



Changes in Mortality Rates with the Introduction of Immuno-Oncology Therapy in Advanced Non-Small Cell Lung Cancer: A SEER-Medicare Analysis

Yeijin Kim^{1,2,3}, Jiyeon Lee^{3,4}, Chanhyun Park¹, Hae Sun Suh^{2,3,4}

¹ Health Outcomes Division, College of Pharmacy, The University of Texas at Austin; ² College of Pharmacy, Kyung Hee University, Republic of Korea;

³ Institute of Regulatory Innovation through Science, Kyung Hee University, Republic of Korea; ⁴ Department of Regulatory Science, Graduate School, Kyung Hee University, Republic of Korea.

BACKGROUND

- Lung cancer remained the leading cause of cancer-related mortality globally, accounting for 18.7% of all cancer fatalities in 2022.¹
- Recent advancements has notably improved survival rates for patients with NSCLC, showing a steeper decrease in mortality rates during the era of immuno-oncology (I-O) therapy.²
- With increased survival in later-stage NSCLC patients in post-I-O era³, there's a growing proportion of non-cancer deaths such as cardiovascular disease (CVD), underscoring the necessity fora comprehensive patient care⁴⁻⁶.
- However, there is limited evidence on the shifts in risk factors for cause-specific death in post-I-O era.

OBJECTIVES

- To evaluate changes in mortality rates and cause of death in the pre– and post-I-O eras
- To investigate the factors associated with competing risk of NSCLC or other cause-specific deaths in elderly patients with advanced NSCLC

METHODS

Data Source

- The 2012-2019 Surveillance, Epidemiology, and End Results (SEER) - Medicare linked database

Study Design

- Retrospective cohort study

Study Population

- Aged 65 years or older
- Diagnosed with advanced (stage IIIB-IV) NSCLC

Outcome

- Three types of mortality: (1) CVD; (2) NSCLC; (3) others

Key Variables

- Demographics: age, sex, race
- Cancer-related factors: cancer stage, histology
- Socioeconomic status: region, primary insurance provider
- Clinical characteristics: smoking history, obesity, comorbidities.

Statistical Analysis

- Descriptive analysis
: independent t-test (Fisher's exact test), chi-square test
- Competing risk models
 - when multiple potential events could preclude the event of interest, to assess CVD or NSCLC mortality and associated factors
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- The Fine-Gray model:** to estimate the cumulative incidence of an event and sub-distribution hazard ratio (sHR) in the presence of competing risks
- Cause-specific Cox regression model:** to understand relationships between covariates and the risk of a specific type of event

RESULTS

- Among 107,021 older patients with advanced NSCLC, a total of 51,612 met the study eligibility criteria.
- Across the whole study period, there were more advanced NSCLC diagnoses in the pre-I-O period compared to the post-I-O period (45.71% vs 54.29%).

Table 1. Baseline characteristics

	Pre-I-O (n=23,592)	Post-I-O (n=28,020)	P-value
Male, n (%)	12,203 (51.73)	14,421 (51.47)	0.5596
Age, mean (SD)	77.40 (6.66)	77.51 (6.75)	0.0827
Race, n (%)			
White	20,796 (88.15)	24,512 (87.48)	0.0002
Black	1,691 (7.17)	1,989 (7.10)	
Others	1,081 (4.58)	1,461 (5.21)	
Unknown	24 (0.10)	58 (0.21)	
Primary payer, n (%)			
Medicaid	1,634 (6.93)	1,733 (6.18)	0.0021
Private insurance	5,178 (21.90)	6,300 (22.48)	
Others	16,771 (71.09)	19,987 (71.30)	
CCI, mean (SD)	4.38 (3.76)	4.49 (3.83)	0.0007
Obesity, n (%)	4,201 (17.81)	6,120 (21.84)	<0.0001
Peripheral vascular disease, n (%)	7,158 (30.34)	8,886 (31.71)	0.0008
Cerebrovascular disease, n (%)	5,632 (23.87)	6,380 (22.77)	0.0032

Table 2. Number and death rate per person-years of deaths by causes

Cause of death	Pre-I-O		Post-I-O	
	N (%)	Death rate per person-years	N (%)	Death rate per person-years
All-causes	21,523	0.63	22,763	0.65
CVD	692 (3.22)	0.20	651 (2.86)	0.02
NSCLC	12,982 (60.32)	0.38	12,738 (55.96)	0.36
Others	7,849(36.47)	0.23	9,374 (41.18)	0.27

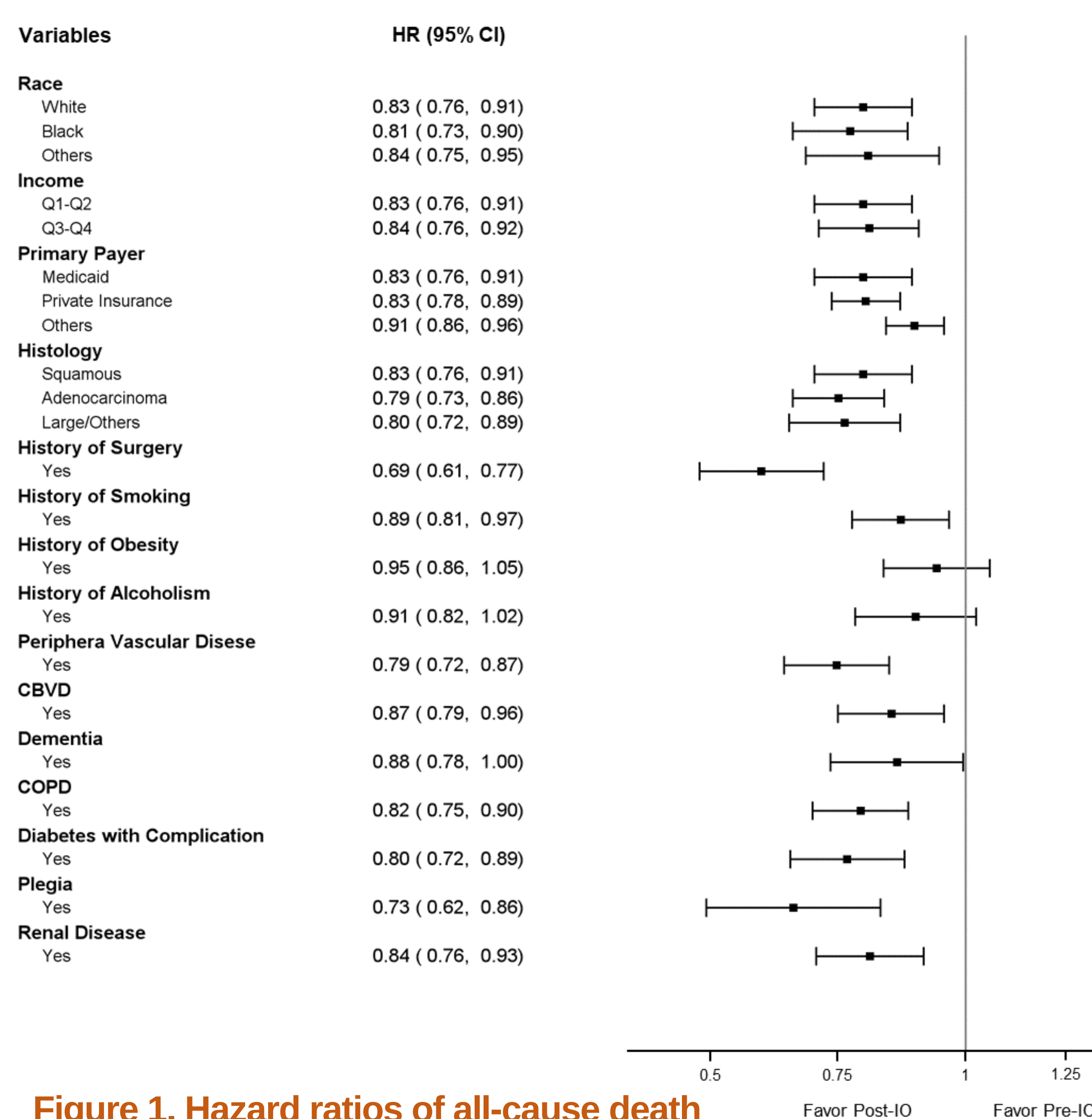
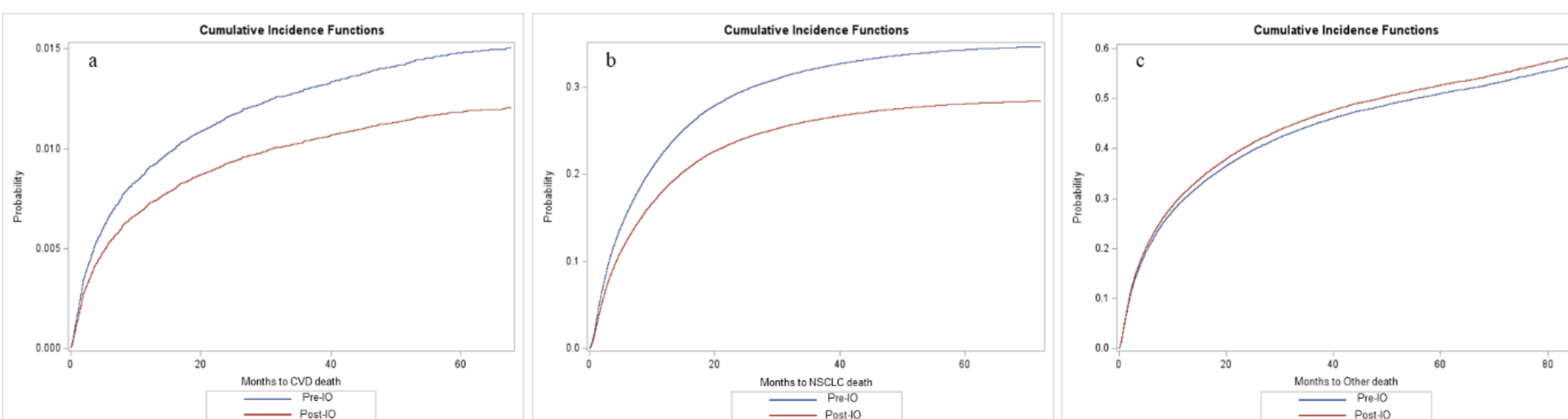


Figure 1. Hazard ratios of all-cause death

- Throughout the study period, the risk of CVD mortality among Black patients increased from 1.49 to 1.56, while the risk of mortality from other causes slightly decreased from 0.88 to 0.86.
- It is notable that **comorbid conditions** associated with **CVD**, such as peripheral vascular disease (pre-I-O: sHR=1.52 [1.29-1.79]; post-I-O: sHR=1.4 [1.25-1.73]) and cerebrovascular disease (pre-I-O: sHR=1.47 [1.24-1.73]; post-I-O: sHR=1.44 [1.20-1.72]), were significant risk factors throughout the period.

Figure 2. CIF curves: Fine-Gray model
[a] CVD mortality; [b] NSCLC mortality; [c] Other-caused mortality

CONCLUSIONS

Key takeaways

- I-O therapies have been associated with a significant reduction in all-cause mortality, CVD and NSCLC-related death among older patients with advanced NSCLC.
- Comorbidities (e.g., renal disease and CVD) significantly influenced mortality rates.
- Persistent racial disparities were observed, with Black patients experiencing higher mortality risks for both CVD and NSCLC compared to White patients.

Strengths

- The study used a large, population-based SEER-Medicare cohort, enhancing the generalizability of the findings.
- The study is one of the first to assess mortality rates, their causes, and associated risk factors before and after the introduction of I-O therapies.

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