

Supplementary file (Part 3 paper)

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Table S3-1 Life expectancy in years by specific age and smoking exposure cohorts

Cohort	Age category					
	65	70	75	80	85	90
US 2017 General population: Men	18	14.5	11.3	8.4	5.9	4.1
US 2017 General population: Women	20.6	16.7	13	9.8	7	4.8
HRS, lung cancer screening eligible	14.2		-	-	-	-
HRS, lung cancer screening eligible	13.2			-	-	-
HRS, Medicare enrolled & screening eligible	12.7 ^a		-	-	-	-

HRS Health Retirement Study (people with smoking exposure consistent with USPSTF lung screening eligibility; HRS life expectancy observed in a 2006 cohort). ^a, age 65-77. Data from Arias (1) and Howard (2).

Table S3-2A Summary of evidence in older patients with typical tumors

	Segment (vs. Lobe)		Wedge (vs. Lobe)		Wedge (vs. Segment)	
	Effect	Conf	Effect	Conf	Effect	Conf
Short-term (90-day) outcomes						
Mortality	= ^a	0	= ^a	+	-	-
Morbidity	= ^a	0	= ^a	0	-	-
QOL 90-day	= ^a	Extpol	= ^a	Extpol	-	-
Pain VATS	= ^a	Extpol	= ^a	Extpol	-	-
Pain Open	= ^a	Extpol	= ^a	Extpol	-	-
Intermediate (1-2 year) outcomes						
Δ FEV1	-	-	-	-	-	-
Dyspnea	-	-	-	-	-	-
QOL VATS	= ^a	Extpol	= ^a	Extpol	-	-
Pain VATS	= ^a	Extpol	= ^a	Extpol	-	-
QOL Open	= ^a	Extpol	= ^a	Extpol	-	-
Pain Open	= ^a	Extpol	= ^a	Extpol	-	-
Long-term (5-year) outcomes						
OS	↓ ^a	++	↓ ^a	++	=/↓	0
LCSS	↓ ^a	++	↓ ^a	++	=/↓	0
FFR	-	-	-	-	-	-
LR- FFR	-	-	-	-	-	-

Table S3-2B Summary of evidence in compromised patients

	Segment (vs. Lobe)		Wedge (vs. Lobe)	
	Effect	Conf	Effect	Conf
Short-term (90-day) outcomes				
Mortality VATS	= ^a	0	= ^a	0
Morbidity VATS	= ^a	0	= ^a	0
Pain VATS	= ^a	Extpol	= ^a	Extpol
Mortality Open	= ^a	0	= ^a	0
Morbidity Open	= ^a	0	= ^a	0
Pain Open	= ^a	Extpol	= ^a	Extpol
QOL 90-day	-	-	-	-
Intermediate (1-2 year) outcomes				
Δ FEV1	= ^a	0	= ^a	0
Dyspnea	= ^a	0	= ^a	0
QOL VATS	= ^a	Extpol	= ^a	Extpol
Pain VATS	= ^a	Extpol	= ^a	Extpol
QOL open	= ^a	Extpol	= ^a	Extpol
Pain Open	= ^a	Extpol	= ^a	Extpol
Long-term (5-year) outcomes				
OS	= ^a	Extpol	= ^a	Extpol
LCSS	-	-	-	-
FFR	-	-	-	-
LR- FFR	-	-	-	-

Table S3-2C Summary of evidence in patients with specific tumors

Tumor type SL (vs. Lobe)	Predominantly GG		Screen detected		Slow growth, low PET avidity		<1 cm (solid tumor)	
	Effect	Conf	Effect	Conf	Effect	Conf	Effect	Conf
Short-term (90-day) outcomes								
Mortality VATS	=	Extrapol	=	Extrapol	=	Extrapol	=	Extrapol
Morbidity VATS	=	Extrapol	=	Extrapol	=	Extrapol	=	Extrapol
Pain VATS	=	Extrapol	=	Extrapol	=	Extrapol	=	Extrapol
Mortality Open	=	Extrapol	=	Extrapol	=	Extrapol	=	Extrapol
Morbidity Open	=	Extrapol	=	Extrapol	=	Extrapol	=	Extrapol
Pain Open	=	Extrapol	=	Extrapol	=	Extrapol	=	Extrapol
QOL 90-day	=	Extrapol	=	Extrapol	=	Extrapol	=	Extrapol
Intermediate (1-2 year) outcomes								
Δ FEV1	= ^a	Extrapol	= ^a	Extrapol	= ^a	Extrapol	= ^a	Extrapol
Dyspnea	= ^a	Extrapol	= ^a	Extrapol	= ^a	Extrapol	= ^a	Extrapol
QOL VATS	=	Extrapol	=	Extrapol	=	Extrapol	=	Extrapol
Pain VATS	=	Extrapol	=	Extrapol	=	Extrapol	=	Extrapol
QOL open	=	Extrapol	=	Extrapol	=	Extrapol	=	Extrapol
Pain Open	=	Extrapol	=	Extrapol	=	Extrapol	=	Extrapol
Long-term (5-year) outcomes								
OS	=	+++	=	Rationale	=	Rationale	↓	++
LCSS	-	-	-	-	-	-	↓	++
FFR	=	+	=	Rationale	=	Rationale	-	-
LR- FFR	=/↓	+	=	Rationale	=	Rationale	-	-

Qualitative assessment of the impact of treatment approaches on various key outcome measures and the confidence in the evidence. Differences are categorized by degree of clinically meaningful differences as defined in the legend insert. The reference (for improvement or worsening) is the treatment in parentheses.

Effect		Confidence in / consistency of evidence	
↑↑↑	2x meaningful improvement	++++	Very High
↑↑	Meaningful improvement	+++	High
↑	Somewhat better	++	Moderate
=	Similar	+	Low
↓	Somewhat worse	0	Very Low
↓↓	Meaningful worsening	Extpol	Extrapolation
↓↓↓	2x meaningful worsening		

A clinically “meaningful” difference is defined as ≥10-unit difference, with “somewhat” being half of the meaningful difference. The units of measure (for categories in parentheses) are: normalized scale points (QOL); 5-year actuarial rate (OS, LCSS); actuarial rate or simple incidence (recurrence, FFR); incidence of Gr ≥3 treatment related complications (morbidity); absolute change in % FEV1 (PFTs in compromised patients). Different thresholds of “meaningful” are: 90-day mortality (2% difference); PFTs in healthy patients (20% difference in FEV1%).

^a, data for sublobar resection not parsed out to segment or wedge. Δ FEV1, change in FEV1 ≥6 months; Conf, confidence in the evidence; Extpol, extrapolation (indirect evidence); FFR, freedom from recurrence (only recurrence counts as an event); Gr, grade; HR, hazard ratio; LCSS, lung cancer specific survival (only a death due to lung cancer counts as an event); Lobe, lobectomy; LR-FFR, locoregional freedom from recurrence; OS, overall survival; PFT, pulmonary function tests; QOL, quality of life; SL, sublobar resection; VATS, video-assisted thoracic surgery.

Table S3-3 Long-term surgical outcomes in compromised patients Ordered by stage, degree of confidence that results reflect effect of treatment, age

1 st author, year (reference)	Study characteristics				Adjustment for confounding							Adjusted % 5-yr OS W/Seg vs. Lobe		Adjusted % 5-yr LCSS W/Seg vs. Lobe									
	Source	Yrs	n	Lobe vs. Stage ^a	Age	Demogr F	CoMorbid	Hi Stage	Time Span	Q Settings	Q Surgery	Fav Tumor	Statistical Methods	# adj for / Subsets	Confid RE Tmt effect	W	Seg	Lobe	HR	W	Seg	Lobe	HR
Compromised patients																							
Salazar 2021 (3)	SEER	05-15	544	W	cI A1,2	≥67 ^b							MV	12	M	39 ^c	-	47 ^c	1.19	70 ^c	-	80 ^c	1.65
Tsutani 2017 (4)	Japan x1	07-15	107	SL	cI-IIA	ILD ^d							MV	7	L	[82] ^{e,f}		[67] ^{e,f}	.36				

Inclusion criteria: Studies using multivariable or propensity adjustment to compare sublobar resection (wedge or segmentectomy) vs. lobectomy, 2000-21, >50 pts per arm, focused specifically on compromised patients; The HR reference is lobectomy, i.e. HR >1 reflects worse outcome compared with Lobectomy. Bold highlights better outcome (>2-point difference); Light green shading highlights statistically significant difference (lighter shade = univariable; darker = multivariable);
^a, 8th edition stage (reported stage is translated into current 8th edition nomenclature for the sake of uniformity and contemporary application); ^b, compromised patients (SEER life expectancy ≤5 years); ^c, unadjusted results; ^d, all patients with interstitial lung disease; ^e, 3-yr OS (in brackets because not comparable to other entries in this column); HR, hazard ratio; ILD, interstitial lung disease; LCSS, lung cancer specific survival; Lobe, lobectomy; OS, overall survival; SEER, Surveillance, Epidemiology, and End Results database; Seg, segmentectomy; W, wedge; Yrs, years (of patient accrual).

Legend for Adjustment for Confounding: Demogr F, demographic factors (age, sex, socioeconomic); Comorbid, comorbidities; Hi Stage, occult stage inaccuracy due to differences in extent of assessment; Time Span, adjustment for changes during the study period or differential use of the interventions; Q settings, discrepancy in the facilities or settings performing the interventions; Q Treatmt, quality of the treatment (e.g. margin distance, adjuvant therapy); Fav Tumor, selection of less aggressive tumors for an intervention; Statistical methods, methods used to adjust for confounding; Subset, additional subset or sensitivity analyses; # adj for, number of factors adjusted for; Conf RE tmt effect, Confidence that results reflect the effect of the treatment vs. confounding factors. MV, Multivariable model (e.g. Cox regression); PA, propensity score adjustment; PM, propensity matching; PQ, analysis of propensity score quintiles

Color code:	Categories of confounding	Addressed	Neutral (likely little effect)	Limited concern	Moderate concern	High concern	Clearly confounded
Confidence RE treatment effect	VH-very high	H-high	M-moderate	L-low	VL-very low confidence		

Table S3-4 Long-term outcomes for small (≤ 1 cm) tumors

Ordered by resection extent, degree of confidence that results reflect effect of treatment

1 st author, year (reference)	Study characteristics					Confid RE Tmt effect	Adjusted % 5-yr OS W/Seg vs. Lobe				Adjusted % 5-yr LCSS W/Seg vs. Lobe			
	Source	Yrs	N	Stage ^a	Lobe vs.		W	Seg	Lobe	HR	W	Seg	Lobe	HR
Wedge/segment vs. lobectomy														
Cao 2018 (5)	SEER	04-13	252 ^b	cIA1	Seg	M	-	74	80	1.1	-	83	90	1.32
Fan 2020 (6)	SEER	04-15	1,684	cIA1	Seg	VL	-	76 ^c	80^c	1.05	-	-	-	-
Dai 2016 (7)	SEER	00-12	1,789	cIA1	Seg	VL	-	71 ^c	78^c	1.39	-	81 ^c	87^c	1.64
Kates ^d 2011 (8)	SEER	88-05	664	cIA1	SL	L	-	-	-	.99	-	-	-	1.44
Cao 2018 (5)	SEER	04-13	1,028 ^b	cIA1	W.	L	74	-	80	1.2	84	-	89	1.3
Fan 2020 (6)	SEER	04-15	2,360	cIA1	W.	VL	71 ^c	-	80^c	1.36	-	-	-	-
Dai 2016 (7)	SEER	00-12	2,450	cIA1	W.	VL	68 ^c	-	78^c	1.45	82 ^c	-	87^c	1.45
Wedge vs. segment							Wedge vs. Seg				Wedge vs. Seg			
Cao 2018 (5)	SEER	04-13	252 ^b	cIA1	W v Seg	L	76	74	-	1.05	91	83	-	.75
Fan 2020 (6)	SEER	04-15	1,026	cIA1	W v Seg	VL	71 ^c	76^c	-	1.42	-	-	-	-
Dai 2016 (7)	SEER	00-12	981	cIA1	W v Seg	VL	68 ^c	71^c	-	1.08	83 ^c	81 ^c	-	.93

Inclusion criteria: studies using multivariable or propensity adjustment to compare wedge resection or segmentectomy vs. lobectomy in cIA1 solid tumors, 2000-21, with >50 pts per arm. The HR reference is lobectomy (or segmentectomy in the wedge vs. segmentectomy section), i.e. HR >1 reflects worse outcome compared with lobectomy. Bold highlights better outcome (>2-point difference); Red font highlights potential weakness, e.g. accrual occurring primarily before 2000; Light green shading highlights statistically significant difference (lighter shade = univariable; darker = multivariable).

^a, 8th edition stage classification; ^b, propensity matched pairs (total); ^c, unadjusted results; ^d, Age ≥ 70 .

Conf RE tmt effect, Confidence that results reflect the effect of the treatment (sublobar resection or lobectomy) vs. confounding factors; HR, hazard ratio; L, low confidence; LCSS, lung cancer specific survival; Lobe, lobectomy; M, moderate confidence; OS, overall survival; SEER, Surveillance, Epidemiology, and End Results database; Seg, segmentectomy; SL, sublobar resection; W, wedge; VL, very low confidence; yr, year.

Life-expectancy in a representative US medicare population

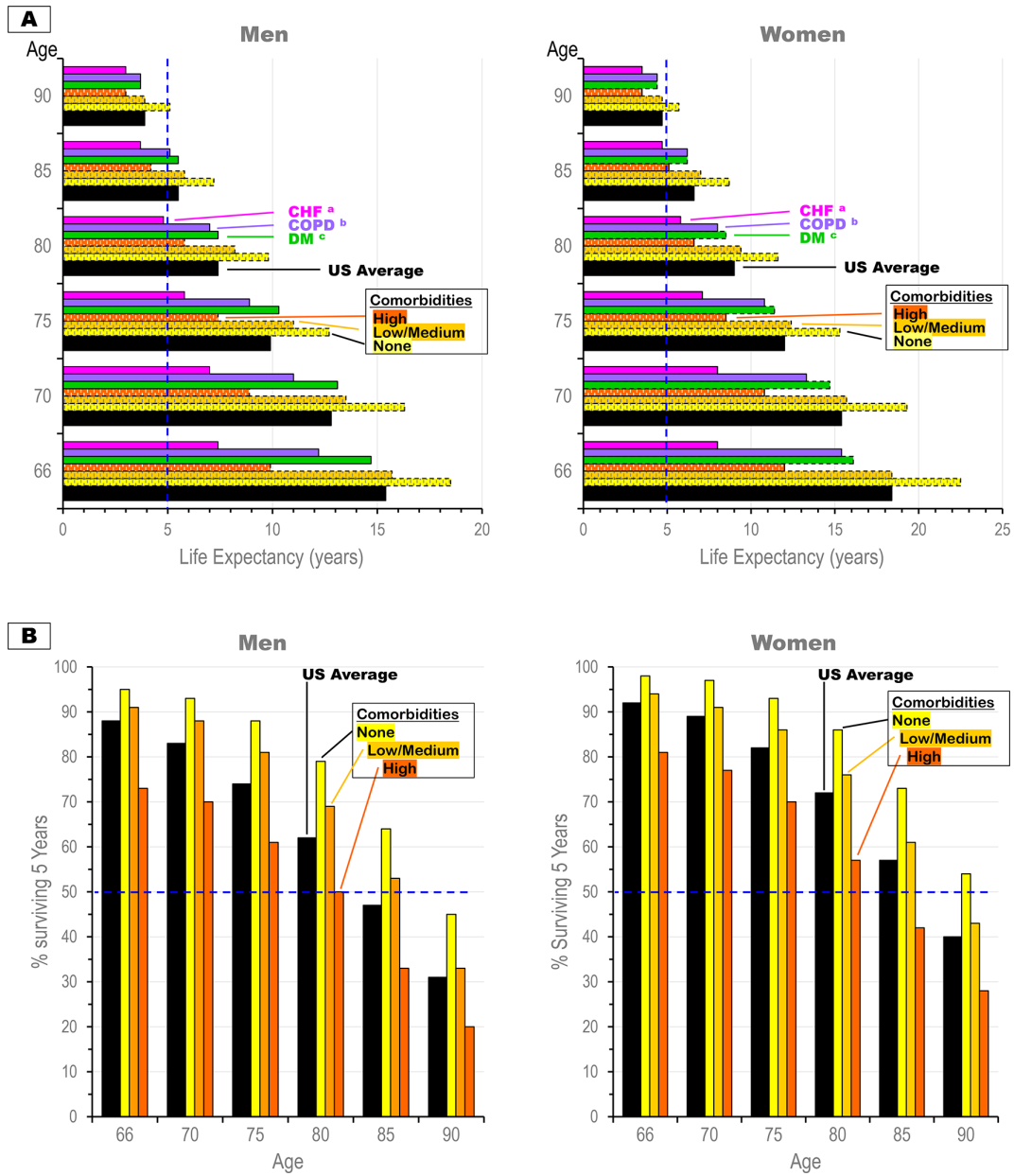


Figure S3-1 Life-expectancy in a representative US Medicare population.

Life-expectancy in a 5% population-representative sample of individuals without cancer in the US Surveillance, Epidemiology, and End Results (SEER) database, age ≥ 66 between 1992-2005, enrolled in Medicare, $n=407,749$. A. Life expectancy in years of age cohorts by degree of comorbidities and common specific comorbidities. B. Percent of patients surviving 5 years. ^a, includes CHF only or with other comorbidities; ^b, includes COPD only or COPD with other comorbidities except CHF; ^c, includes DM only or with other comorbidities other than COPD or CHF. CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus. Data taken from Cho *et al.*, *Ann Intern Med* 2013;159:667-76. (9)

Sublobar resection vs. lobectomy in older patients

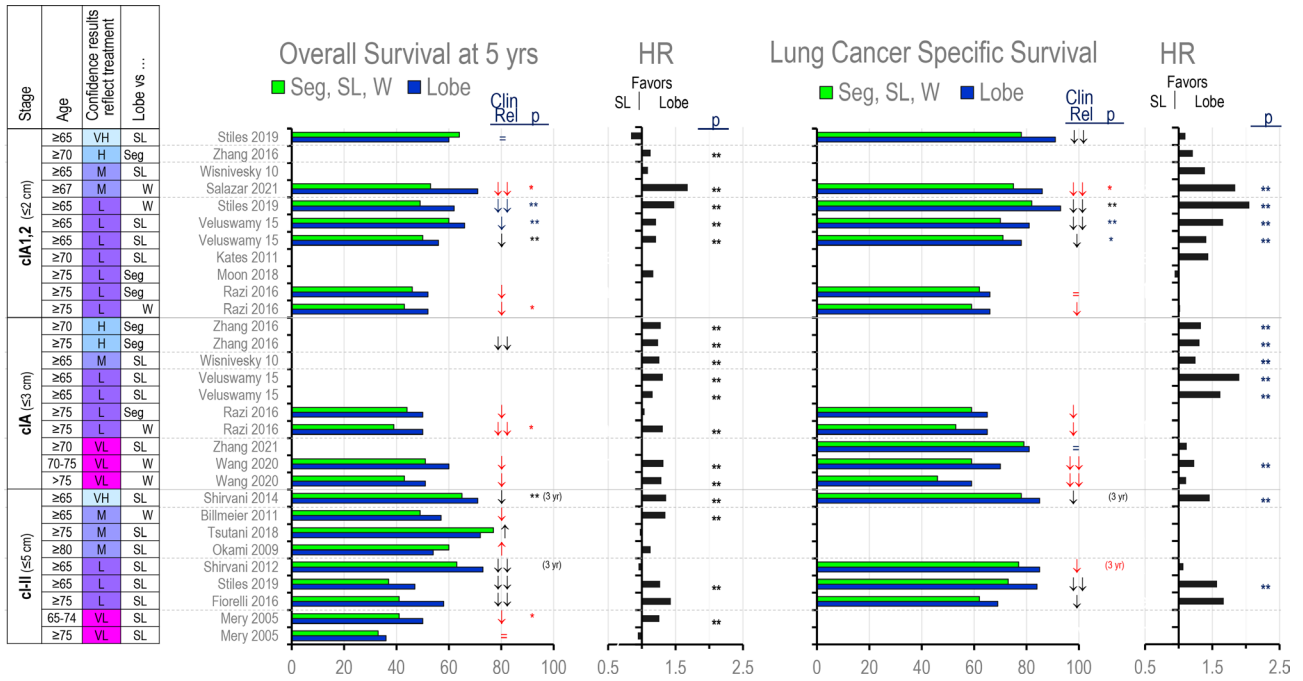


Figure S3-2 Graphic depiction of outcomes in Table 2, Part 3 paper. Figure rows correspond to the respective table rows. Also depicted is the confidence that the outcomes reflect the treatment (vs. confounders), the level of clinical relevance and statistical significance. The HR reference is lobectomy, i.e., HR >1 reflects worse outcome compared with lobectomy. Red font indicates unadjusted survival rates.

Confidence results reflect the treatment		Relevance of Effect	
VH	Very High	↑↑↑	2x meaningfully better
H	High	↑↑	Meaningfully better
M	Moderate	↑	Somewhat better
L	Low	=	Similar
VL	Very Low	↓	Somewhat worse
See Table 1 for details		↓↓	Meaningfully worse
		↓↓↓	2x meaningfully worse

* reported as statistically significant by univariable analysis; ** reported as statistically significant by multivariable analysis; Clin Rel, clinical relevance of effect. A clinically relevant difference is defined as ≥5-point difference in the 5-year actuarial rate (overall survival, lung cancer specific survival). Details of this categorization is provided in the Part 1 paper (Tab. S1-1) (10). HR, hazard ratio; Lobe, lobectomy; Seg, segment; SL, sublobar resection; W, wedge; yrs, years.

Incidence of comorbidities in SEER-medicare 1992–2005
in non-cancer and lung cancer patients

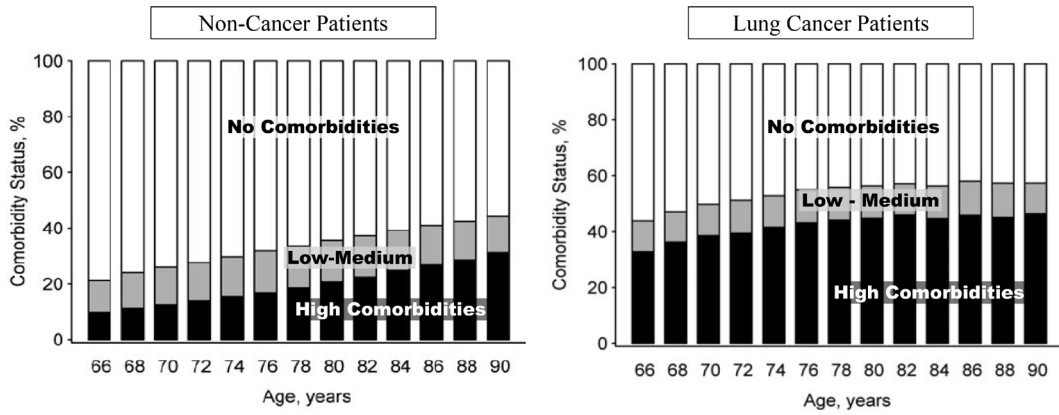


Figure S3-3 Incidence of co-morbidities in lung cancer patients.

Incidence of comorbidities in SEER-Medicare 1992–2005 in non-cancer (left) and lung cancer patients (right). Reproduced with permission from Cho *et al.* (11).

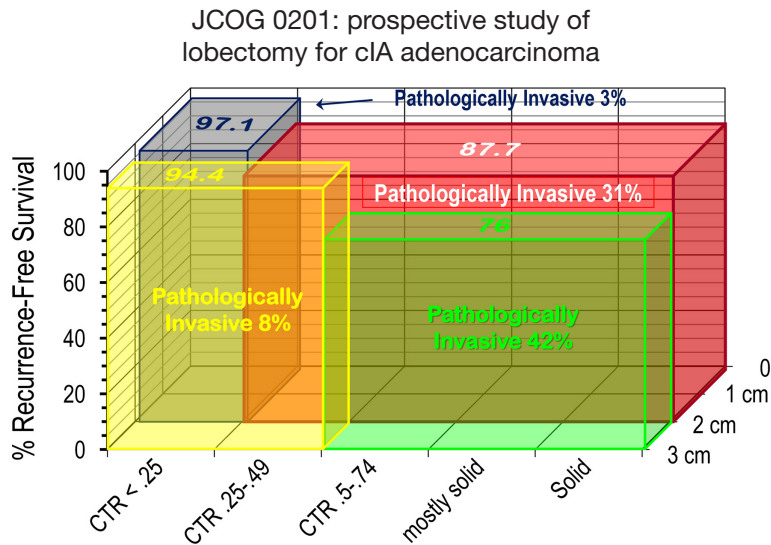


Figure S3-4 Prospective study of lobectomy for cI adenocarcinoma (JCOG0201).

Prospective study of invasiveness and recurrence free survival after lobectomy for cI adenocarcinoma by size and ground glass proportion (12,13). CTR, consolidation/tumor ratio (size of consolidation on lung windows/total tumor size including ground glass component).

Wedge/segment resection vs. lobectomy

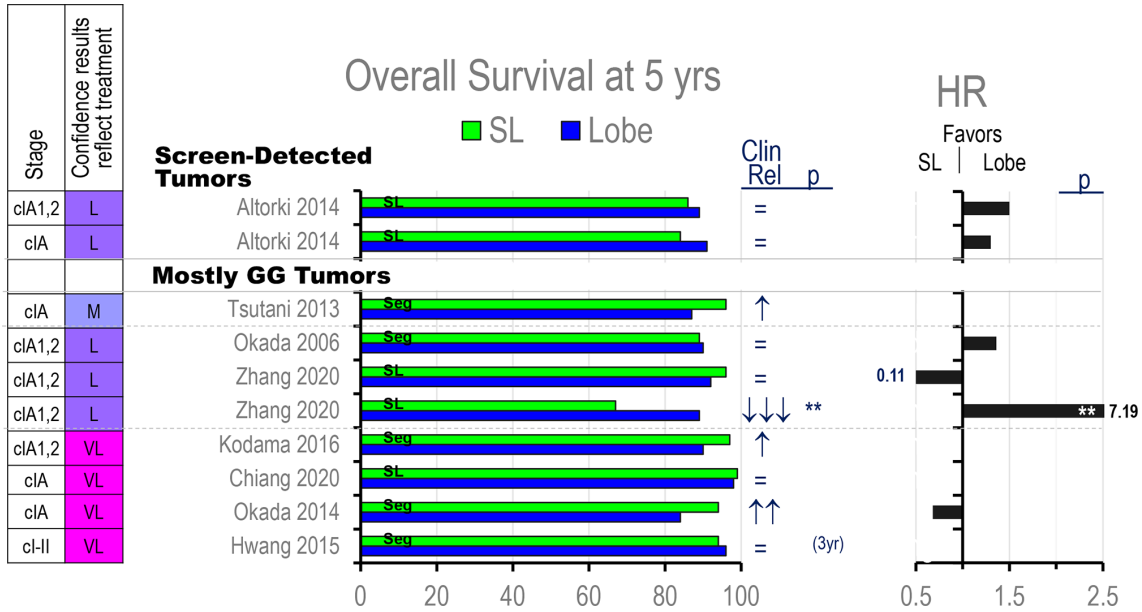


Figure S3-5 Graphic depiction of outcomes in Table 5, Part 3 paper.

Figure rows correspond to the respective table rows. Also depicted is the confidence that the outcomes reflect the treatment (*vs.* confounders), the level of clinical relevance and statistical significance. The HR reference is lobectomy, i.e. HR >1 reflects worse outcome compared with lobectomy. Red font indicates unadjusted survival rates.

Confidence results reflect the treatment		Relevance of Effect	
VH	Very High	↑↑↑	2x meaningfully better
H	High	↑↑	Meaningfully better
M	Moderate	↑	Somewhat better
L	Low	=	Similar
VL	Very Low	↓	Somewhat worse
See Table 1 for details		↓↓	Meaningfully worse
		↓↓↓	2x meaningfully worse

* reported as statistically significant by univariable analysis; ** reported as statistically significant by multivariable analysis; Clin Rel, clinical relevance of effect. A clinically relevant difference is defined as ≥5-point difference in the 5-year actuarial rate (overall survival, lung cancer specific survival). Details of this categorization is provided in the Part 1 paper (*Tab. S1-1*) (10). GG, ground glass; HR, hazard ratio; Lobe, lobectomy; Seg, segment; SL, sublobar resection; W, wedge; yrs, years.

Sublobar resection vs. lobectomy for ≤ 1 cm tumors

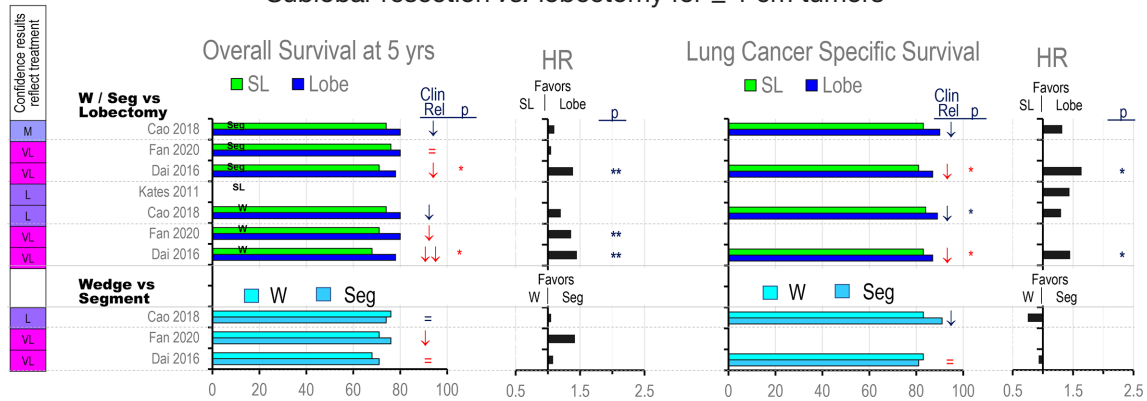


Figure S3-6 Graphic depiction of outcomes in Table S3-4, Part 3 paper.

Figure rows correspond to the respective table rows. Also depicted is the confidence that the outcomes reflect the treatment (*vs.* confounders), the level of clinical relevance and statistical significance. The HR reference is lobectomy (or segmentectomy in the bottom section), i.e., HR >1 reflects worse outcome compared with lobectomy (or segmentectomy in the bottom section). Red font indicates unadjusted survival rates.

Confidence results reflect the treatment		Relevance of Effect	
VH	Very High	↑↑↑	2x meaningfully better
H	High	↑↑	Meaningfully better
M	Moderate	↑	Somewhat better
L	Low	=	Similar
VL	Very Low	↓	Somewhat worse
		↓↓	Meaningfully worse
		↓↓↓	2x meaningfully worse

* reported as statistically significant by univariable analysis; ** reported as statistically significant by multivariable analysis; Clin Rel, clinical relevance of effect. A clinically relevant difference is defined as ≥5-point difference in the 5-year actuarial rate (overall survival, lung cancer specific survival). Details of this categorization is provided in the part 1 paper (*Tab. S1-1*) (10). HR, hazard ratio; Lobe, lobectomy; Seg, segment; SL, sublobar resection; W, wedge; yrs, years.

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