

SUPPLEMENTARY MATERIAL

Treatment patterns and survival trends among patients with advanced-stage non-small cell lung cancer in Pakistan: a cancer registry-based flexible parametric analysis

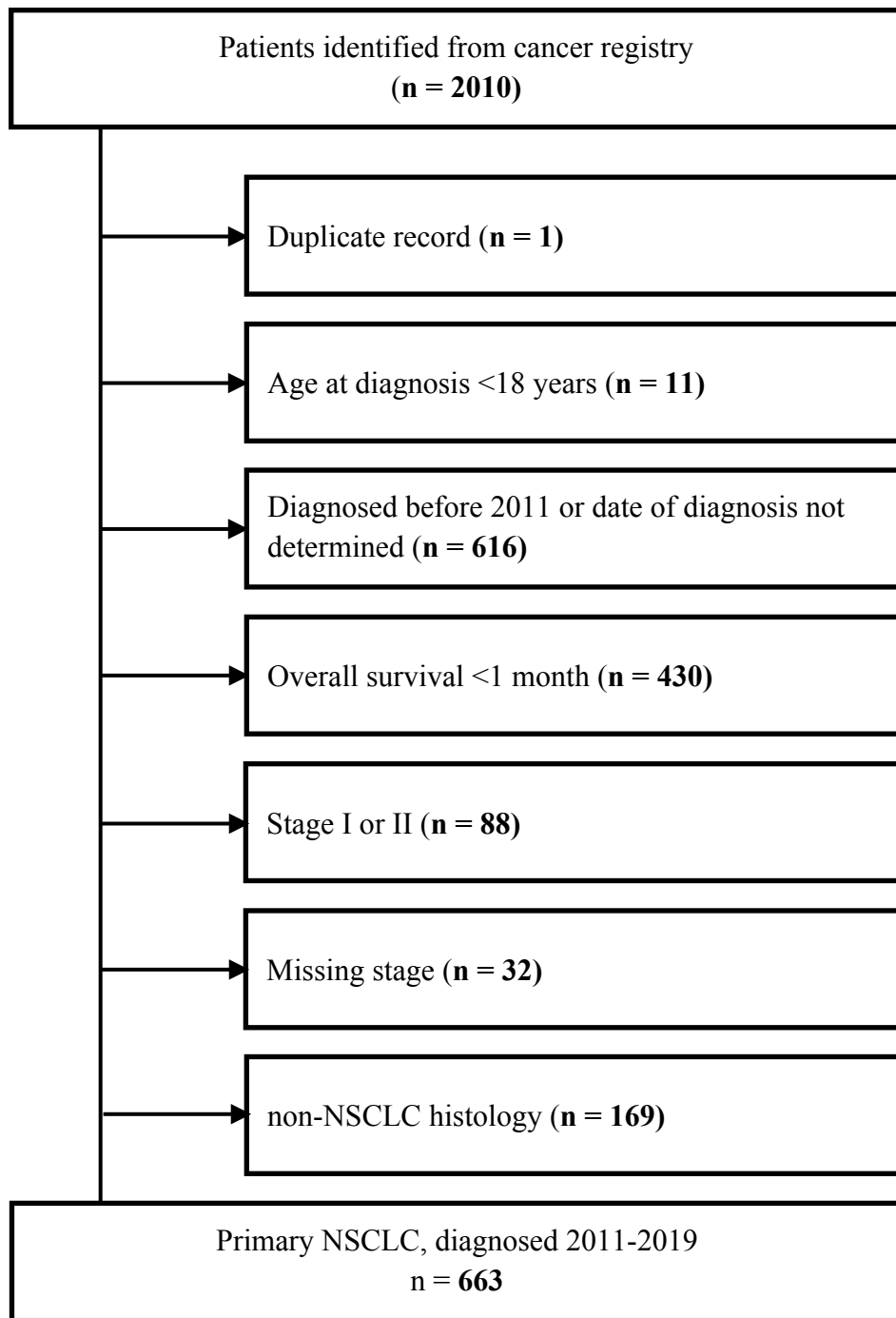
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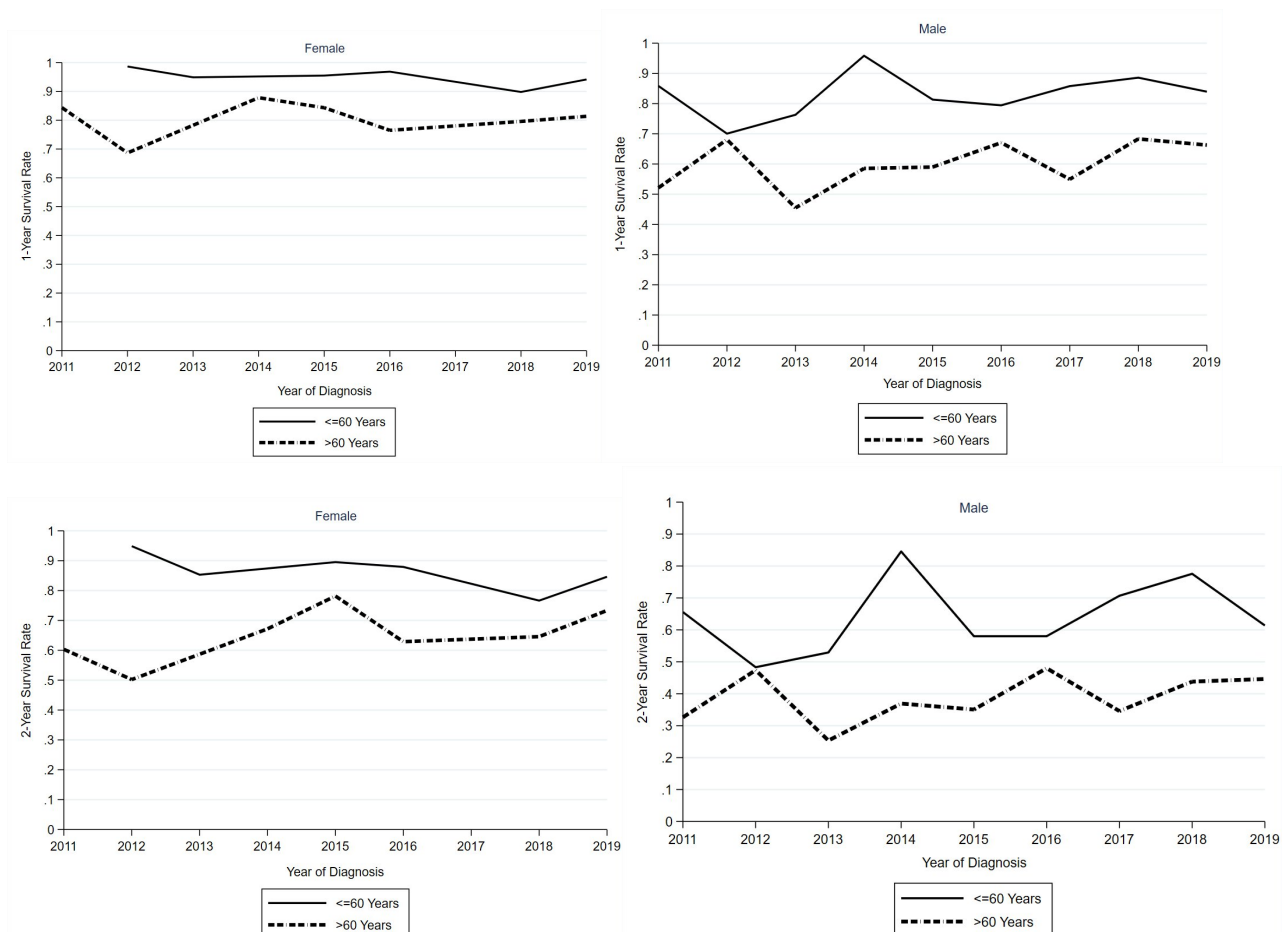
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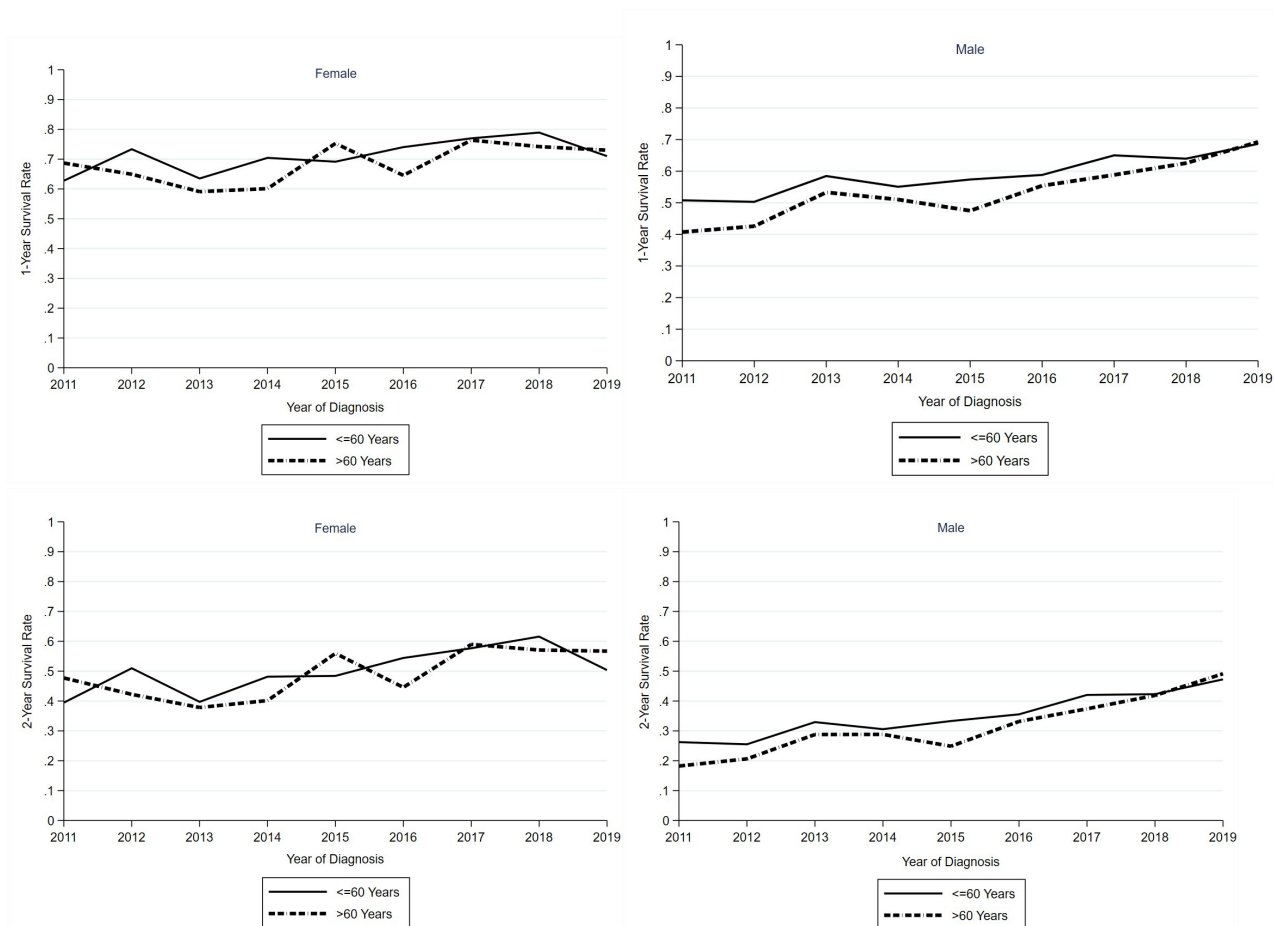
Key words: non-small cell lung cancer, advanced-stage, treatment pattern, survival trend, flexible parametric model.



Supplementary Figure 1. Flow diagram for primary non-small cell lung cancer patient inclusion.



Supplementary Figure 2. Trends in 1-year and 2-year survival rate by sex and age group in patients with primary non-small cell lung cancer stage III. Note: No cases were diagnosed among females aged ≤ 60 years in 2011; the corresponding trend line is therefore plotted from 2012 onward.



Supplementary Figure 3. Trends in 1-year and 2-year survival rate by sex and age group in patients with primary non-small cell lung cancer stage IV.

Supplementary Table 1. Trends of treatment modalities in primary non-small cell lung cancer stage III patients (2011 to 2019).

Year of diagnosis	No Treatment			Radiotherapy Only			Systemic Therapy Only			Systemic Therapy with Radiotherapy			Surgery ± Additional Treatment		
	n=40			n=14			n=34			n=30			n=19		
	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
2011	4	19.05	7.27-41.39	5	23.81	10.19-46.26	3	14.29	4.63-36.39	6	28.57	13.34-50.97	3	14.29	4.63-36.39
2012	4	25.00	9.62-51.08	2	12.50	93.10-38.91	5	31.25	13.53-56.91	2	12.50	3.10-38.91	3	18.75	6.11-45.02
2013	3	33.33	10.99-66.93	-	-	-	5	55.56	24.91-82.49	1	11.11	1.51-50.45	-	-	-
2014	3	33.33	10.99-66.93	1	11.11	1.51-50.45	-	-	-	4	44.44	17.51-75.09	1	11.11	1.51-50.45
2015	3	14.29	4.63-36.39	5	23.81	10.19-46.26	5	23.81	10.19-46.26	4	19.05	7.27-41.39	4	19.05	7.27-41.39
2016	5	33.33	14.48-59.63	-	-	-	4	26.67	10.28-53.57	3	20.00	6.52-47.26	3	20.00	6.52-47.26
2017	8	50.00	27.12-72.88	1	6.25	0.86-33.95	4	25.00	9.62-51.08	2	12.50	3.10-38.91	1	6.25	0.86-33.95
2018	5	38.46	16.83-65.87	-	-	-	4	30.77	11.93-59.33	2	15.38	3.82-45.40	2	15.38	3.82-45.40
2019	8	29.41	12.70-54.42	-	-	-	4	23.53	9.04-48.80	6	35.29	16.67-59.81	2	11.76	2.92-37.14

NSCLC, non-small cell lung cancer. Note: 2011 (n=21), 2012 (n=16), 2013 (n=9), 2014 (n=9), 2015 (n=21), 2016 (n=15), 2017 (n=16), 2018 (n=13), and 2019 (n=17). Overall p for Trend: 0.149

Supplementary Table 2. Trends of treatment modalities in primary non-small cell lung cancer stage IV patients (2011 to 2019).

Year of diagnosis	No Treatment			Radiotherapy Only			Systemic Therapy Only			Systemic Therapy with Radiotherapy			Surgery ± Additional Treatment		
	n=155			n=67			n=183			n=106			n=15		
	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
2011	16	34.78	22.50-49.49	8	17.39	8.93-31.13	11	23.91	13.75-38.26	8	17.39	8.93-31.13	3	6.52	2.13-18.40
2012	14	31.11	19.35-45.95	7	15.56	7.59-29.24	14	31.11	19.35-45.95	8	17.78	9.13-31.75	2	4.44	1.11-16.15
2013	8	14.29	7.30-26.08	10	17.86	9.87-30.14	23	41.07	29.02-54.30	15	26.79	16.82-39.83	-	-	-
2014	18	27.69	18.18-39.77	11	16.92	9.61-28.07	21	32.31	22.09-44.56	13	20.00	11.97-31.49	2	3.08	0.77-11.52
2015	17	29.82	19.40-42.88	7	12.28	5.96-23.63	18	31.58	20.87-44.68	15	26.32	16.51-39.20	-	-	-
2016	19	27.94	18.57-39.74	9	13.24	7.02-23.55	21	30.88	21.06-42.80	17	25.00	16.13-36.62	2	2.94	0.73-11.04
2017	22	31.88	21.98-43.74	7	10.14	4.91-19.81	25	36.23	25.78-48.17	12	17.39	10.14-28.21	3	4.35	1.41-12.66
2018	29	35.80	26.13-46.79	3	3.70	1.20-10.89	37	45.68	35.17-56.58	10	12.35	6.76-21.47	2	2.47	0.62-9.37
2019	12	30.77	18.35-46.77	5	12.82	5.43-27.37	13	33.33	20.42-49.35	8	20.51	10.59-36.00	1	2.56	0.36-16.15

NSCLC, non-small cell lung cancer. Note: 2011 (n=46), 2012 (n=45), 2013 (n=56), 2014 (n=65), 2015 (n=57), 2016 (n=68), 2017 (n=69), 2018 (n=81), and 2019 (n=39). Overall p for trend: 0.077.

Supplementary Table 3. Absolute change in 1-year and 2-year survival from 2011 to 2019 by treatment modality in patients with primary non-small cell lung cancer stage III.

Treatment Modalities	1-Year Survival	1-Year Survival	Absolute Change	2-Year Survival	2-Year Survival	Absolute Change
	2011	2019		2011	2019	
No Treatment	61.55%	69.12%	7.57%	52.20%	57.60%	5.40%
Radiotherapy Only	35.46%	61.17%	25.71%	18.66%	39.28%	20.62%
Systemic Therapy Only	54.02%	64.13%	10.11%	24.73%	36.11%	11.38%
Systemic Therapy with Radiotherapy	84.64%	88.16%	3.52%	61.20%	68.22%	7.02%
Surgery ± Additional Treatment	89.77%	96.44%	6.67%	66.66%	86.23%	19.57%

Supplementary Table 4. Absolute change in 1-year and 2-year survival from 2011 to 2019 by treatment modality in patients with primary non-small cell lung cancer stage IV.

Treatment Modalities	1-Year Survival	1-Year Survival	Absolute Change	2-Year Survival	2-Year Survival	Absolute Change
	2011	2019		2011	2019	
No Treatment	42.67%	67.11%	24.44%	24.52%	50.87%	26.35%
Radiotherapy Only	43.64%	55.74%	12.1%	21.11%	34.92%	13.81%
Systemic Therapy Only	58.91%	74.33%	15.42%	34.10%	54.31%	20.21%
Systemic Therapy with Radiotherapy	60.38%	75.10%	14.72%	30.39%	52.20%	21.81%
Surgery ± Additional Treatment	67.22%	86.93%	19.71%	36.50%	69.96%	33.46%

Supplementary Table 5. Absolute change in 1-year and 2-year survival from 2011 to 2019 by sex and age group in patients with primary non-small cell lung cancer stage III.

Sex	Age Group	1-Year Survival	1-Year Survival	Absolute Change	2-Year Survival	2-Year Survival	Absolute Change
		2011	2019		2011	2019	
Female	≤60*	98.65%	94.16%	-4.49%	94.86%	84.62%	-10.24%
	>60	84.38%	81.36%	-3.02%	60.33%	73.32%	12.99%
Male	≤60	85.84%	81.36%	-4.48%	65.58%	61.37%	-4.21%
	>60	52.11%	66.27%	14.16%	32.62%	44.62%	12.00%

*For females aged ≤60 years, absolute change in 1- and 2-year survival was calculated for 2012-2019, as no cases were diagnosed in this subgroup in 2011.

Supplementary Table 6. Absolute change in 1-year and 2-year survival from 2011 to 2019 by sex and age group in patients with primary non-small cell lung cancer stage IV.

Sex	Age Group	1-Year Survival	1-Year Survival	Absolute Change	2-Year Survival	2-Year Survival	Absolute Change
		2011	2019		2011	2019	
Female	≤60	62.77%	71.01%	8.24%	39.46%	50.36%	10.90%
	>60	68.68%	73.01%	4.33%	47.72%	56.71%	8.99%
Male	≤60	50.78%	68.65%	17.87%	26.25%	47.27%	21.02%
	>60	40.73%	69.24%	28.51%	18.24%	49.12%	30.88%

Supplementary Table 7. Predictors of receiving radiotherapy only for patients with primary non-small cell lung cancer stage III (2011 to 2019).

	Radiotherapy Only (n = 14)					
	Univariable			Multivariable		
	OR	95% CI	p value	OR	95% CI	p value
Sex						
Female	Reference			-	-	-
Male	1.78	0.31-10.28	0.518			
Age at Diagnosis (Years)						
≤60	Reference			Reference		
>60	3.44	0.84-13.99	0.085	3.00	0.73-12.43	0.129
Period of Diagnosis						
2011-2013	Reference			Reference		
2014-2016	0.87	0.28-2.71	0.806	0.80	0.25-2.53	0.699
2017-2019	0.17	0.03-1.05	0.057	0.19	0.03-1.16	0.072
Tobacco (Current/Past)						
No	Reference			-	-	-
Yes	1.07	0.30-3.80	0.914			
Alcohol (Current/Past)						
No	Reference			-	-	-
Yes	3.83	0.52-28.09	0.187			
Histology						
Other	Reference			-	-	-
Squamous Cell Carcinoma	1.67	0.39-7.23	0.491			
Adenocarcinoma	0.49	0.08-3.07	0.449			

NSCLC, non-small cell lung cancer; OR, odds ratio; CI, confidence interval.

Supplementary Table 8. Predictors of receiving radiotherapy only for patients with primary non-small cell lung cancer stage IV (2011 to 2019).

	Radiotherapy Only (n = 67)					
	Univariable			Multivariable		
	OR	95% CI	p value	OR	95% CI	p value
Sex						
Female	Reference			-	-	-
Male	1.46	0.80-2.66	0.218			
Age at Diagnosis (Years)						
≤60	Reference			-	-	-
>60	1.30	0.77-2.21	0.330			
Period of Diagnosis						
2011-2013	Reference			Reference		
2014-2016	0.81	0.45-1.45	0.477	0.88	0.48-1.60	0.670
2017-2019	0.43	0.22-0.84	0.013	0.46	0.23-0.92	0.027
Tobacco (Current/Past)						
No	Reference			Reference		
Yes	2.28	1.29-4.01	0.004	1.73	0.95-3.15	0.072
Alcohol (Current/Past)						
No	Reference			-	-	-
Yes	0.60	0.16-2.25	0.449			
Histology						
Other	Reference			Reference		
Squamous Cell Carcinoma	2.46	1.19-5.10	0.015	2.23	1.06-4.71	0.036
Adenocarcinoma	0.79	0.41-1.54	0.495	0.90	0.46-1.76	0.761

NSCLC, non-small cell lung cancer; OR, odds ratio; CI, confidence interval.

Supplementary Table 9. Predictors of receiving surgery ± additional treatment for patients with primary non-small cell lung cancer stage III (2011 to 2019).

	Surgery ± Additional Treatment (n = 19)					
	Univariable			Multivariable		
	OR	95% CI	p value	OR	95% CI	p value
Sex Female Male	Reference 0.59	0.19-1.91	0.381	- -	- -	- -
Age at Diagnosis (Years) ≤60 >60	Reference 0.24	0.09-0.66	0.006	Reference 0.25	0.09-0.70	0.008
Period of Diagnosis 2011-2013 2014-2016 2017-2019	Reference 1.41 0.83	0.46-4.30 0.24-2.78	0.543 0.758	- - -	- - -	- - -
Tobacco (Current/Past) No Yes	Reference 0.37	0.14-0.99	0.048	Reference 0.40	0.15-1.12	0.081
Alcohol (Current/Past) No Yes	Reference 2.68	0.37-19.28	0.329	- -	- -	- -
Histology Other Squamous Cell Carcinoma Adenocarcinoma	Reference 0.66 1.72	0.16-2.65 0.46-6.44	0.558 0.421	- - -	- - -	- - -

NSCLC, non-small cell lung cancer; OR, odds ratio; CI, confidence interval.

Supplementary Table 10. Predictors of receiving surgery ± additional treatment for patients with primary non-small cell lung cancer stage IV (2011 to 2019).

	Surgery ± Additional Treatment (n = 15)					
	Univariable			Multivariable		
	OR	95% CI	<i>p</i> value	OR	95% CI	<i>p</i> value
Sex						
Female	Reference			-	-	-
Male	1.49	0.45-4.94	0.517			
Age at Diagnosis (Years)						
≤60	Reference			-	-	-
>60	0.62	0.23-1.67	0.341			
Period of Diagnosis						
2011-2013	Reference			-	-	-
2014-2016	0.63	0.18-2.21	0.467			
2017-2019	0.92	0.29-2.92	0.884			
Tobacco (Current/Past)						
No	Reference			-	-	-
Yes	0.87	0.32-2.36	0.786			
Alcohol (Current/Past)						
No	Reference			-	-	-
Yes	1.75	0.31-9.83	0.522			
Histology						
Other	Reference			-	-	-
Squamous Cell Carcinoma	0.85	0.22-3.35	0.819			
Adenocarcinoma	0.50	0.16-1.53	0.225			

NSCLC, non-small cell lung cancer; OR, odds ratio; CI, confidence interval.

STATA CODE FOR ANALYSIS (Stage III)

Stpm2

- `stpm2 i.sex age_diagnosis year_diagnosis i.tobacco_cat i.histology i.trt if staging==3, df(3) tvc(trt year_diagnosis) dftvc(1) scale(hazard) eform diff nolog`

Predicting Trends in 1-Year and 2-Year Survival Rate

- `stpm2 i.sex age_diagnosis year_diagnosis i.tobacco_cat i.histology i.trt if staging==3, df(3) tvc(trt year_diagnosis) dftvc(1) scale(hazard) eform diff nolog`
- `gen time1=1`
- `predict surv1yr if staging==3, survival timevar(time1)`
- `gen time2=2`
- `predict surv2yr if staging==3, survival timevar(time2)`
- `bysort trt year_diagnosis: egen surv1m=mean(surv1yr)`
- `bysort trt year_diagnosis: egen surv2m=mean(surv2yr)`
- `bysort trt year_diagnosis: gen count=_n`
- `twoway (line surv1m year_diagnosis if trt==0 & count==1, sort lp(solid) lc(black) lw(medthick)) (line surv1m year_diagnosis if trt==1 & count==1, sort lp(shortdash) lc(black) lw(medthick)) (line surv1m year_diagnosis if trt==2 & count==1, sort lp(longdash) lc(black) lw(medthick)) (line surv1m year_diagnosis if trt==3 & count==1, sort lp("-.") lc(black) lw(medthick)) (line surv1m year_diagnosis if trt==4 & count==1, sort lp("--.") lc(black) lw(thick)), ytitle("1-Year Survival Rate", size(3)) ylabel(0(0.1)1, angle(horizontal)) xtitle("Year of Diagnosis", size(3)) xlabel(2011(1)2019) ysize(4) xsize(5.5) plotregion(margin(zero)) legend(order(1 "No Treatment" 2 "Radiotherapy Only" 3 "Systemic Therapy Only" 4 "Systemic Therapy with Radiotherapy" 5 "Surgery ± Additional Treatment")) rows(5)) graphregion(color(white)) name(trt1, replace)`
- `twoway (line surv2m year_diagnosis if trt==0 & count==1, sort lp(solid) lc(black) lw(medthick)) (line surv2m year_diagnosis if trt==1 & count==1, sort lp(shortdash) lc(black) lw(medthick)) (line surv2m year_diagnosis if trt==2 & count==1, sort lp(longdash) lc(black) lw(medthick)) (line surv2m year_diagnosis if trt==3 & count==1, sort lp("-.") lc(black) lw(medthick)) (line surv2m year_diagnosis if trt==4 & count==1, sort lp("--.") lc(black) lw(thick)), ytitle("2-Year Survival Rate", size(3)) ylabel(0(0.1)1, angle(horizontal)) xtitle("Year of Diagnosis", size(3)) xlabel(2011(1)2019) ysize(4) xsize(5.5) plotregion(margin(zero)) legend(order(1 "No Treatment" 2 "Radiotherapy Only" 3 "Systemic Therapy Only" 4 "Systemic Therapy with Radiotherapy" 5 "Surgery ± Additional Treatment")) rows(5)) graphregion(color(white)) name(trt12, replace)`

Absolute Change in 1-Year and 2-Year Survival by Treatment Modalities

- `gen surv1_2011 = .`
- `gen surv1_2019 = .`
- `gen surv2_2011 = .`
- `gen surv2_2019 = .`
- `replace surv1_2011 = surv1m if year_diagnosis == 2011`
- `replace surv1_2019 = surv1m if year_diagnosis == 2019`
- `replace surv2_2011 = surv2m if year_diagnosis == 2011`
- `replace surv2_2019 = surv2m if year_diagnosis == 2019`
- `bysort trt (year_diagnosis): replace surv1_2011 = surv1_2011[_n-1] if missing(surv1_2011)`

- bysort trt (year_diagnosis): replace surv2_2011 = surv2_2011[_n-1] if missing(surv2_2011)
- gen surv1_absdiff = surv1_2019 - surv1_2011
- gen surv2_absdiff = surv2_2019 - surv2_2011
- list trt surv1_2011 surv1_2019 surv1_absdiff surv2_2011 surv2_2019 surv2_absdiff if year_diagnosis == 2019, sep(0)

Trends in 1-Year Survival Rate based on Sex and Age Group

- capture drop surv1m -count
- bysort sex age60 year_diagnosis: egen surv1m=mean(surv1yr)
- bysort sex age60 year_diagnosis: gen count=_n
- twoway (line surv1m year_diagnosis if age60==0 & count==1 & sex==0, sort lp(solid) lc(black) lw(medthick)) (line surv1m year_diagnosis if age60==1 & count==1 & sex==0, lp("--.") lc(black) lw(thick)), title("Female", size(5)) ytitle("1-Year Survival Rate", size(3)) ylabel(0(0.1)1, angle(horizontal)) xtitle("Year of Diagnosis", size(3)) xlabel(2011(1)2019) ysize(4) xsize(5.5) plotregion(margin(zero)) legend(order(1 "<=60 Years" 2 ">60 Years") rows(2)) graphregion(color(white)) name(female, replace)
- twoway (line surv1m year_diagnosis if age60==0 & count==1 & sex==1, sort lp(solid) lc(black) lw(medthick)) (line surv1m year_diagnosis if age60==1 & count==1 & sex==1, lp("--.") lc(black) lw(thick)), title("Male", size(5)) ytitle("1-Year Survival Rate", size(3)) ylabel(0(0.1)1, angle(horizontal)) xtitle("Year of Diagnosis", size(3)) xlabel(2011(1)2019) ysize(4) xsize(5.5) plotregion(margin(zero)) legend(order(1 "<=60 Years" 2 ">60 Years") rows(2)) graphregion(color(white)) name(male, replace)

Trends in 2-Year Survival Rate based on Sex and Age Group

- drop count
- bysort sex age60 year_diagnosis: egen surv2m=mean(surv2yr)
- bysort sex age60 year_diagnosis: gen count=_n
- twoway (line surv2m year_diagnosis if age60==0 & count==1 & sex==0, sort lp(solid) lc(black) lw(medthick)) (line surv2m year_diagnosis if age60==1 & count==1 & sex==0, lp("--.") lc(black) lw(thick)), title("Female", size(5)) ytitle("2-Year Survival Rate", size(3)) ylabel(0(0.1)1, angle(horizontal)) xtitle("Year of Diagnosis", size(3)) xlabel(2011(1)2019) ysize(4) xsize(5.5) plotregion(margin(zero)) legend(order(1 "<=60 Years" 2 ">60 Years") rows(2)) graphregion(color(white)) name(female, replace)
- twoway (line surv2m year_diagnosis if age60==0 & count==1 & sex==1, sort lp(solid) lc(black) lw(medthick)) (line surv2m year_diagnosis if age60==1 & count==1 & sex==1, lp("--.") lc(black) lw(thick)), title("Male", size(5)) ytitle("2-Year Survival Rate", size(3)) ylabel(0(0.1)1, angle(horizontal)) xtitle("Year of Diagnosis", size(3)) xlabel(2011(1)2019) ysize(4) xsize(5.5) plotregion(margin(zero)) legend(order(1 "<=60 Years" 2 ">60 Years") rows(2)) graphregion(color(white)) name(male, replace)

Absolute Change in 1-Year and 2-Year Survival by Sex and Age Group

- capture drop surv1_2011 surv1_2019 surv1_absdiff surv2_2011 surv2_2019 surv2_absdiff
- gen surv1_2011 = .
- gen surv1_2019 = .

- gen surv2_2011 = .
- gen surv2_2019 = .
- replace surv1_2011 = surv1m if year_diagnosis == 2011
- replace surv1_2019 = surv1m if year_diagnosis == 2019
- replace surv2_2011 = surv2m if year_diagnosis == 2011
- replace surv2_2019 = surv2m if year_diagnosis == 2019
- bysort sex age60 (year_diagnosis): replace surv1_2011 = surv1_2011[_n-1] if missing(surv1_2011)
- bysort sex age60 (year_diagnosis): replace surv1_2011 = surv1_2011[_n-1] if missing(surv1_2011)
- bysort sex age60 (year_diagnosis): replace surv1_2019 = surv1_2019[_n-1] if missing(surv1_2019)
- bysort sex age60 (year_diagnosis): replace surv1_2019 = surv1_2019[_n-1] if missing(surv1_2019)
- bysort sex age60 (year_diagnosis): replace surv2_2011 = surv2_2011[_n-1] if missing(surv2_2011)
- bysort sex age60 (year_diagnosis): replace surv2_2011 = surv2_2011[_n-1] if missing(surv2_2011)
- bysort sex age60 (year_diagnosis): replace surv2_2019 = surv2_2019[_n-1] if missing(surv2_2019)
- bysort sex age60 (year_diagnosis): replace surv2_2019 = surv2_2019[_n-1] if missing(surv2_2019)
- gen surv1_absdiff = surv1_2019 - surv1_2011
- gen surv2_absdiff = surv2_2019 - surv2_2011
- list sex age60 surv1_2011 surv1_2019 surv1_absdiff surv2_2011 surv2_2019 surv2_absdiff if year_diagnosis == 2019, sep(0)

STATA CODE FOR ANALYSIS (Stage IV)

Stpm2

- stpm2 i.sex age_diagnosis year_diagnosis i.tobacco_cat i.histology i.trt if staging==4, df(3) tvc(trt year_diagnosis) dftvc(1) scale(hazard) eform diff nolog

Predicting Trends in 1-Year and 2-Year Survival Rate

- stpm2 i.sex age_diagnosis year_diagnosis i.tobacco_cat i.histology i.trt if staging==4, df(3) tvc(trt year_diagnosis) dftvc(1) scale(hazard) eform diff nolog
- gen time1=1
- predict surv1yr if staging==4, survival timevar(time1)
- gen time2=2
- predict surv2yr if staging==4, survival timevar(time2)
- bysort trt year_diagnosis: egen surv1m=mean(surv1yr)
- bysort trt year_diagnosis: egen surv2m=mean(surv2yr)
- bysort trt year_diagnosis: gen count=_n
- twoway (line surv1m year_diagnosis if trt==0 & count==1, sort lp(solid) lc(black) lw(medthick)) (line surv1m year_diagnosis if trt==1 & count==1, sort lp(shortdash) lc(black) lw(medthick)) (line surv1m year_diagnosis if trt==2 & count==1, sort lp(longdash) lc(black) lw(medthick)) (line surv1m year_diagnosis if trt==3 & count==1, sort lp("-.") lc(black) lw(medthick)) (line surv1m year_diagnosis if trt==4 & count==1, sort lp("--.") lc(black) lw(thick)), ytitle("1-Year Survival Rate", size(3)) ylabel(0(0.1)1, angle(horizontal)) xtitle("Year of Diagnosis", size(3)) xlabel(2011(1)2019) ysize(4) xsize(5.5) plotregion(margin(zero)) legend(order(1 "No Treatment" 2 "Radiotherapy Only" 3 "Systemic Therapy Only" 4 "Systemic Therapy with Radiotherapy" 5 "Surgery ± Additional Treatment") rows(5)) graphregion(color(white)) name(trt1, replace)
- twoway (line surv2m year_diagnosis if trt==0 & count==1, sort lp(solid) lc(black) lw(medthick)) (line surv2m year_diagnosis if trt==1 & count==1, sort lp(shortdash) lc(black) lw(medthick)) (line surv2m year_diagnosis if trt==2 & count==1, sort lp(longdash) lc(black) lw(medthick)) (line surv2m year_diagnosis if trt==3 & count==1, sort lp("-.") lc(black) lw(medthick)) (line surv2m year_diagnosis if trt==4 & count==1, sort lp("--.") lc(black) lw(thick)), ytitle("2-Year Survival Rate", size(3)) ylabel(0(0.1)1, angle(horizontal)) xtitle("Year of Diagnosis", size(3)) xlabel(2011(1)2019) ysize(4) xsize(5.5) plotregion(margin(zero)) legend(order(1 "No Treatment" 2 "Radiotherapy Only" 3 "Systemic Therapy Only" 4 "Systemic Therapy with Radiotherapy" 5 "Surgery ± Additional Treatment") rows(5)) graphregion(color(white)) name(trt12, replace)

Absolute Change in 1-Year and 2-Year Survival by Treatment Modalities

- gen surv1_2011 = .
- gen surv1_2019 = .
- gen surv2_2011 = .
- gen surv2_2019 = .
- replace surv1_2011 = surv1m if year_diagnosis == 2011
- replace surv1_2019 = surv1m if year_diagnosis == 2019
- replace surv2_2011 = surv2m if year_diagnosis == 2011
- replace surv2_2019 = surv2m if year_diagnosis == 2019

- bysort trt (year_diagnosis): replace surv1_2011 = surv1_2011[_n-1] if missing(surv1_2011)
- bysort trt (year_diagnosis): replace surv2_2011 = surv2_2011[_n-1] if missing(surv2_2011)
- gen surv1_absdiff = surv1_2019 - surv1_2011
- gen surv2_absdiff = surv2_2019 - surv2_2011
- list trt surv1_2011 surv1_2019 surv1_absdiff surv2_2011 surv2_2019 surv2_absdiff if year_diagnosis == 2019, sep(0)

Trends in 1-Year Survival Rate based on Sex and Age Group

- capture drop surv1m -count
- bysort sex age60 year_diagnosis: egen surv1m=mean(surv1yr)
- bysort sex age60 year_diagnosis: gen count=_n
- twoway (line surv1m year_diagnosis if age60==0 & count==1 & sex==0, sort lp(solid) lc(black) lw(medthick)) (line surv1m year_diagnosis if age60==1 & count==1 & sex==0, lp("--") lc(black) lw(thick)), title("Female", size(5)) ytitle("1-Year Survival Rate", size(3)) ylabel(0(0.1)1, angle(horizontal)) xtitle("Year of Diagnosis", size(3)) xlabel(2011(1)2019) ysize(4) xsize(5.5) plotregion(margin(zero)) legend(order(1 "<=60 Years" 2 ">60 Years") rows(2)) graphregion(color(white)) name(female, replace)
- twoway (line surv1m year_diagnosis if age60==0 & count==1 & sex==1, sort lp(solid) lc(black) lw(medthick)) (line surv1m year_diagnosis if age60==1 & count==1 & sex==1, lp("--") lc(black) lw(thick)), title("Male", size(5)) ytitle("1-Year Survival Rate", size(3)) ylabel(0(0.1)1, angle(horizontal)) xtitle("Year of Diagnosis", size(3)) xlabel(2011(1)2019) ysize(4) xsize(5.5) plotregion(margin(zero)) legend(order(1 "<=60 Years" 2 ">60 Years") rows(2)) graphregion(color(white)) name(male, replace)

Trends in 2-Year Survival Rate based on Sex and Age Group

- drop count
- bysort sex age60 year_diagnosis: egen surv2m=mean(surv2yr)
- bysort sex age60 year_diagnosis: gen count=_n
- twoway (line surv2m year_diagnosis if age60==0 & count==1 & sex==0, sort lp(solid) lc(black) lw(medthick)) (line surv2m year_diagnosis if age60==1 & count==1 & sex==0, lp("--") lc(black) lw(thick)), title("Female", size(5)) ytitle("2-Year Survival Rate", size(3)) ylabel(0(0.1)1, angle(horizontal)) xtitle("Year of Diagnosis", size(3)) xlabel(2011(1)2019) ysize(4) xsize(5.5) plotregion(margin(zero)) legend(order(1 "<=60 Years" 2 ">60 Years") rows(2)) graphregion(color(white)) name(female, replace)
- twoway (line surv2m year_diagnosis if age60==0 & count==1 & sex==1, sort lp(solid) lc(black) lw(medthick)) (line surv2m year_diagnosis if age60==1 & count==1 & sex==1, lp("--") lc(black) lw(thick)), title("Male", size(5)) ytitle("2-Year Survival Rate", size(3)) ylabel(0(0.1)1, angle(horizontal)) xtitle("Year of Diagnosis", size(3)) xlabel(2011(1)2019) ysize(4) xsize(5.5) plotregion(margin(zero)) legend(order(1 "<=60 Years" 2 ">60 Years") rows(2)) graphregion(color(white)) name(male, replace)

Absolute Change in 1-Year and 2-Year Survival by Sex and Age Group

- capture drop surv1_2011 surv1_2019 surv1_absdiff surv2_2011 surv2_2019 surv2_absdiff
- gen surv1_2011 = .

- `gen surv1_2019 = .`
- `gen surv2_2011 = .`
- `gen surv2_2019 = .`
- `replace surv1_2011 = surv1m if year_diagnosis == 2011`
- `replace surv1_2019 = surv1m if year_diagnosis == 2019`
- `replace surv2_2011 = surv2m if year_diagnosis == 2011`
- `replace surv2_2019 = surv2m if year_diagnosis == 2019`
- `bysort sex age60 (year_diagnosis): replace surv1_2011 = surv1_2011[_n-1] if missing(surv1_2011)`
- `bysort sex age60 (year_diagnosis): replace surv1_2011 = surv1_2011[_n-1] if missing(surv1_2011)`
- `bysort sex age60 (year_diagnosis): replace surv1_2019 = surv1_2019[_n-1] if missing(surv1_2019)`
- `bysort sex age60 (year_diagnosis): replace surv1_2019 = surv1_2019[_n-1] if missing(surv1_2019)`
- `bysort sex age60 (year_diagnosis): replace surv2_2011 = surv2_2011[_n-1] if missing(surv2_2011)`
- `bysort sex age60 (year_diagnosis): replace surv2_2011 = surv2_2011[_n-1] if missing(surv2_2011)`
- `bysort sex age60 (year_diagnosis): replace surv2_2019 = surv2_2019[_n-1] if missing(surv2_2019)`
- `bysort sex age60 (year_diagnosis): replace surv2_2019 = surv2_2019[_n-1] if missing(surv2_2019)`
- `gen surv1_absdiff = surv1_2019 - surv1_2011`
- `gen surv2_absdiff = surv2_2019 - surv2_2011`
- `list sex age60 surv1_2011 surv1_2019 surv1_absdiff surv2_2011 surv2_2019 surv2_absdiff if year_diagnosis == 2019, sep(0)`

Sensitivity Analysis to Number of Knots

- `range temptime 0 5 200`
- `forvalues i = 1/6 {`
`quietly stpm2 trt, df(`i') scale(hazard)`
`predict h0_df `i', hazard timevar(temptime) per(1000) zeros`
`predict s0_df `i', survival timevar(temptime) zeros`
`estimates store df `i'`
`}`
- `estimates table df*, keep(trt) b(%6.5f) se(%6.5f) stats(AIC BIC) stfmt(%6.2f)`