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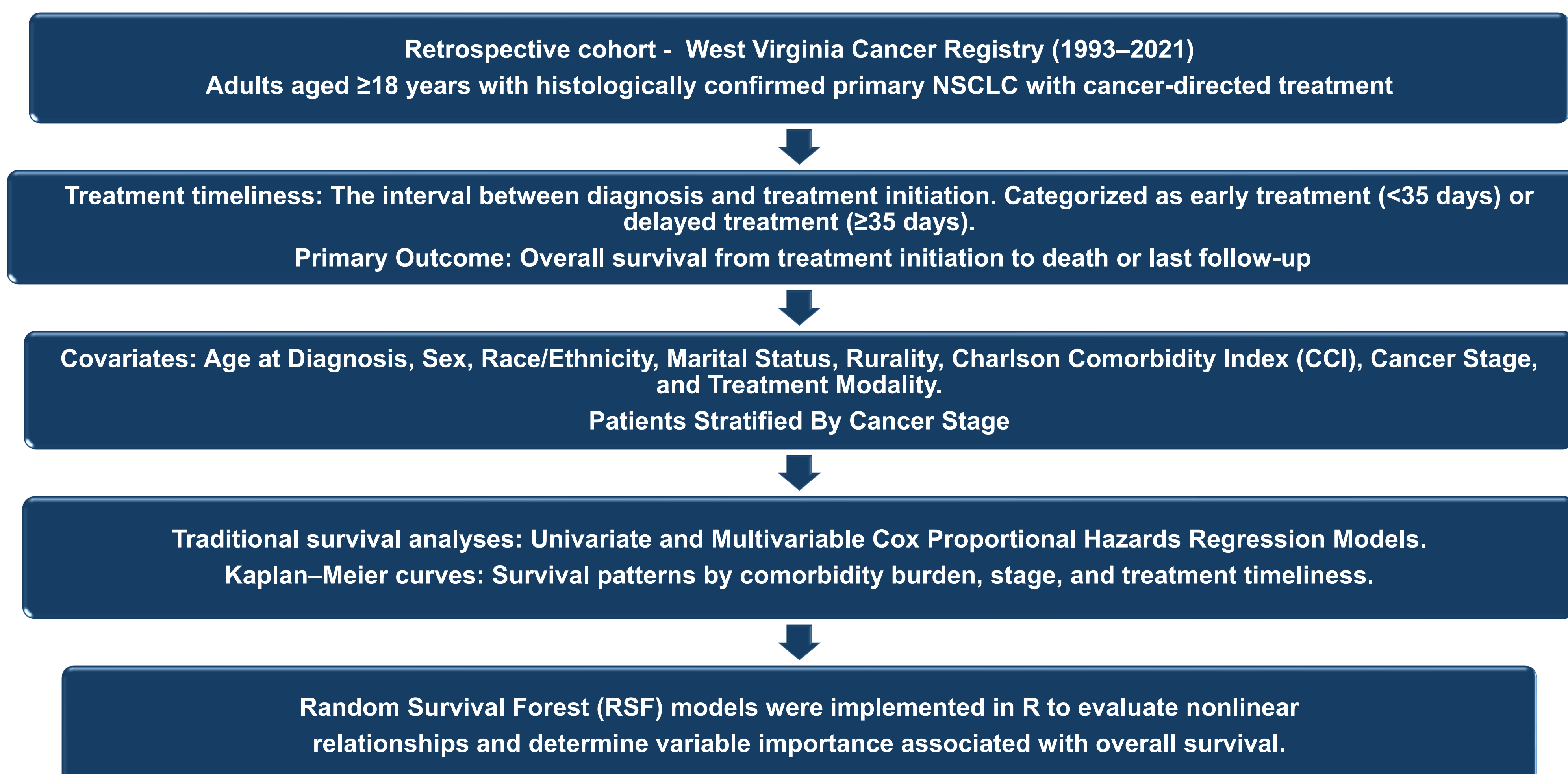
## INTRODUCTION

- Lung cancer is among one of the leading causes of cancer-related mortality in the United States, with non-small cell lung cancer (NSCLC) accounting for approximately 85% of cases. Treatment delays are common and may influence survival outcomes.
- Treatment timeliness is frequently used as a quality-of-care metric in oncology; however, studies evaluating its association with survival in NSCLC have reported inconsistent findings. Some studies show delayed treatment worsens outcomes, particularly in early-stage disease, while others report neutral or paradoxically improved survival with delayed care.
- These inconsistent findings may be driven by confounding from cancer stage, disease severity, frailty, comorbidity burden, and treatment prioritization. Patients with advanced-stage disease often receive faster treatment because of aggressive clinical presentation but may still experience poorer survival.
- A previous West Virginia Cancer Registry study reported that approximately 61% of patients with NSCLC initiated treatment within 35 days of diagnosis, with earlier treatment more common among advanced-stage patients. The study suggested that cancer stage strongly influences both treatment timing and survival outcomes.
- Traditional survival models may not be able to capture nonlinear and stage-dependent relationships between treatment timeliness and mortality. Random Survival Forest (RSF), a machine learning-based survival method for right-censored data, can model complex interactions and identify important predictors of survival without assuming linearity.

## STUDY OBJECTIVE

The study objective was to evaluate the association between treatment timeliness and overall survival in NSCLC stratified by cancer stage, while identifying additional effect modifiers using both traditional survival analysis and Random Survival Forest models.

## METHODS

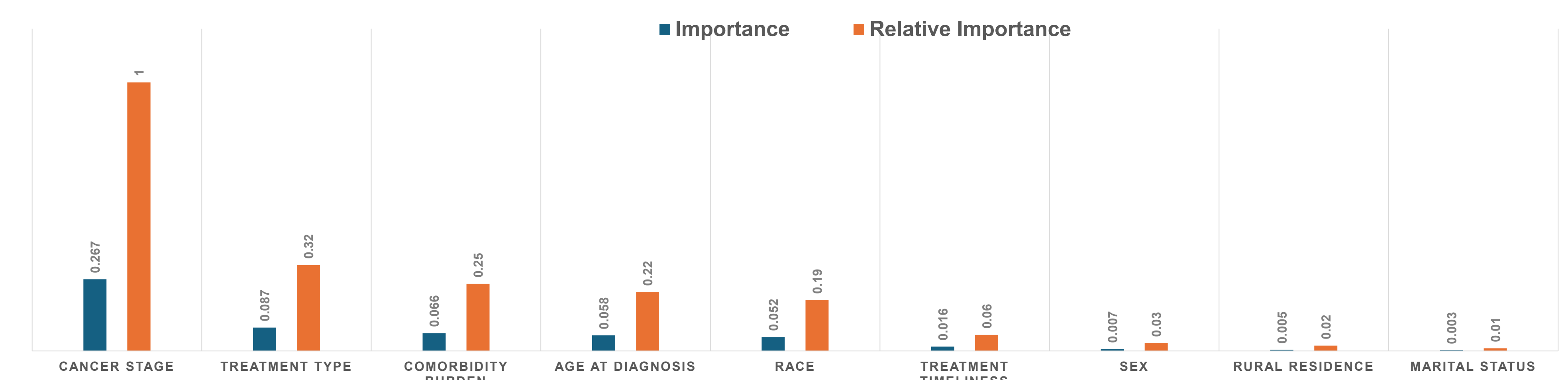


## RESULTS

- A total of 10,463 treated patients with NSCLC were included, of whom 61% received early treatment (<35 days). Patients receiving delayed treatment were older and more likely to present with stage I disease.
- In stage-stratified Cox models, delayed treatment was associated with worse survival in stage I NSCLC (HR=1.11, 95% CI: 1.02–1.20, p=0.011), but lower mortality in stage II (HR=0.85, 95% CI: 0.74–0.96, p=0.0095), stage III (HR=0.85, 95% CI: 0.77–0.92, p=0.0002), and stage IV disease (HR=0.64, 95% CI: 0.60–0.69, p<0.0001)
- Increasing age, higher Charlson Comorbidity Index, and male sex were consistently associated with poorer overall survival across stages. Rural residence was associated with higher mortality in stage II disease.
- Random Survival Forest analysis identified cancer stage, treatment type, comorbidity burden, and age as the strongest predictors of survival, while treatment timeliness showed a comparatively smaller relative contribution.

Variable	Stage 1		Stage 2		Stage 3		Stage 4	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
<b>Treatment Time</b>								
Early Treatment	Ref	-	-	-	-	-	-	-
Delayed Treatment	1.107 (1.024-1.197)	0.011	0.845 (0.744-0.960)	0.0095	0.845 (0.774-0.922)	0.0002	0.643 (0.596-0.693)	<0.0001
<b>Age at Diagnosis</b>	1.026 (1.022-1.031)	<0.0001	1.022 (1.015-1.029)	<0.0001	1.011 (1.007-1.016)	<0.0001	1.006 (1.002-1.009)	0.001
<b>Charlson Comorbidity Index</b>	1.093 (1.054-1.133)	<0.0001	1.073 (1.011-1.139)	0.0212	1.065 (1.022-1.111)	0.0029	1.055 (1.024-1.087)	0.0004
<b>Region</b>								
Urban	Ref	-	-	-	-	-	-	-
Rural	1.073 (0.914-1.260)	0.3892	1.331 (1.009-1.754)	0.0427	0.937 (0.796-1.104)	0.4398	1.123 (0.984-1.281)	0.0858
<b>Sex</b>								
Female	Ref	-	-	-	-	-	-	-
Male	1.285 (1.189-1.389)	<0.0001	1.319 (1.155-1.506)	<0.0001	1.219 (1.112-1.337)	<0.0001	1.127 (1.050-1.209)	0.0009
<b>Race</b>								
Non-Hispanic White	Ref	-	-	-	-	-	-	-
Hispanic	2.021 (0.840-4.865)	0.1162	2.743 (0.383-19.628)	0.315	2.586 (0.646-10.344)	0.1792	1.510 (0.676-3.376)	0.315
Non-Hispanic Black	1.035 (0.801-1.337)	0.7933	1.171 (0.783-1.753)	0.442	0.830 (0.608-1.132)	0.2382	0.900 (0.710-1.142)	0.3862
Others	1.811 (0.752-4.361)	0.1855	1.419 (0.353-5.705)	0.6218	1.053 (0.262-4.230)	0.9415	0.838 (0.450-1.562)	0.5775
<b>Marital status</b>								
Not Married	Ref	-	-	-	-	-	-	-
Married	0.868 (0.802-0.904)	0.0005	0.897 (0.788-1.021)	0.1	0.975 (0.890-1.068)	0.5866	0.960 (0.895-1.030)	0.2564
<b>Treatment Type</b>								
Other treatments	Ref	-	-	-	-	-	-	-
Radiation	0.844 (0.210-3.396)	0.811	0.122 (0.030-0.502)	0.0036	0.109 (0.044-0.267)	<0.0001	0.402 (0.260-0.620)	<0.0001
Surgery	0.383 (0.095-1.534)	0.175	0.048 (0.012-0.198)	<0.0001	0.058 (0.023-0.141)	<0.0001	0.236 (0.151-0.367)	<0.0001
Systemic	0.658 (0.164-2.645)	0.555	0.049 (0.012-0.203)	<0.0001	0.054 (0.022-0.133)	<0.0001	0.191 (0.124-0.293)	<0.0001

VARIABLE IMPORTANCE MEASURES FROM RANDOM SURVIVAL FOREST ANALYSIS



## DISCUSSION

- Treatment timeliness demonstrated stage-dependent associations with survival in NSCLC, with delayed treatment associated with worse outcomes in stage I but lower mortality in advanced stages.
- Random Survival Forest analyses identified cancer stage and treatment modality as stronger predictors of survival than treatment timeliness alone.
- Future research should focus on evaluation of treatment delays in NSCLC based on the stage and underlying factors.