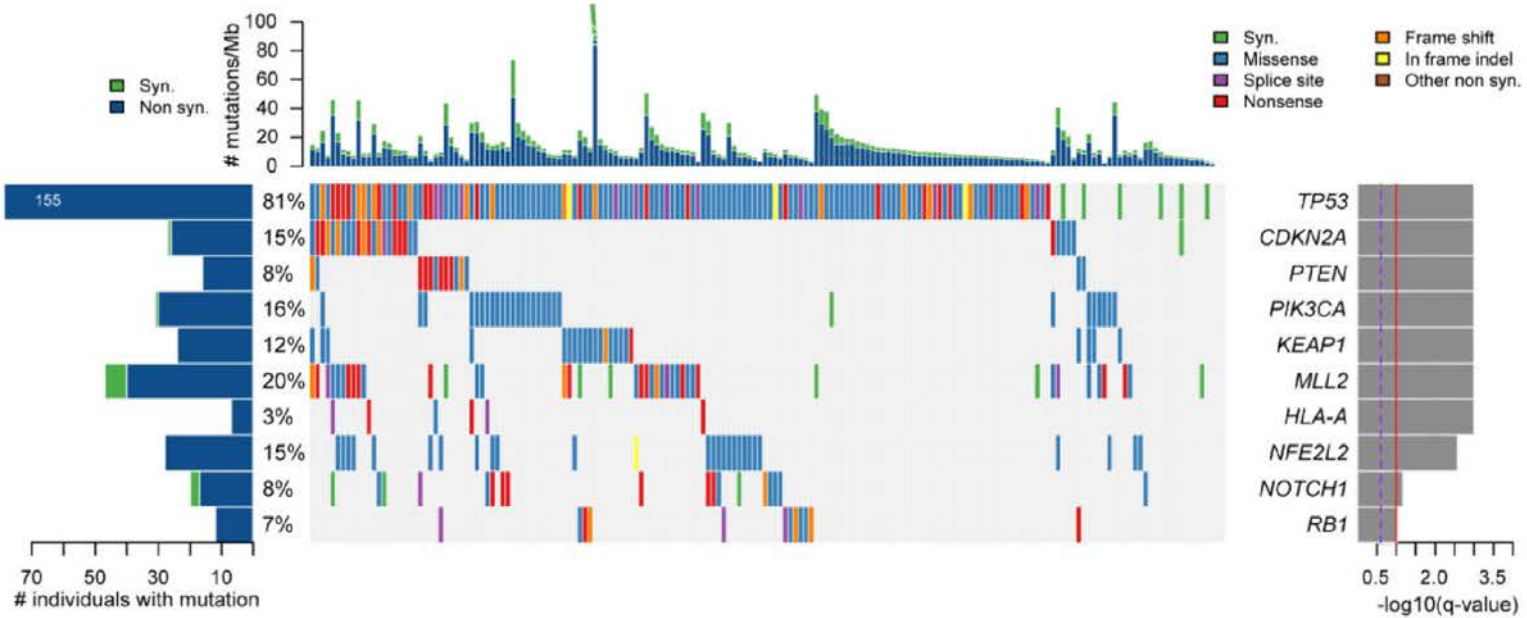
Molecular Profiling

WHO Classification

1. Use of immunohistochemistry throughout the classification.
2. New emphasis on genetic studies.
3. New classification for small biopsies and cytology.
4. Different approach to lung adenocarcinomas.
5. Restricting the diagnosis of large cell carcinoma.
6. Reclassifying squamous cell carcinomas.
7. Grouping neuroendocrine tumors in one category.

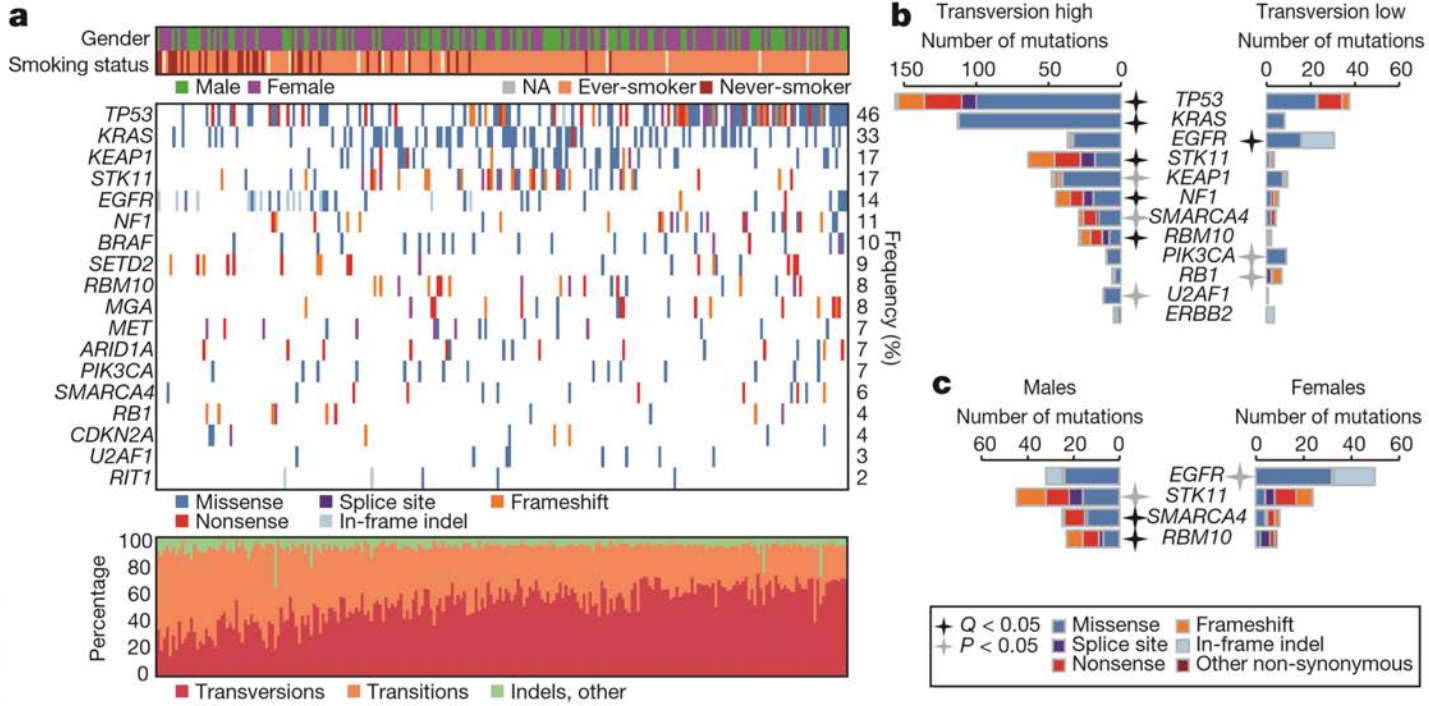
Travis, J Thorac Oncol 2015.

Squamous Cell Genomic Characterization



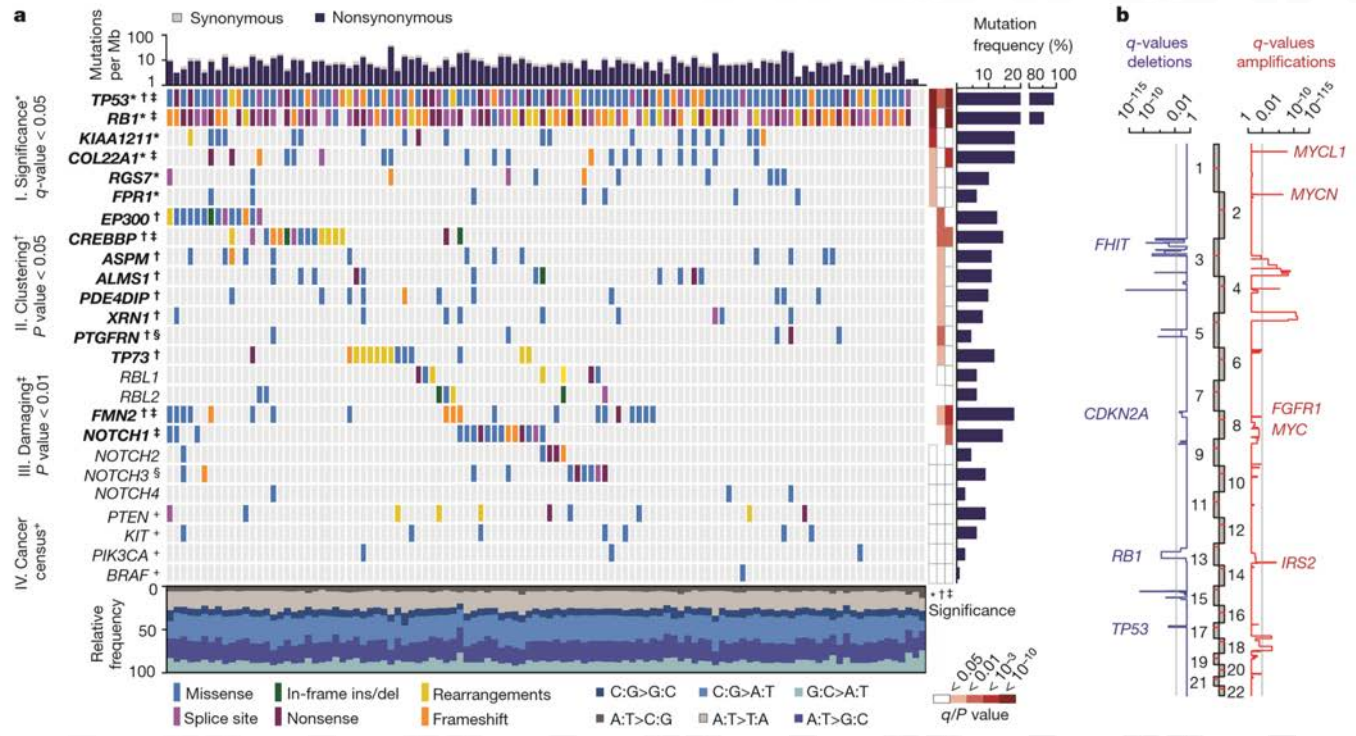
Cancer Genome Atlas Research Network, Nature 2012.

Adenocarcinoma Molecular Profiling



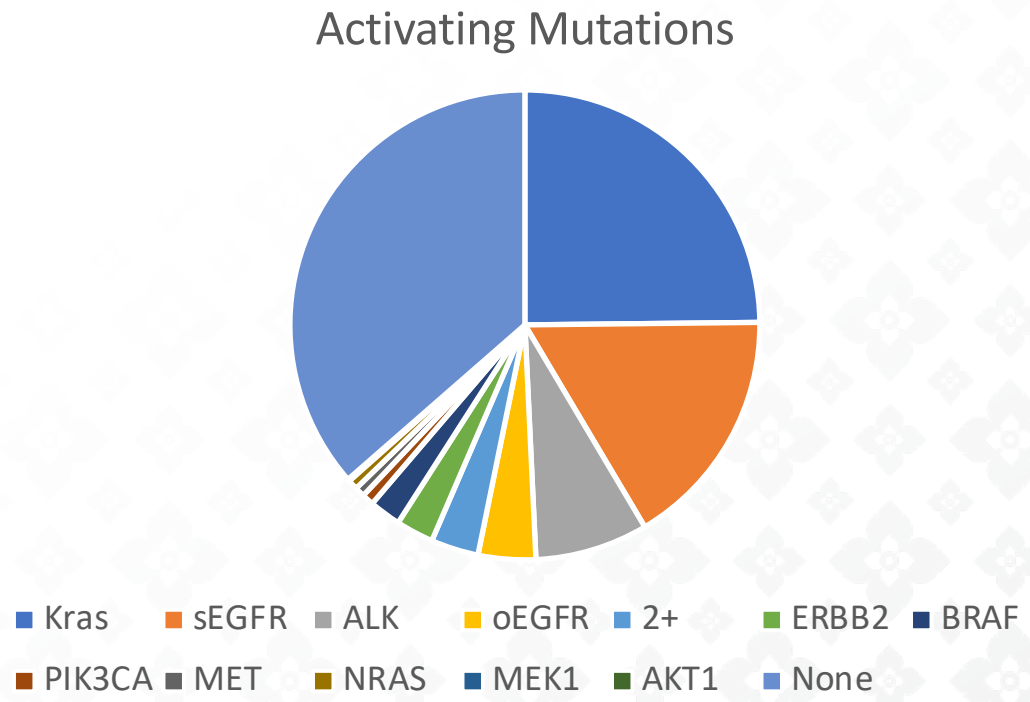
Cancer Genome Atlas Research Network, Nature 2014.

Small Cell Genomic Characterization



George, Nature 2015.

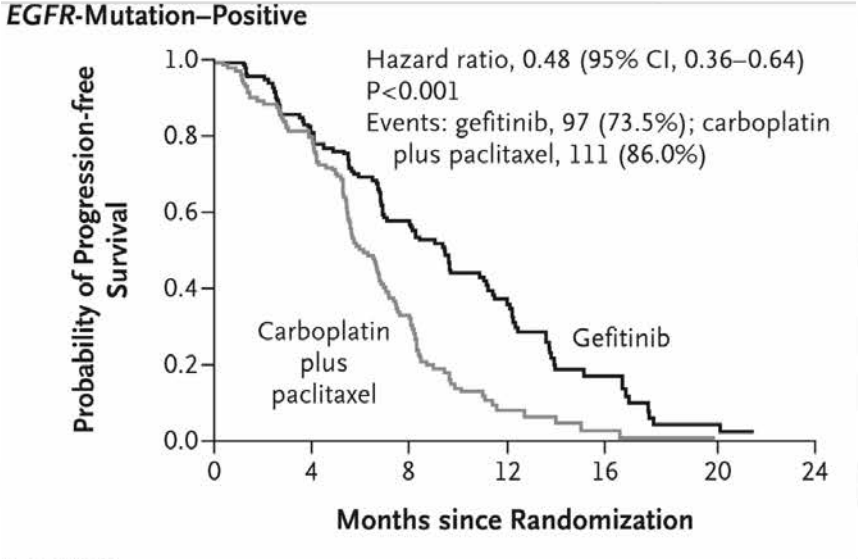
Multiplexed Profiling

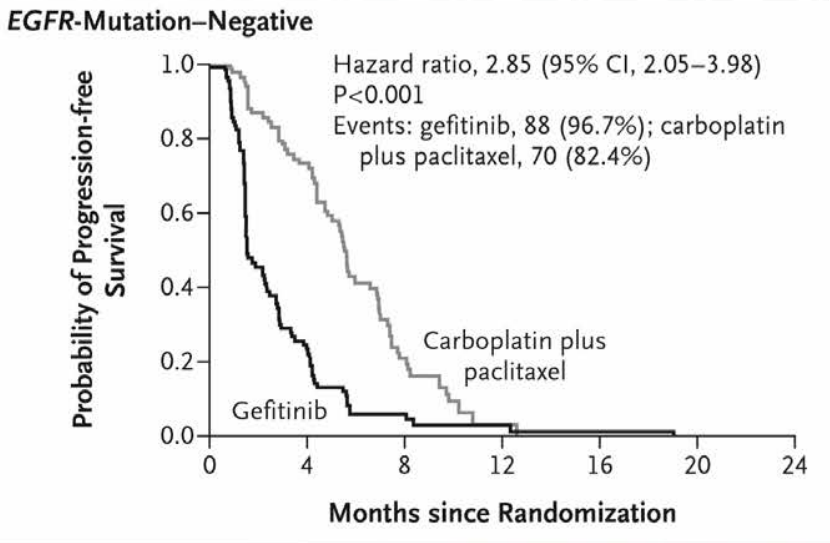


Kris, JAMA 2014.

Targeted Therapy

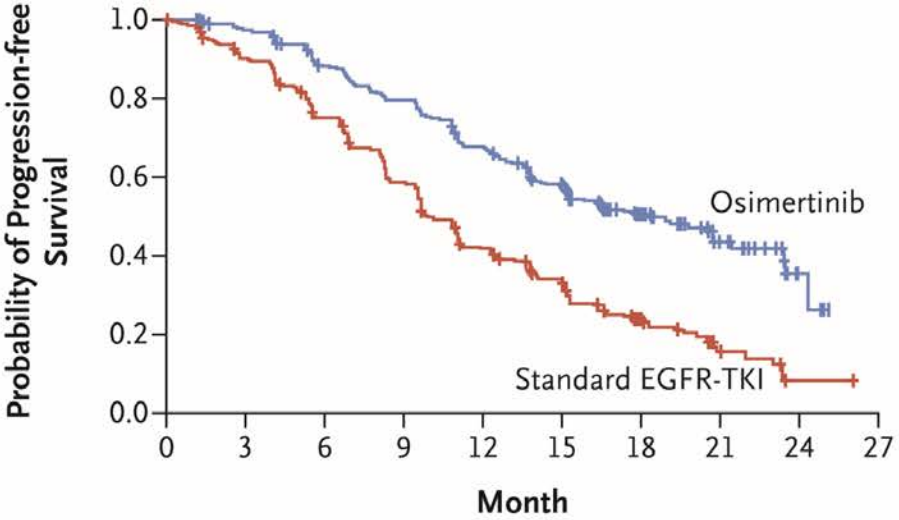
EGFR Mutations

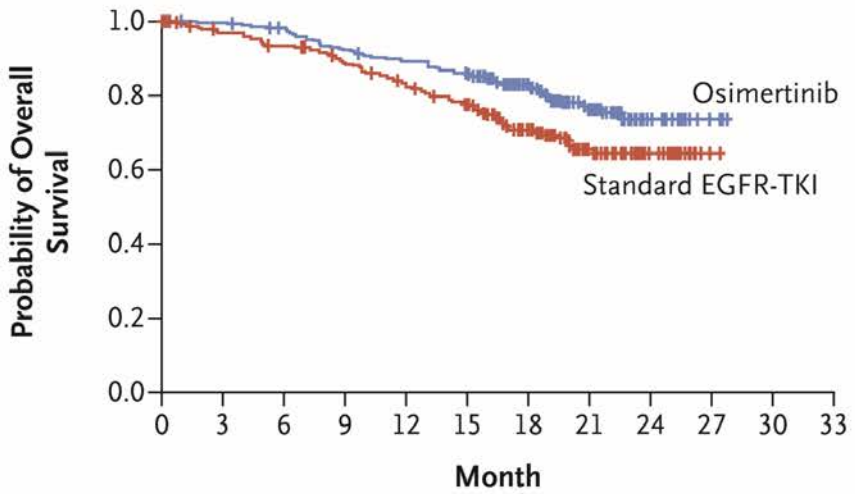




Mok, N Engl J Med 2009.

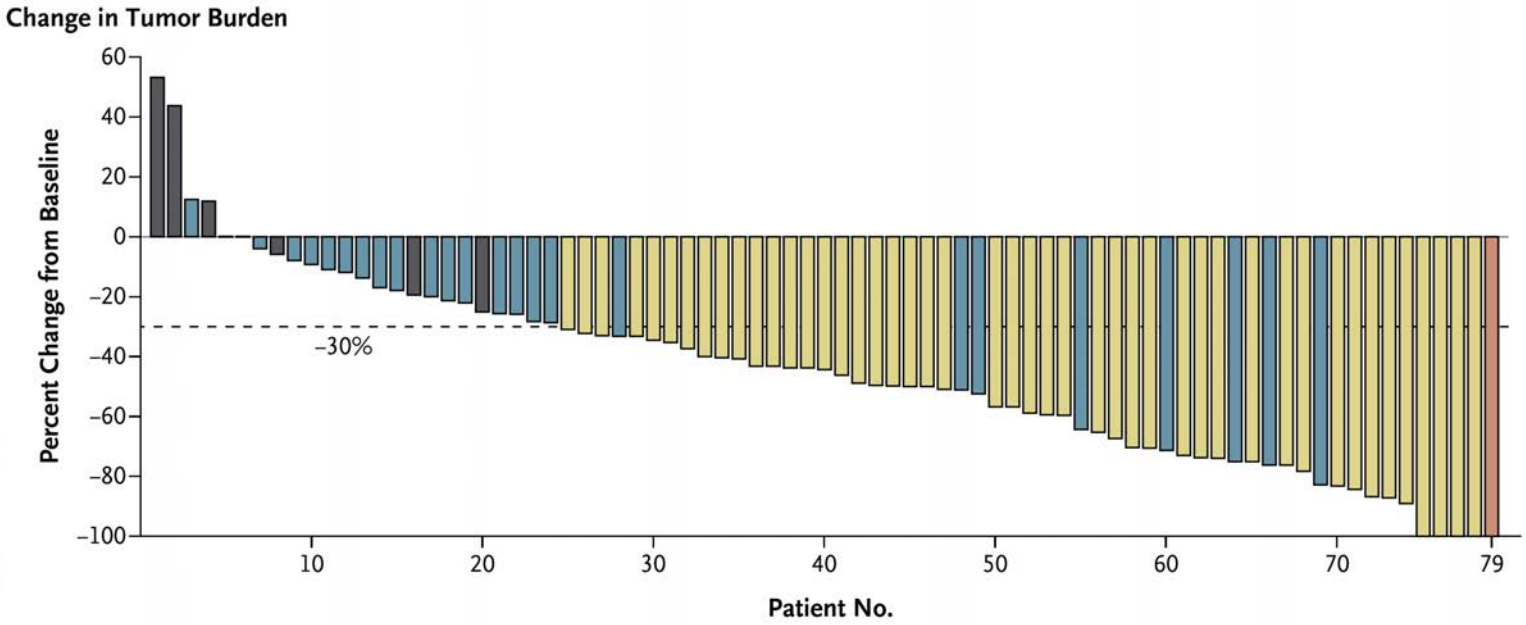
EGFR Mutations





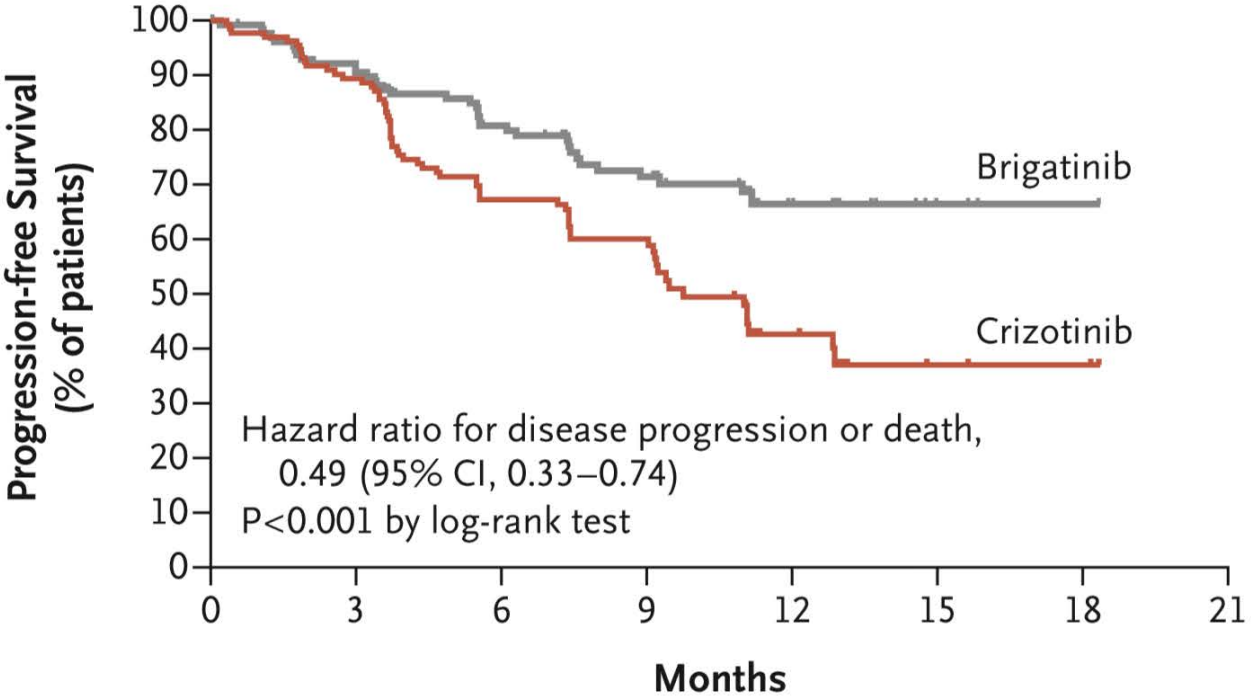
Soria, N Engl J Med 2018.

EML4-ALK Translocation



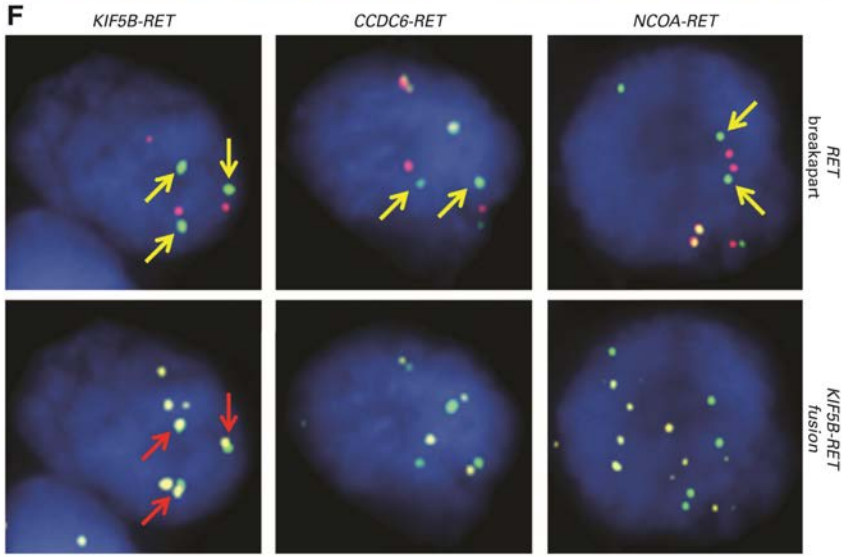
Kwak, N Engl J Med 2010.

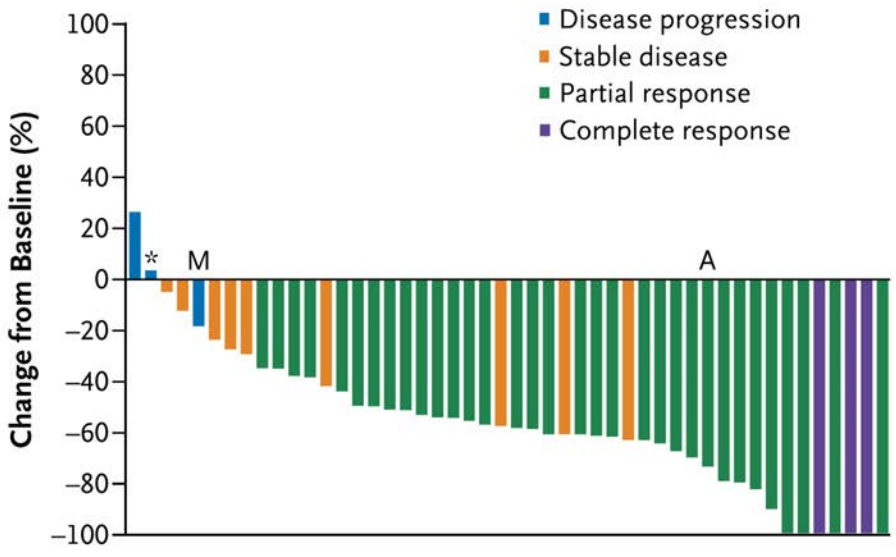
EML4-ALK Translocation



Camidge, N Engl J Med 2018.

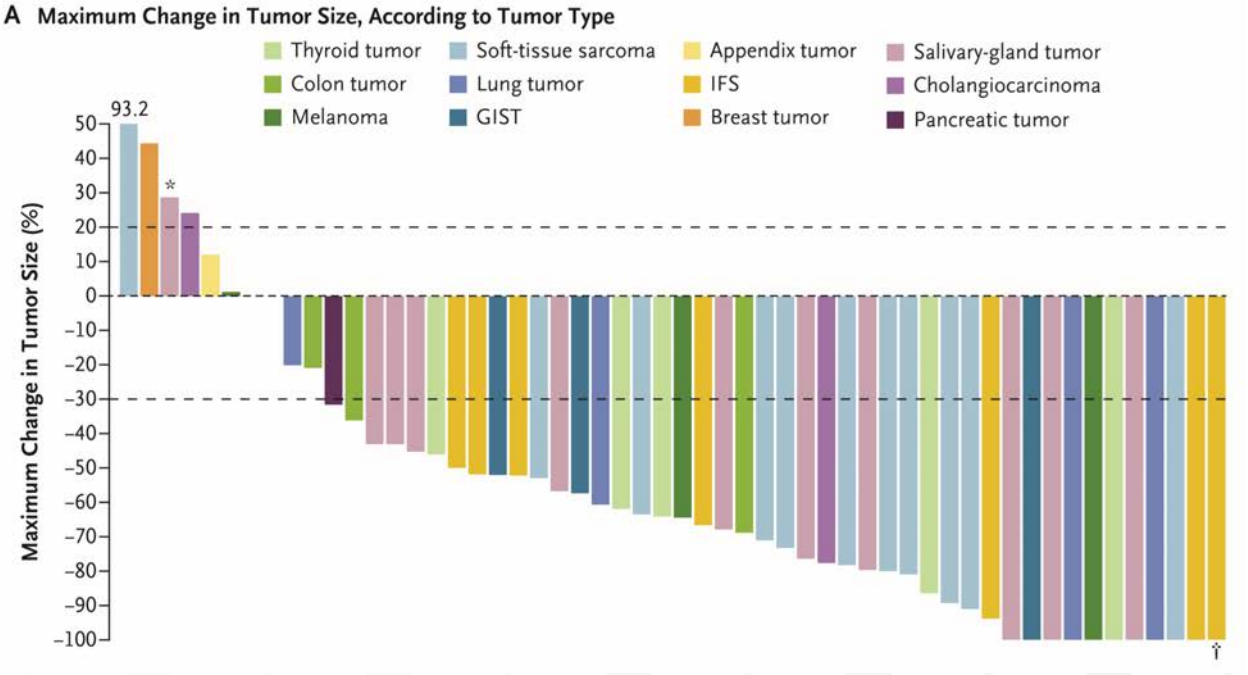
Other Targets





Wang, J Clin Oncol 2012. Shaw, N Engl J Med 2014.

Cross-Cancer Targets



Drilon, N Engl J Med 2018.

Molecular Testing Guidelines

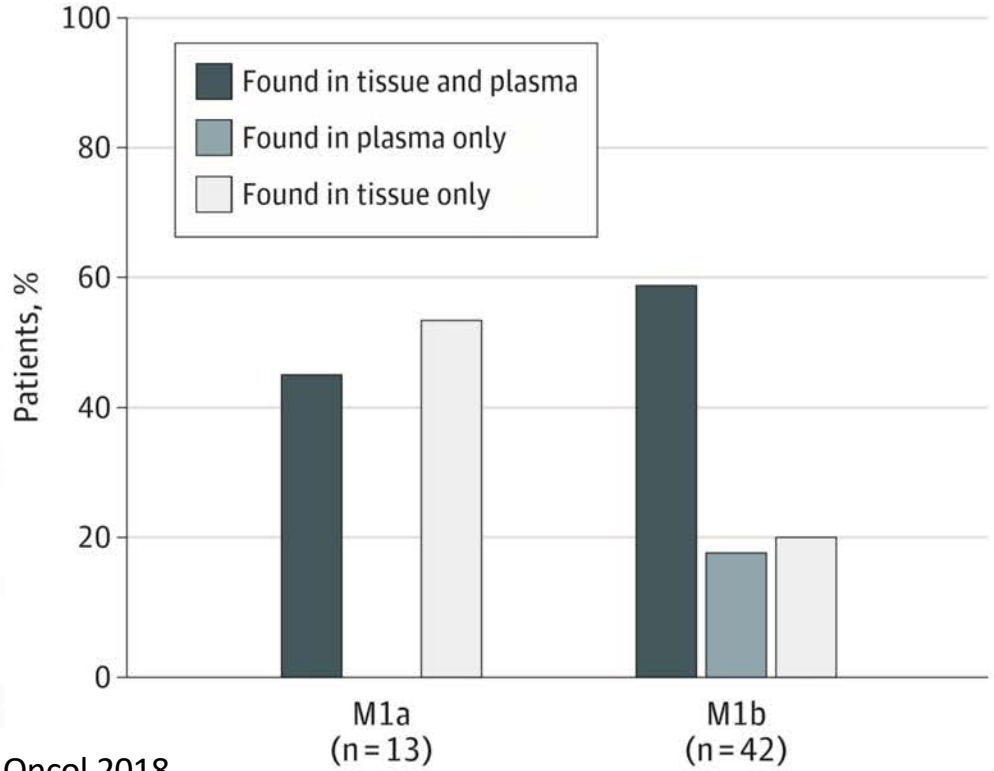
	Stand Alone	Panel
EGFR	X	X
ALK	X	X
ROS1	X	X
BRAF	X	X
RET		X
ERBB2		X
KRAS		X
MET		X

Table 5. Emerging Markers for Molecular Testing in Lung Cancer

Mitogen-activated protein kinase kinase 1 (*MEK1/MAP2K1*)
Fibroblast growth factor receptor 1–4 (*FGFR 1–4*)
Neurotrophic tyrosine kinase, receptor, type 1–3 (*NTRK1-3*)
Neuregulin 1 (*NRG1*)
Ras-like without CAAX 1 (*RIT1*)
Neurofibromin 1 (*NF1*)
Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (*PIK3CA*)
AKT serine/threonine kinase 1 (*AKT1*)
NRAS proto-oncogene, GTPase (*NRAS*)
Mechanistic target of rapamycin (*MTOR*)
Tuberous sclerosis 1 (*TSC1*)
Tuberous sclerosis 2 (*TSC2*)
KIT proto-oncogene receptor tyrosine kinase (*KIT*)
Platelet-derived growth factor receptor alpha (*PDGFRA*)
Discoidin domain receptor tyrosine kinase 2 (*DDR2*)

Lindeman, Arch Path Lab Med 2018; Kalemkerian, J Clin Oncol 2018.

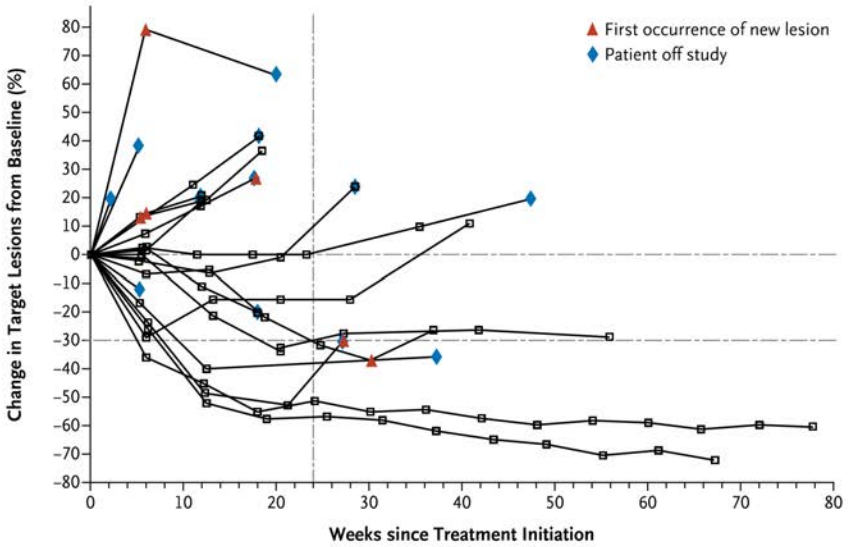
Plasma Genotyping

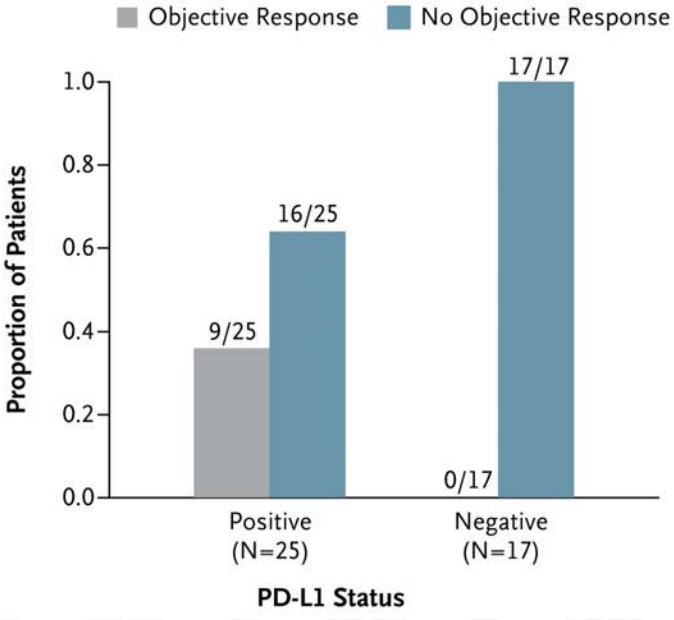


Aggarwal, JAMA Oncol 2018.

Immune Checkpoint Inhibitors

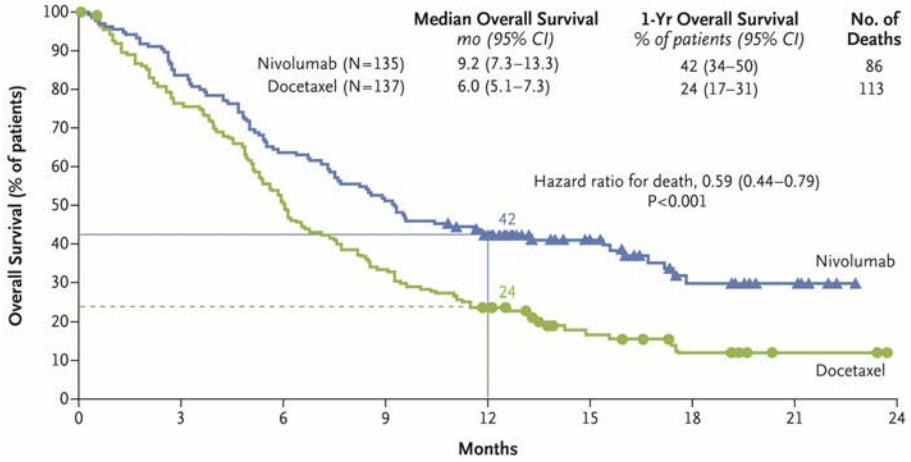
Immune Checkpoint Inhibitors

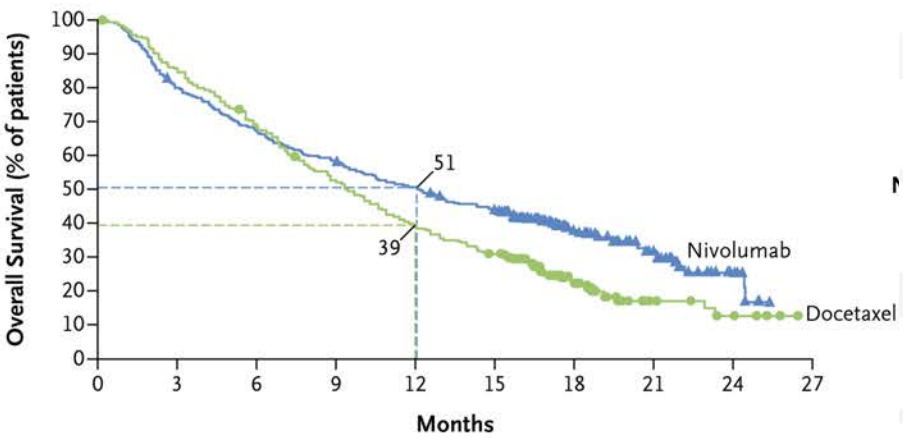




Brahmer, N Engl J Med 2012. Topalian, N Engl J Med 2012.

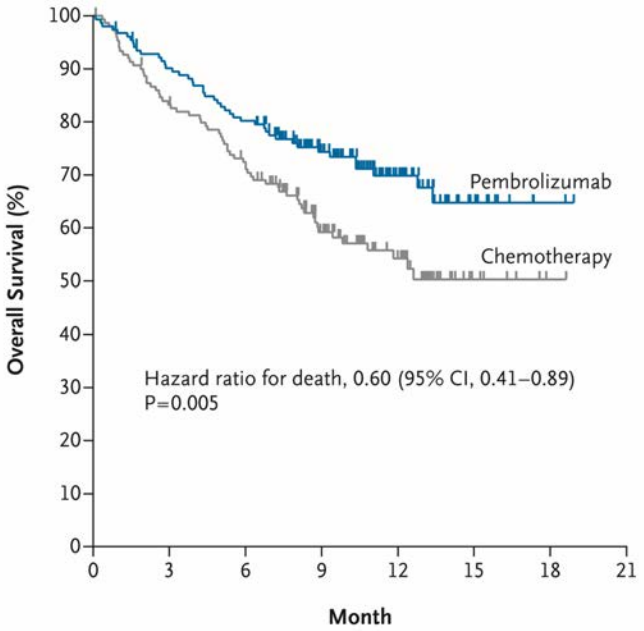
Second Line Therapy

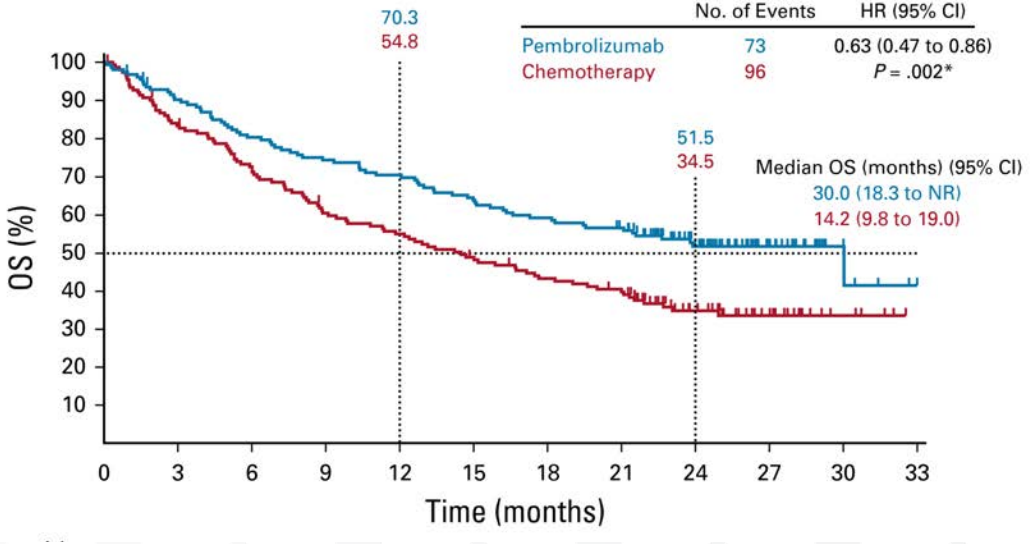




Brahmer, N Engl J Med 2015. Borghaei, N Engl J Med 2015.

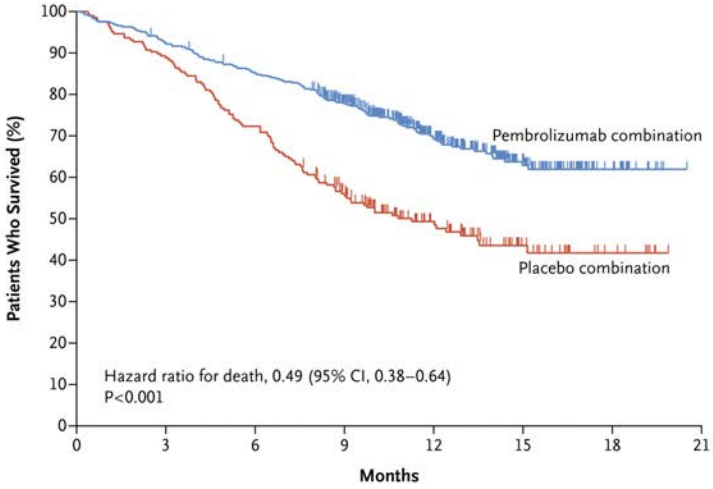
First Line Therapy Alone PD-L1 Positive

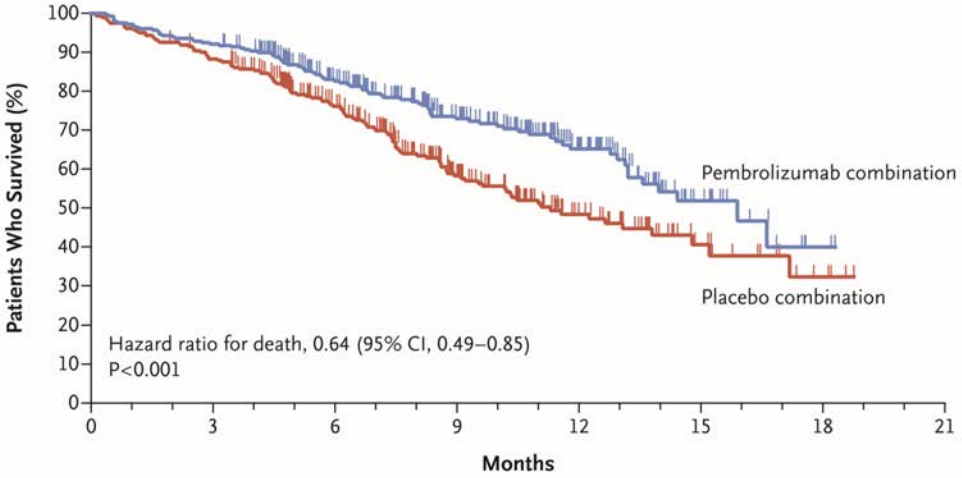




Reck, N Engl J Med 2016. Reck, J Clin Oncol 2019.

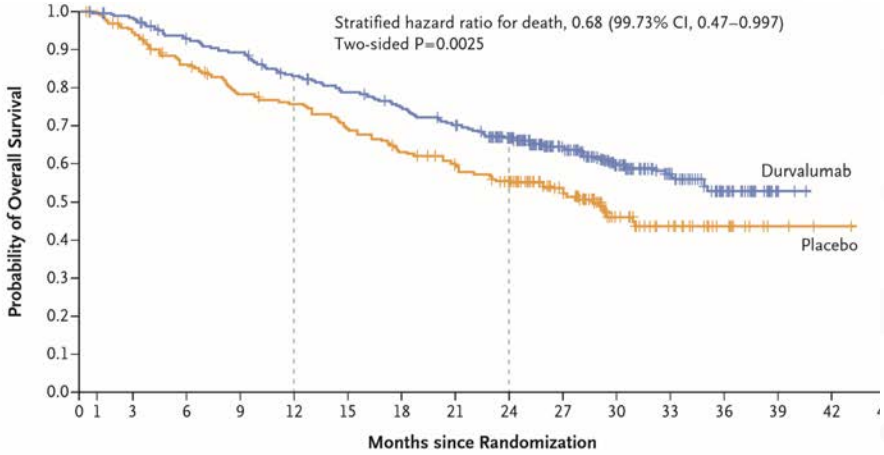
ICI + Chemotherapy



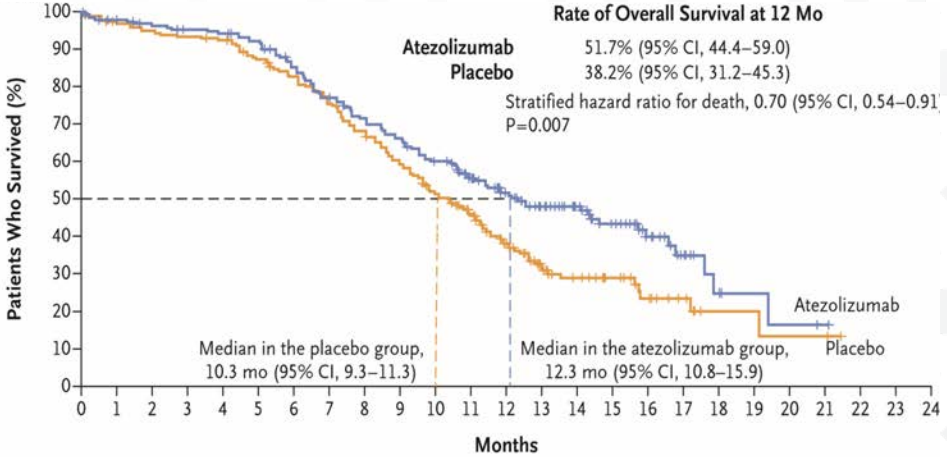


Gandhi, N Engl J Med 2018. Paz-Ares, N Engl J Med 2018.

Stage III

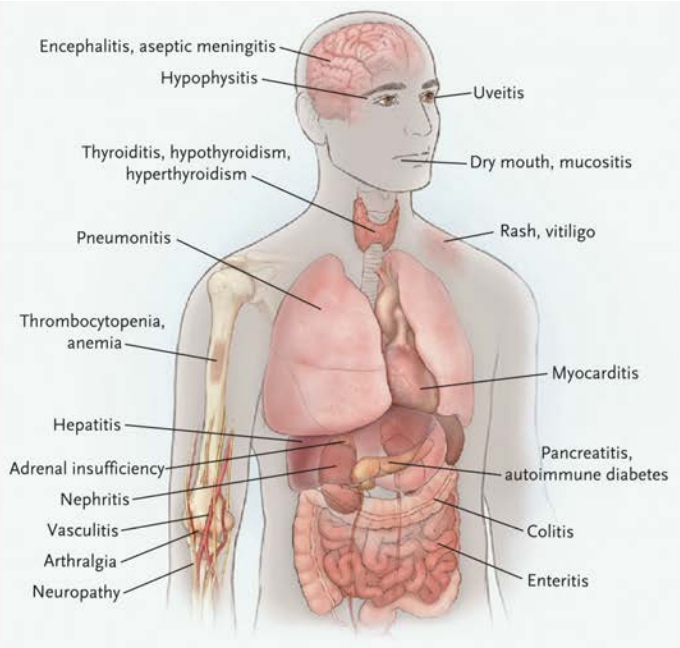


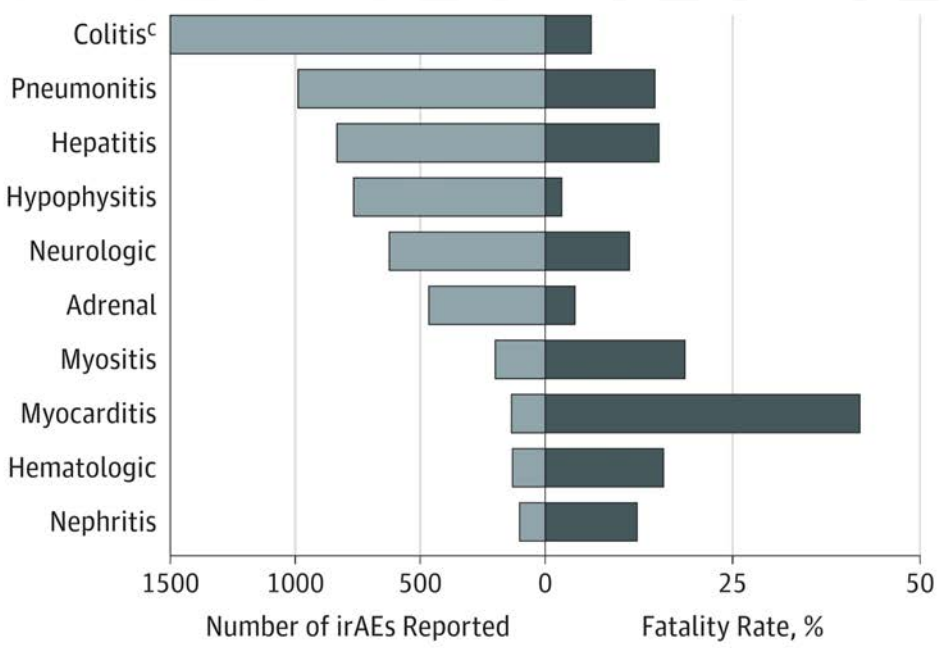
Small Cell



Antonia, N Engl J Med 2018. Horn, N Engl J Med 2018.

Immune Related Adverse Events

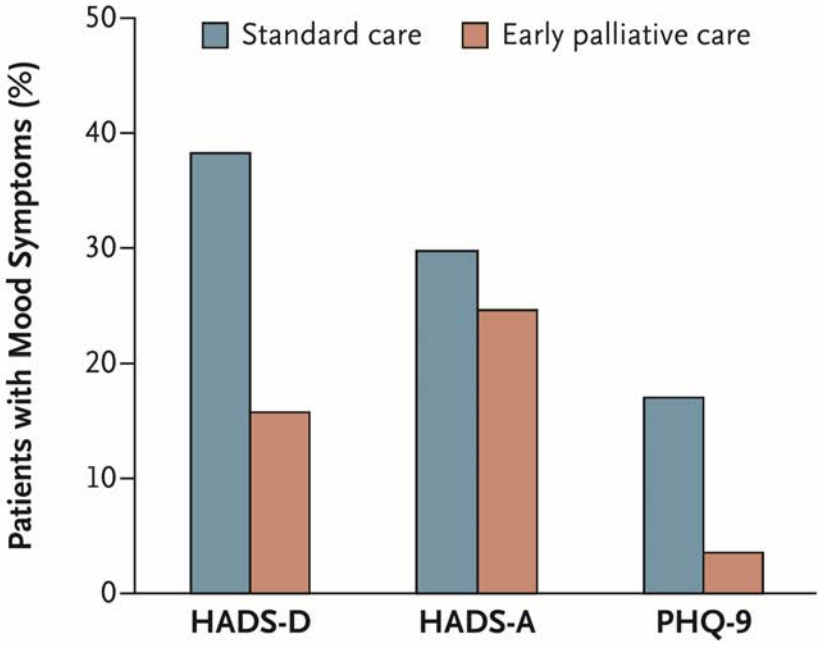


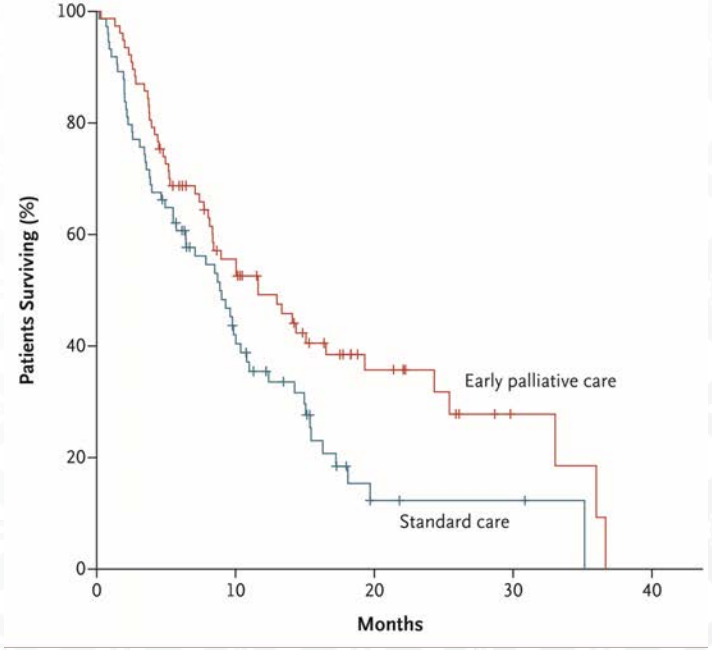


Postow, N Engl J Med 2018. Wang JAMA Oncol 2018.

Supportive Care

Early Palliative Care





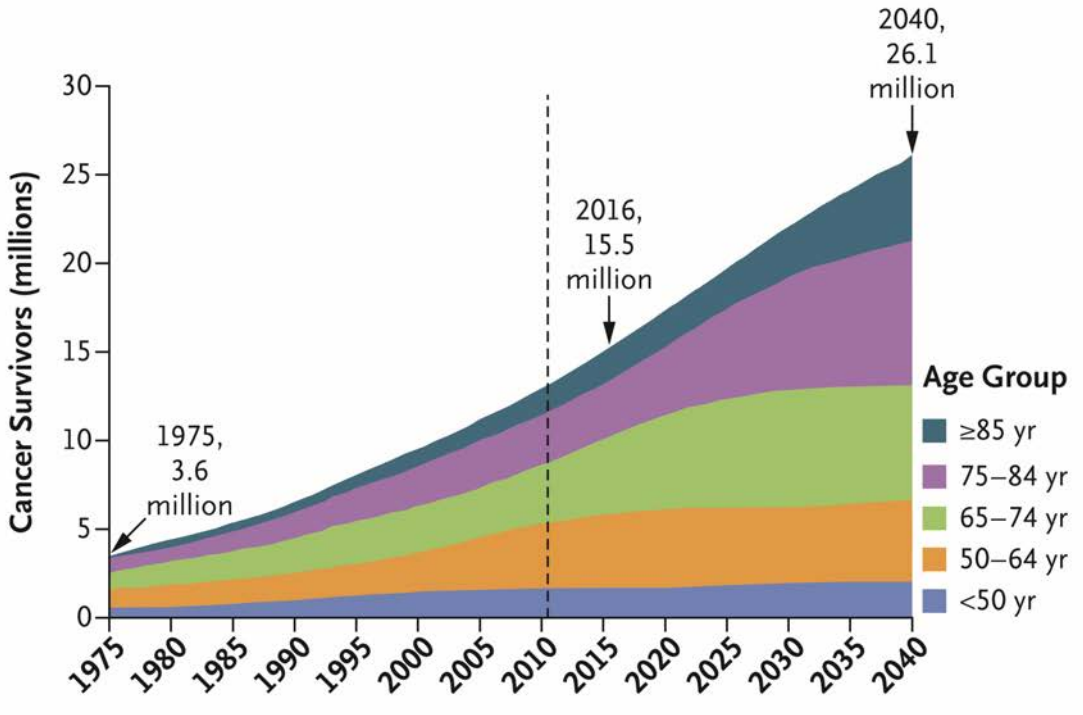
Temel, N Engl J Med 2010.

Perception of Quality of End-of-Life Care

	Excellent End-of-Life Care (%)
Intensive Care Unit (Y vs. N)	43.1 vs. 52.5
No Hospice (Y vs. N)	42.8 vs. 59.3
Death in Hospital (Y vs. N)	41.0 vs. 58.0

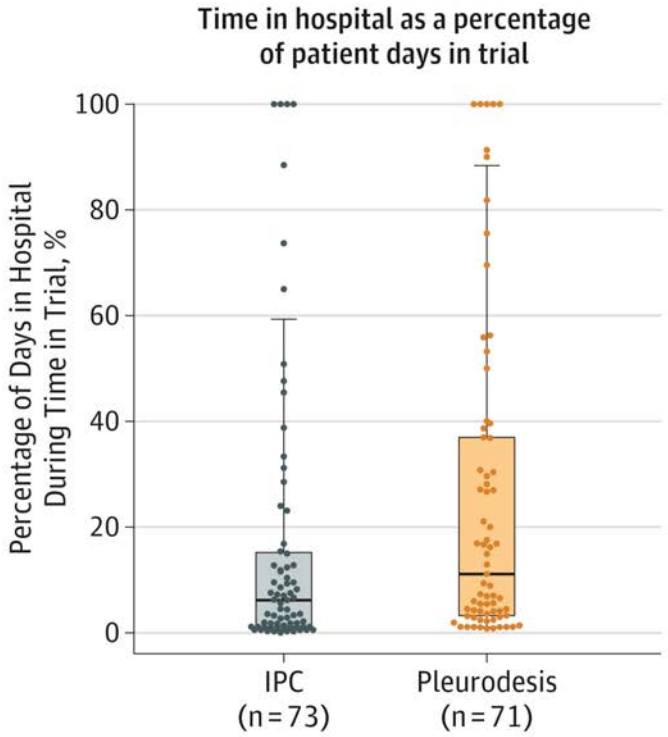
Wright, JAMA 2016.

Survivorship



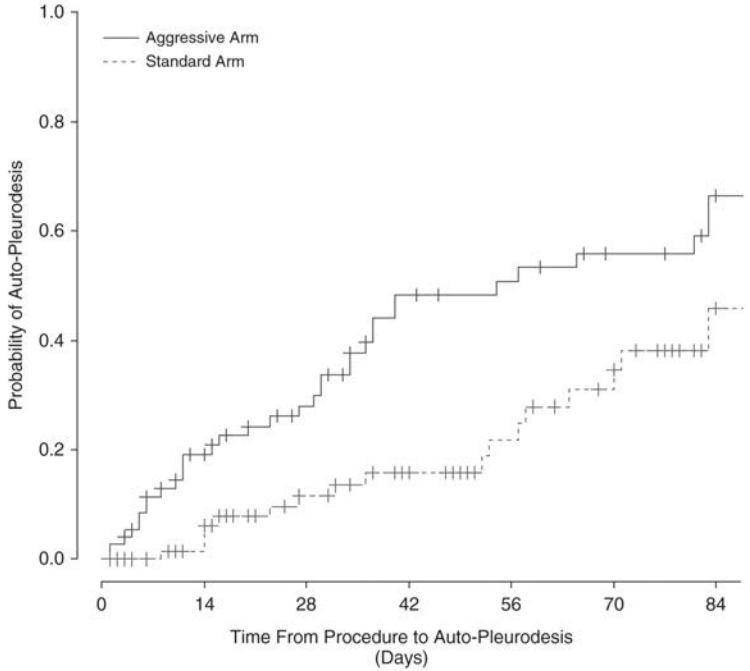
Shapiro, N Engl J Med 2018.

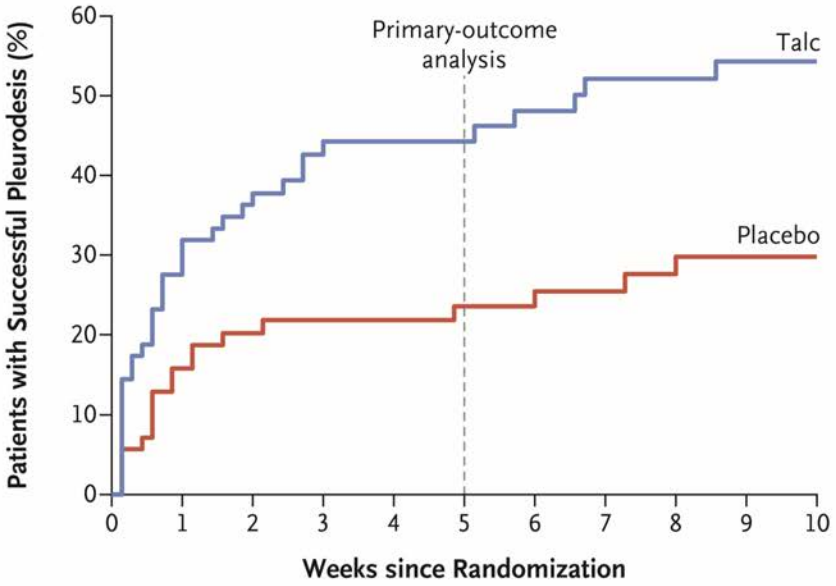
Indwelling Pleural Catheter vs. Pleurodesis



Thomas, JAMA 2017.

Indwelling Pleural Catheter





Wahidi, Am J Respir Crit Care Med 2017. Bhatnagar, N Engl J Med 2018.