

Evolving Landscape of Cardiovascular Disease-Associated Mortality in Lung Cancer: A 25-Year National Population Analysis (1999–2024)

Siqi Yang^{1,2}, James A. Diao^{3,4}, Chirag J. Patel⁴, Matthew S. Ning⁵, Bing Yu^{1,2}, Zhongxing Liao⁵, Yixuan He^{1,2}, **David C. Qian⁵**

¹Department of Epidemiology, University of Texas Health Science Center at Houston School of Public Health, Houston/TX/USA, ²Human Genetics Center, University of Texas Health Science Center at Houston School of Public Health, Houston/TX/USA, ³Department of Cardiology, Massachusetts General Hospital, Boston/MA/USA, ⁴Department of Biomedical Informatics, Harvard Medical School, Boston/MA/USA, ⁵Department of Thoracic Radiation Oncology, University of Texas MD Anderson Cancer Center, Houston/TX/USA

Correspondence: DQian@mdanderson.org



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BACKGROUND & AIM

Global lung cancer mortality has declined following advancements in treatment and smoking cessation.¹ However, treatment-related toxicities and comorbidities have limited further survival gains.^{2,3} Cardiovascular disease (CVD) is the leading non-cancer cause of death among individuals with lung cancer,⁴ yet its long-term trends remain poorly characterized.

We present the national trajectory of lung cancer deaths associated with CVD and its subtypes over the past 25 years.

METHODS

This serial cross-sectional study used multiple cause of death data from the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER). We obtained mortality information from January 1, 1999 to December 31, 2024.⁵ The underlying cause of death was identified using International Classification of Diseases, Tenth Edition (ICD-10) codes corresponding to lung cancer (ICD-10 C34) and CVD with subtype specifications: ischemic heart disease (I20-I25), heart failure (I50), arrhythmia (I44-I49), hypertensive heart disease (I11, I13), rheumatic/valvular heart disease (I00-I09, I34-I38), cerebrovascular disease (I60-I69), and other cardiovascular disease (I26-I28, I30-I33, I40-I43, I51). Lung cancer mortality associated with CVD was defined as death with lung cancer as the underlying cause and one or more of the CVD conditions as contributing causes. This study was deemed exempt from the UT Health institutional review board.

Age-adjusted mortality rates (AAMR) per 100,000 were collected for the overall population. To assess change in trends over time, we fitted segmented log-linear regression models to estimate annual percent change (APC) in AAMRs, with 2013 as the specified breakpoint to compare trends before and after the observed trajectory change. Differences in APC before and after 2013 were evaluated using Wald tests. P-values were calculated using 2-sided tests. Relative contribution of CVD-associated mortality was calculated by dividing the AAMR for lung cancer deaths with CVD by the overall lung cancer AAMR and multiplying by 100. 95% confidence intervals were estimated using the delta method with standard errors derived from the log-transformed AAMRs.

RESULTS

Table 1. Cardiovascular Disease (CVD) and Lung Cancer Aged-Adjusted Mortality Rates and Annual Relative Rates of Change in the United States, 1999 - 2024

Disease	AAMR ^a			Annual relative rate of change (95% CI)		P value ^b
	1999	2013	2024	1999 – 2013	2014 – 2024	
Lung Cancer	55.3	43.4	28.9	-1.93 (-2.14, -1.73)	-4.11 (-4.37, -3.85)	<0.001
Lung Cancer associated with CVD	10.9	8.3	7.0	-2.16 (-2.41, -1.91)	-1.73 (-2.06, -1.39)	0.12
Lung Cancer associated with CVD subtypes						
Arrhythmias	5.9	4.4	3.5	-2.13 (-2.27, -1.99)	-2.37 (-2.68, -2.07)	0.22
Ischemic Heart Disease	2.9	2.2	1.7	-2.30 (-2.85, -1.74)	-2.77 (-3.51, -2.04)	0.43
Heart Failure	1.4	1.0	1.4	-2.40 (-2.72, -2.20)	2.46 (2.03, 2.86)	<0.001
Cerebrovascular Disease	1.0	0.8	0.8	-2.82 (-3.14, -2.50)	1.06 (0.69, 1.42)	<0.001
Other CVD ^c	0.8	1.0	1.1	1.18 (0.82, 1.55)	0.98 (0.50, 1.46)	0.61
Rheumatic/Valvular Heart Disease	0.2	0.1	0.1	-1.50 (-2.06, -0.94)	0.57 (-0.18, 1.33)	0.002
Hypertensive Heart Disease	0.1	0.1	0.3	-2.84 (-3.91, -1.75)	15.21 (13.96, 16.48)	<0.001
Lung Cancer not associated with CVD	45.3	35.6	22.1	-2.61 (-2.91, -2.30)	-6.23 (-7.95, -4.48)	<0.001
CVD	328.1	206.0	196.2	-3.46 (-3.69, -3.23)	0.21 (-0.10, 0.53)	<0.001

a. AAMR: aged-adjusted mortality rate; AAMR is expressed per 100,000 persons.

b. P values were derived from Wald tests comparing annual relative rates of change before and after 2013.

c. Other CVD included pulmonary vascular/heart disease and inflammatory heart disease.

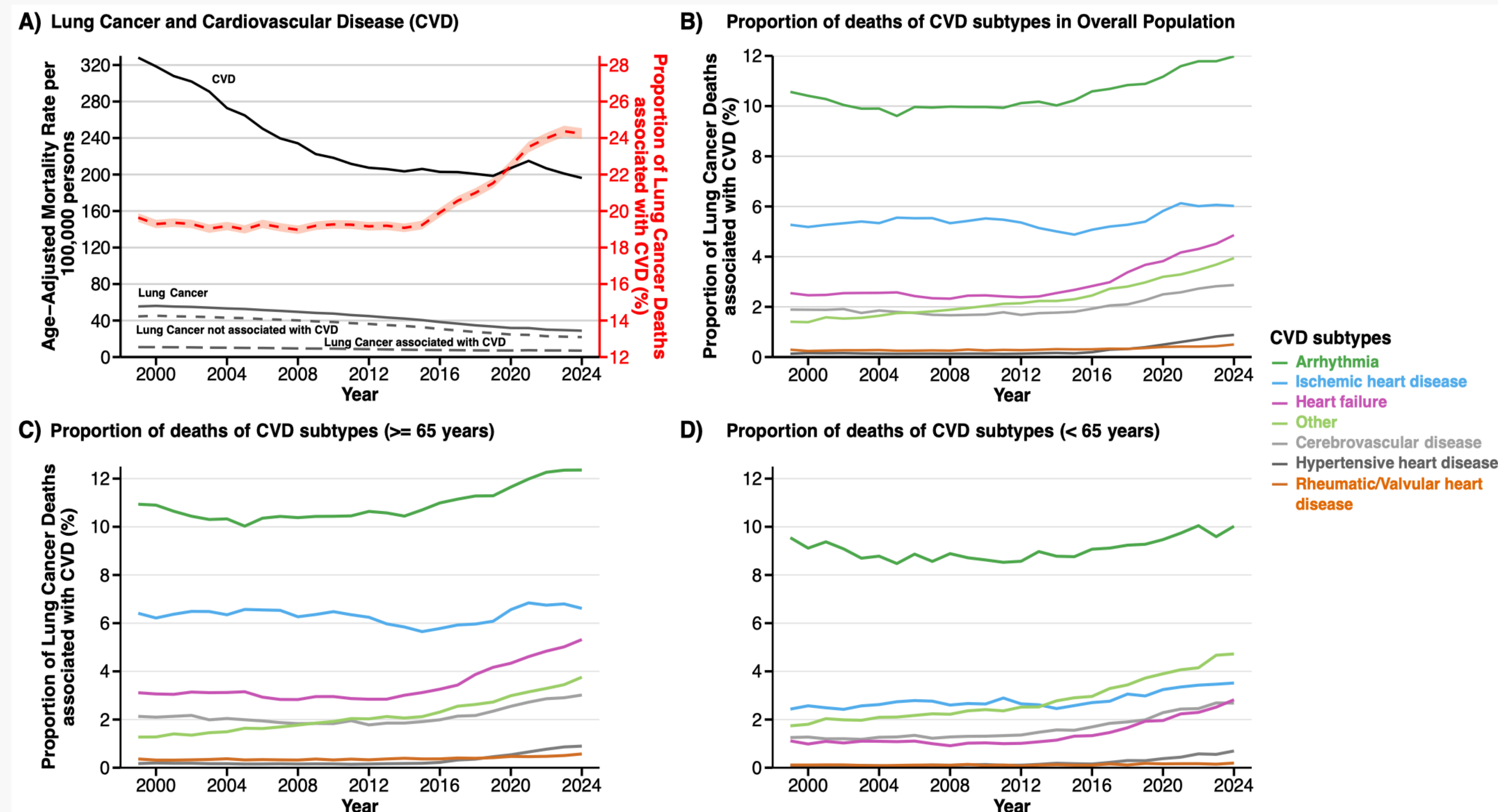


Figure 1. Trends in Lung Cancer Deaths associated with cardiovascular disease (CVD), 1999 - 2024

(A) Age-adjusted mortality rates (per 100,000 persons) for lung cancer and overall cardiovascular disease, along with the proportion of lung cancer deaths associated with CVD. The shaded area represents 95% confidence interval of the proportion of lung cancer deaths associated with CVD over time.

(B) Proportion of lung cancer deaths associated with specific cardiovascular disease subtypes, including arrhythmias, ischemic heart disease, heart failure, hypertensive heart disease, cerebrovascular disease, rheumatic/valvular heart disease, and other cardiovascular conditions (such as inflammatory heart disease).

(C, D) Proportion of lung cancer deaths associated with specific CVD subtypes stratified by age of decedents (C) ≥ 65 years and (D) < 65 years.

Among 3,907,472 lung cancer decedents (45% female, mean age of 71 years), AAMR for total CVD initially decreased and then plateaued ($-3.46\%/year$ within 1999–2013 and $+0.21\%/year$ within 2013–2024) (Table 1). In contrast, lung cancer AAMR declined throughout entire study period ($-1.93\%/year$ within 1999–2013 and $-4.11\%/year$ within 2014–2024). Despite this decline, the proportion of lung cancer deaths associated with CVD (Figure 1A) increased from 19.6% in 2013 to 24.2% in 2024 ($P<0.001$), with greater increase among men (29.4% to 25.3%, $P<0.001$) than women (16.3% to 21.0%, $P<0.001$).

Arrhythmias represented the most common contributing CVD, followed by ischemic heart disease and heart failure (Table 1/Figure 1B). While most CVD subtypes had declining AAMRs, heart failure increased from -2.40% before 2013 to $+2.46\%$ thereafter ($P<0.001$). In age-stratified analyses (Figures 1C-D), the relative contribution of heart failure and ischemic heart disease to lung cancer deaths among individuals ≥ 65 years at death more than doubled that of their younger counterparts; other CVD subtypes were similar between groups.

CONCLUSION

Overall lung cancer mortality continues to decrease in the U.S., though CVD's contribution to lung cancer deaths has grown over the past 25 years. Our findings underscore the importance of cardio-oncology collaborations and CVD risk assessment within routine lung cancer treatment pathways.

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