

Prognosis and Survival Analysis of 922,317 Lung Cancer Patients from the US Based on the Most Recent Data from the SEER Database (April 15, 2021)

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Background: On April 15, 2021, the Surveillance, Epidemiology, and End Results (SEER) database released the latest lung cancer follow-up data. We selected 922,317 lung cancer patients diagnosed from 2000 to 2017 for survival analysis to provide updated data for lung cancer researchers.

Research Question: This study explored the latest trends of survival time in terms of gender, race, nationality, age, income, address, histological type and primary site.

Study Design and Methods: The SEER database covers 27.8% of the US population. We used life table, Kaplan–Meier, log-rank, Breslow and Tarone–Ware tests to calculate survival rate, time, and curve and to compare differences in survival distribution. We performed univariate and multivariate Cox proportional hazards analyses.

Results: The median survival time of all lung cancer patients diagnosed in 2017 increased by 41.72% compared to 2000. Median survival time of female patients diagnosed in 2017 increased by 70.94% compared to 2000. Median survival time of those diagnosed in 2017 for different primary sites was as follows: right middle lobe was the longest, then left lower lobe, right upper lobe, right lower lobe, and left upper lobe. Lung cancer patients older than 75 years had a significantly shorter median survival time. Patients living in metropolitan areas of 250,000 to 1 million had a longer median survival time. Median survival time in the adenocarcinoma group was significantly greater than other patients. Median survival of Asian and other races diagnosed in 2017 was 97.87% higher than those diagnosed in 2000. Survival rate of lung cancer increased gradually with the year of diagnosis.

Interpretation: The rapid improvement of the prognosis of female and young lung cancer patients contributes to the improvement of the overall prognosis. Primary lung cancer in the right middle lobe has the best prognosis.

Keywords: Cox regression analysis, Kaplan Meier survival analysis, lung cancer, prognosis, SEER

Introduction

The Surveillance, Epidemiology, and End Results (SEER) database released the most recent lung cancer follow-up data on 15 April 2021 (<https://www.cancer.gov/>). Although previous articles^{1–3} analyzed patient survival,^{4–6} these predated this release and therefore the data were not up to date. Our study therefore aimed to provide lung cancer researchers with accurate and updated survival data.

SEER is an authoritative source of cancer statistics in the United States and the SEER Program provides statistics on the cancer burden among the US population.

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The SEER database collects and publishes cancer incidence and survival data from population-based cancer registries. These data are collected on every cancer case reported from 18 US geographic areas. Because these areas are representative of the entire US population, SEER can account for diverse populations. SEER also reports mortality data, which are provided by the National Center for Health Statistics.⁷

Our study analyzed the survival of 922,317 lung cancer patients diagnosed from 2000–2017 in detail. Grouped by gender, race, ethnicity, age, income, address, histologic type, and primary site, respectively, our study found large variations in survival times and conditions among different groups of lung cancer patients by factors, and this variation has further expanded in recent years. And we tabulated the hazard ratios corresponding to each group in each item in detail.

We consider our study meaningful in being able to inform researchers and policy makers on the survival differences of lung cancer patients from different perspectives and to support the latest data in research and policy. It may help public health authorities and policy makers to identify and monitor public health problems and focus interventions to reduce potential excess deaths in these areas.⁸

Methods

Data Sources

We selected 922,317 lung cancer cases from the latest available data from the SEER database on April 15, 2021. Incidence - SEER Research Data, 18 Registries, Nov 2020 Sub (2000–2018). SEER 18 covers approximately 27.8% of the US population (based on the 2010 census). Geographic areas (registries) covered San Francisco-Oakland SMSA, Connecticut, Detroit (Metropolitan), Hawaii, Iowa, New Mexico, Seattle (Puget Sound), Utah, Atlanta (Metropolitan), San Jose-Monterey, Los Angeles, Alaska Natives, Rural Georgia, California excluding, Kentucky, Louisiana, New Jersey, and Greater Georgia. We selected 13 entries including ID, survival months, status, sex, age, year of diagnosis, race recode (White, Black, American Indian/Alaska Native, Asian or Pacific Islander), origin recode the National Health Insurance Authority (Hispanic, Non-Hispanic), primary site-labeled, laterality, median household income inflation adjusted to 2019, the Rural-Urban Continuum Code, and ICD-O-3 (International

Classification of Disease for Oncology-3) histologic type. The specific type of histologic type is shown in [Table S1](#), but all lung tumors designed for this study refer to malignancies of the lung. Epithelial neoplasms including small cell carcinoma. Unless otherwise indicated, all text within the National Cancer Institute (NCI) products is free of copyright and may be reused without permission. Credit the NCI as the source. Each entry is integrated and grouped, and the specific grouping is shown in [Table 1](#).

Data Processing and Statistical Analysis

Because the data volume and analysis items were too large and limited to the length of the paper, the focus was briefly described in the results, and detailed and specific contents are detailed in the tables, figures, and other supplementary materials. We used frequency function statistics, and statistical analysis was performed with SPSS v. 24 (IBM). We used GraphPad Prism 8 to plot the trend of median survival time in different subgroups. We performed life table analysis, Kaplan Meier survival analysis, univariate and multivariate Cox proportional hazards analysis to analyze patient data.

Log rank (Mantel-Cox), Breslow (generalized Wilcoxon) and Tarone-Ware tests were used to compare the distribution of survival data between groups. To explore the factors influencing survival time (survival speed) and predict survival probability, we used univariate and multivariate Cox proportional hazard analysis using the backward Wald method. Taking the first group of each project as the comparison object, the confidence interval of the Hazard Ratio (HR) was 95%, the step probability of entering was 0.05, the step probability of going out was 0.10, and the maximum number of iterations was 20.

Results

The median survival time of all lung cancer patients diagnosed in 2017 (14.030 months) increased by 41.72% compared with 2000 (9.900 months). [Table 1](#) describes the 3-, 5-, and 10-year survival rates, median survival time, and mean survival time according to the variables defined in the Methods section. [Table 2](#) describes the chi square and P values of the three test methods of population comparison and pairwise comparison in Kaplan Meier survival analysis. [Figure 2](#) shows the survival curves according to primary lung cancer site and patient demographics. [Table 3](#) describes the univariate and multivariate Cox proportional HR, for which the first group of each item is taken as the comparison object.

Table 1 Basic Characteristics of Patients and Survival Analysis According to Different Factors

	Number of Patients	Percentage of Total Patients (%)	3-Year Survival Rate (%)	Probability Density	5-Year Survival Rate (%)	Probability Density	10-Year Survival Rate (%)	Probability Density	Median Survival Time (Months)	Standard Error	95.0% CI		Mean Survival Time (Months)	Standard Error	95.0% CI	
											Lower	Upper			Lower	Upper
Total	9,22,317	100	19	0.003	14	0.002	8	0.001	9	0.021	8.959	9.041	32.793	0.066	32.663	32.922
Sex																
Female	4,32,762	46.9	23	0.004	18	0.002	10	0.001	11	0.039	10.923	11.077	38.805	0.107	38.595	39.015
Male	4,89,555	53.1	16	0.003	12	0.002	6	0.001	8	0.025	7.952	8.048	27.522	0.08	27.365	27.68
Age																
< 45 years	15,701	1.7	32	0.003	28	0.001	24	0.001	16	0.284	15.443	16.557	67.082	0.763	65.586	68.579
45–54 years	74,518	8.1	24	0.003	20	0.001	15	0.001	12	0.088	11.827	12.173	46.308	0.29	45.74	46.876
55–64 years	1,98,128	21.5	23	0.003	18	0.002	12	0.001	11	0.051	10.9	11.1	41.111	0.165	40.788	41.433
65–74 years	3,00,953	32.6	21	0.004	16	0.002	8	0.001	11	0.041	10.92	11.08	34.554	0.115	34.33	34.779
75–84 years	2,54,341	27.6	15	0.003	10	0.002	3	0.001	7	0.034	6.933	7.067	23.075	0.087	22.904	23.246
≥ 85 years	78,676	8.5	7	0.002	4	0.001	1	0	3	0.034	2.933	3.067	12.349	0.091	12.171	12.527
Race																
White	7,65,078	83	19	0.003	14	0.002	8	0.001	9	0.023	8.955	9.045	32.726	0.072	32.585	32.867
Black	1,00,450	10.9	17	0.003	12	0.002	7	0.001	9	0.06	8.882	9.118	29.497	0.191	29.124	29.871
Asian and others (a)	56,789	6.2	23	0.004	17	0.002	11	0.001	12	0.124	11.757	12.243	40.002	0.32	39.375	40.629
Origin recode NHIA																
Non-Spanish-Hispanic-Latino	8,72,814	94.6	19	0.003	14	0.002	8	0.001	9	0.021	8.958	9.042	32.686	0.068	32.553	32.818
Spanish-Hispanic-Latino	49,503	5.4	20	0.003	15	0.002	9	0.001	9	0.094	8.816	9.184	35.001	0.321	34.373	35.629
Median household income																
inflation adj to 2019																
< \$35,000	19,711	2.1	15	0.003	11	0.001	5	0.001	7	0.111	6.783	7.217	25.872	0.405	25.079	26.665
\$35,000-\$44,999	76,395	8.3	16	0.003	12	0.002	6	0.001	8	0.064	7.875	8.125	28.092	0.219	27.663	28.521
\$45,000-\$54,999	1,52,943	16.6	17	0.003	13	0.002	6	0.001	8	0.049	7.905	8.095	28.94	0.151	28.645	29.235
\$55,000-\$64,999	2,18,082	23.6	18	0.003	14	0.002	8	0.001	9	0.042	8.917	9.083	31.782	0.132	31.522	32.041
\$65,000-\$74,999	1,95,430	21.2	20	0.003	15	0.002	8	0.001	9	0.05	8.901	9.099	33.927	0.147	33.639	34.215
\$75,000+	2,59,669	28.2	22	0.004	16	0.002	9	0.001	11	0.045	10.911	11.089	36.832	0.133	36.571	37.92
Others (b)	87	0	13	0.01	10	0.002	0	0	14	2.287	9.517	18.483	25.118	3.734	17.799	32.438
Rural-Urban Continuum																
Code																
Counties in metropolitan areas greater than 1 million population	5,24,354	56.9	20	0.003	15	0.002	9	0.001	10	0.031	9.939	10.061	34.716	0.091	34.537	34.895
Counties in metropolitan areas of 250,000 to 1 million population	1,76,075	19.1	19	0.003	14	0.002	8	0.001	9	0.047	8.907	9.093	32.469	0.151	32.172	32.765
Counties in metropolitan areas of less than 250 thousand population	81,081	8.8	18	0.003	13	0.002	7	0.001	9	0.068	8.867	9.133	29.798	0.205	29.396	30.199

(Continued)

Table 1 (Continued).

	Number of Patients	Percentage of Total Patients (%)	3-Year Survival Rate (%)	Probability Density	5-Year Survival Rate (%)	Probability Density	10-Year Survival Rate (%)	Probability Density	Median Survival Time (Months)	Standard Error	95.0%, CI	
											Lower	Upper
Nonmetropolitan counties adjacent to a metropolitan area	80,876	8.8	16	0.003	12	0.002	6	0.001	8	0.064	7.875	8.125
Nonmetropolitan counties not adjacent to a metropolitan area	58,676	6.4	16	0.003	11	0.002	6	0.001	8	0.07	7.863	8.137
Others (c)	1,255	0.1	14	0.003	11	0.001	5	0	9	0.475	8.069	9.931
Primary site												
Right upper lobe	2,44,392	26.5	23	0.004	17	0.002	10	0.001	12	0.052	11.898	12.102
Right middle lobe	38,374	4.2	26	0.004	20	0.002	12	0.001	13	0.151	12.705	13.295
Right lower lobe	1,23,735	13.4	22	0.004	17	0.002	9	0.001	11	0.072	10.859	11.141
Left upper lobe	1,95,234	21.2	22	0.004	16	0.002	9	0.001	11	0.053	10.896	11.104
Left lower lobe	99,281	10.8	23	0.004	18	0.002	10	0.001	11	0.078	10.848	11.152
Main bronchus	43,133	4.7	8	0.002	6	0.001	4	0	5	0.055	4.892	5.108
Overlapping lesion of lung	10,731	1.2	17	0.003	13	0.001	7	0.001	7	0.164	6.678	7.322
Lung, NOS	1,64,777	17.9	7	0.002	4	0.001	2	0	4	0.026	3.949	4.051
Others (d)	2,660	0.3	8	0.002	5	0.001	2	0.001	5	0.22	4.569	5.431
Histologic type (ICD-O-3)												
Neoplasia, NAS	67,189	7.3	6	0.002	4	0.001	2	0	2	0.027	1.946	2.054
Epithelial Neoplasms, NAS	2,94,702	32	9	0.002	6	0.001	3	0	6	0.024	5.954	6.046
Squamous cell neoplasms	1,79,942	19.5	20	0.004	15	0.002	7	0.001	11	0.055	10.893	11.107
Adenoma and adenocarcinomas	3,47,366	37.7	28	0.004	22	0.002	13	0.001	15	0.061	14.88	15.12
Cystic, mucinous and serous neoplasms	12,070	1.3	29	0.004	23	0.002	14	0.001	15	0.377	14.261	15.739
Acinous cell neoplasm	7044	0.8	67	0.005	55	0.004	34	0.002	86	2.44	81.217	90.783
Complex epithelial neoplasms	10,523	1.1	26	0.004	20	0.002	11	0.001	14	0.319	13.375	14.625
Others (e)	3481	0.4	30	0.003	26	0.002	19	0.001	12	0.566	10.891	13.109
Year of diagnosis												
2000	48,893	5.3	15	0.003	11	0.001	6	0.001	8	0.071	7.862	8.138
2001	49,520	5.37	15	0.003	11	0.001	6	0.001	8	0.07	7.863	8.137
2002	49,658	5.38	15	0.003	11	0.001	6	0.001	8	0.07	7.863	8.137
2003	50,123	5.43	16	0.003	12	0.001	7	0.001	8	0.075	7.854	8.146
2004	49,890	5.41	16	0.003	12	0.002	7	0.001	8	0.076	7.851	8.149
2005	50,749	5.5	17	0.003	13	0.002	7	0.001	8	0.082	7.839	8.161
2006	51,223	5.55	18	0.003	13	0.002	7	0.001	9	0.085	8.833	9.167
2007	51,598	5.59	18	0.003	14	0.002	7	0.001	9	0.089	8.826	9.174
2008	51,869	5.62	19	0.003	14	0.002	8	0.001	9	0.086	8.831	9.169
2009	52,587	5.7	19	0.003	14	0.002	N/A	N/A	9	0.087	8.829	9.171
2010	51,355	5.57	20	0.003	15	0.002	N/A	N/A	9	0.087	8.829	9.171

2011	50,918	5,52	21	0.003	15	0.002	N/A	N/A	9,803	10,197	25,461	0.145	25,177	25,745
2012	51,591	5,59	20	0.003	15	0.002	N/A	N/A	9,806	10,194	23,689	0.129	23,435	23,943
2013	51,787	5,61	21	0.003	16	0.002	N/A	N/A	9,8	10,2	22,55	0.115	22,324	22,776
2014	52,469	5,69	23	0.004	N/A	N/A	N/A	N/A	10,796	11,204	21,215	0.1	21,019	21,411
2015	52,702	5,71	24	0.004	N/A	N/A	N/A	N/A	10,757	11,243	19,492	0.083	19,33	19,654
2016	52,642	5,71	N/A	N/A	N/A	N/A	N/A	N/A	11,736	12,264	16,725	0.064	16,601	16,85
2017	52,743	5,72	N/A	N/A	N/A	N/A	N/A	N/A	12,703	13,297	12,966	0.042	12,883	13,05
Summary stage														
Distant	4,80,617	52.1	5	0.002	3	0.001	2	0	3,974	4,026	12,89	0.047	12,798	12,982
Localized	1,69,955	18.4	51	0.006	40	0.004	24	0.002	48,494	49,506	78,295	0.22	77,863	78,726
Regional	2,03,809	22.1	28	0.005	21	0.003	11	0.001	17,851	18,149	45,042	0.154	44,739	45,344
Unknown/unstaged	67,936	7.4	10	0.003	7	0.001	3	0	5,863	6,137	19,61	0.186	19,245	19,976

Notes: (a) included Asian or Pacific Islander and American Indian/Alaska Native. (b) Others included unknown/missing/no match/Not 1990–2018. (c) Others included Unknown/missing/no match (Alaska or Hawaii - Entire State) and Unknown/missing/no match/Not 1990–2018. (d) Others included Only one side - side unspecified, Bilateral, single primary and Paired site, but no information concerning laterality. (e) Others included all the histological types of lung cancer except the above seven types.

Sex

The median survival time of female patients increased faster than in males (Figure 1A and B). The median survival time of female patients diagnosed in 2017 (18.000 months, Table S2) increased by 70.94% (Table S3) compared with 2000 (10.530 months, Table S1). In males, the trend was similar although the increase was smaller: from 9.450 months in 2000 to 11.540 months in 2017 (Table S2), an increase of 22.12% (Table S3). Surprisingly, the difference in median survival time between female and male patients increased from 1.08 months to 6.46 months (Table S2). The 3-, 5-, and 10-year survival rates for female patients were 23%, 18%, and 10%, respectively; and for male patients these were 16%, 12%, and 6%, respectively (Table 1). The log rank (Mantel-Cox) for the overall comparison of females with males was 3,119.588, Breslow (generalized Wilcoxon) was 2,577.577, and Tarone-Ware was 2934.977. For the pairwise comparison, the log rank (Mantel-Cox) was 9,473.321, Breslow (generalized Wilcoxon) was 7,344.132, and Tarone-Ware was 8697.481. All had $P < 0.001$ (Table 2). The HR for univariate Cox analyses of male:female was 1.240 (1.234–1.246), $P < 0.001$. The HR for multivariate Cox analyses of male:female was 1.217 (1.212–1.223), $P < 0.001$ (Table 3).

Primary Site

The median survival time when the primary site was in one lobe was greater than in patients whose primary site was in the main bronchus with an overlapping lesion in the lung (Figure 1C and D). Patients diagnosed in 2017 with a primary site in the right middle lobe had the longest median survival time (20.370 months), then in the left lower lobe (19.000 months), right upper lobe (17.930 months), right lower lobe (17.690 months), and left upper lobe (17.120 months, Table S4). The survival time of patients with single-lobe cancer increased markedly since 2000: the number of patients diagnosed in 2017 at the primary site of the right middle lobe, left lower lobe, right lower lobe, right upper lobe, and left upper lobe increased by 85.35%, 78.91%, 66.89, 65.56%, and 55.92%, respectively (Table S5). The specific values of the 3-year, 5-year, and 10-year survival rates of lung cancer patients of different primary sites were shown in Table 1.

The log rank (Mantel-Cox) for the overall comparison was 56,749.667, the Breslow (generalized Wilcoxon) was

Table 2 Overall Comparison and Pairwise Comparison of Each Group in Kaplan–Meier Survival Analysis

Comparison Type	Comparative Factor	Log Rank (Mantel-Cox)		Breslow (Generalized Wilcoxon)		Tarone-Ware	
		Chi Square	Sig.	Chi Square	Sig.	Chi Square	Sig.
Overall comparison	Sex	3,119.588	0.000	2,577.577	0.000	2,934.977	0.000
	Age	36,486.760	0.000	33,627.846	0.000	34,681.780	0.000
	Race	1,300.355	0.000	1,210.942	0.000	1,311.907	0.000
	Origin recode NHIA	10.506	0.001	0.624	0.429	0.323	0.570
	Median household income inflation adj to 2019	3,119.588	0.000	2,577.577	0.000	2,934.977	0.000
	Rural-Urban Continuum Code	1,952.945	0.000	1,397.391	0.000	1,696.331	0.000
	Primary site	56,749.667	0.000	57,432.600	0.000	59,443.510	0.000
	Histologic type (ICD-O-3)	82,913.123	0.000	79,928.300	0.000	84,548.100	0.000
	Year of diagnosis	7,532.042	0.000	5,692.115	0.000	6,834.910	0.000
	Summary stage	240,670.146	0.000	219,186.158	0.000	239,656.003	0.000
Pairwise comparison	Sex	9,473.321	0.000	7,344.132	0.000	8,697.481	0.000
	Female vs Male						
	Age	658.146	0.000	451.420	0.000	535.237	0.000
	< 45 years vs 45–54 years						
	< 45 years vs 55–64 years	1,186.997	0.000	755.752	0.000	891.847	0.000
	< 45 years vs 65–74 years	2,134.621	0.000	1,209.475	0.000	1,450.388	0.000
	< 45 years vs 75–84 years	5,280.355	0.000	3,281.758	0.000	3,847.412	0.000
	< 45 years vs ≥ 85 years	9,405.387	0.000	7,374.587	0.000	8,275.701	0.000
	45–54 years vs 55–64 years	168.537	0.000	131.890	0.000	125.492	0.000
	45–54 years vs 65–74 years	1,135.723	0.000	766.972	0.000	783.114	0.000
	45–54 years vs 75–84 years	7,332.664	0.000	5,949.599	0.000	6,199.769	0.000
	45–54 years vs ≥ 85 years	16,522.957	0.000	16,185.395	0.000	16,484.200	0.000
	55–64 years vs 65–74 years	734.202	0.000	495.365	0.000	520.272	0.000
	55–64 years vs 75–84 years	9,978.407	0.000	8,503.476	0.000	8,906.353	0.000
	55–64 years vs ≥ 85 years	21,880.320	0.000	21,656.557	0.000	22,006.761	0.000
	65–74 years vs 75–84 years	7,052.078	0.000	6,213.807	0.000	6,581.952	0.000
	65–74 years vs ≥ 85 years	19,673.925	0.000	19,042.105	0.000	19,640.948	0.000
	75–84 years vs ≥ 85 years	6,915.700	0.000	6,358.064	0.000	6,757.770	0.000
	Race						
	White vs Black	278.487	0.000	106.505	0.000	189.853	0.000
	White vs Asian and other races	918.554	0.000	1,032.227	0.000	1,028.928	0.000

Black vs Asian and other races	1,325.507	0.000	1,162.642	0.000	1,310.095	0.000
Origin recode NHIA	10.506	0.001	0.624	0.429	0.323	0.570
Non-Spanish-Hispanic-Latino vs Spanish-Hispanic-Latino	42.062	0.000	33.672	0.000	40.737	0.000
Median household income inflation adj to 2019	85.564	0.000	68.062	0.000	81.767	0.000
< \$35,000 vs \$35,000-\$44,999	230.631	0.000	172.090	0.000	206.247	0.000
< \$35,000 vs \$45,000-\$54,999	431.627	0.000	337.420	0.000	396.074	0.000
< \$35,000 vs \$55,000-\$64,999	811.362	0.000	684.642	0.000	774.900	0.000
< \$35,000 vs \$65,000-\$74,999	2.197	0.138	4.895	0.027	4.144	0.042
< \$35,000 vs \$75,000+	16.965	0.000	12.927	0.000	15.542	0.000
< \$35,000 vs Others	214.341	0.000	144.686	0.000	176.486	0.000
\$35,000-\$44,999 vs \$45,000-\$54,999	588.760	0.000	440.256	0.000	520.033	0.000
\$35,000-\$44,999 vs \$55,000-\$64,999	1,464.530	0.000	1,219.404	0.000	1,378.889	0.000
\$35,000-\$44,999 vs \$65,000-\$74,999	1.005	0.316	3.174	0.075	2.395	0.122
\$35,000-\$44,999 vs Others	176.365	0.000	107.494	0.000	134.260	0.000
\$45,000-\$54,999 vs \$55,000-\$64,999	636.716	0.000	461.262	0.000	549.033	0.000
\$45,000-\$54,999 vs \$65,000-\$74,999	1,882.057	0.000	1,547.162	0.000	1,755.248	0.000
\$45,000-\$54,999 vs \$75,000+	0.699	0.403	2.703	0.100	1.938	0.164
\$45,000-\$54,999 vs Others	177.901	0.000	155.032	0.000	175.937	0.000
\$55,000-\$64,999 vs \$65,000-\$74,999	1,064.955	0.000	995.599	0.000	1,088.148	0.000
\$55,000-\$64,999 vs \$75,000+	0.219	0.640	1.752	0.186	1.068	0.301
\$55,000-\$64,999 vs Others	314.574	0.000	308.995	0.000	328.720	0.000
\$65,000-\$74,999 vs \$75,000+	0.007	0.933	0.987	0.321	0.450	0.502
\$65,000-\$74,999 vs Others	0.160	0.690	0.267	0.605	0.029	0.864
\$75,000+ vs Others	154.789	0.000	89.246	0.000	118.829	0.000
Rural-Urban Continuum Code	489.541	0.000	339.405	0.000	414.594	0.000
Counties in metropolitan areas greater than 1 million population vs Counties in metropolitan areas of 250,000 to 1 million population	898.955	0.000	628.695	0.000	771.331	0.000
Counties in metropolitan areas greater than 1 million population vs Counties in metropolitan areas of less than 250 thousand population	1,002.371	0.000	758.392	0.000	899.192	0.000
Counties in metropolitan areas greater than 1 million population vs Nonmetropolitan counties adjacent to a metropolitan area	22.407	0.000	9.820	0.002	15.310	0.000
Counties in metropolitan areas greater than 1 million population vs Nonmetropolitan counties not adjacent to a metropolitan area	132.516	0.000	103.077	0.000	119.878	0.000
Counties in metropolitan areas greater than 1 million population vs Others						
Counties in metropolitan areas of 250,000 to 1 million population vs Counties in metropolitan areas of less than 250 thousand population						

(Continued)

Table 2 (Continued).

Comparison Type	Comparative Factor	Log Rank (Mantel-Cox)		Breslow (Generalized Wilcoxon)		Tarone-Ware	
		Chi Square	Sig.	Chi Square	Sig.	Chi Square	Sig.
	Counties in metropolitan areas of 250,000 to 1 million population vs Nonmetropolitan counties adjacent to a metropolitan area	343.469	0.000	256.190	0.000	307.174	0.000
	Counties in metropolitan areas of 250,000 to 1 million population vs Nonmetropolitan counties not adjacent to a metropolitan area	471.405	0.000	381.350	0.000	441.650	0.000
	Counties in metropolitan areas of 250,000 to 1 million population vs Others	12.395	0.000	4.685	0.030	7.959	0.005
	Counties in metropolitan areas of less than 250 thousand population vs Nonmetropolitan counties adjacent to a metropolitan area	36.154	0.000	24.804	0.000	31.550	0.000
	Counties in metropolitan areas of less than 250 thousand population vs Nonmetropolitan counties not adjacent to a metropolitan area	102.205	0.000	84.179	0.000	98.169	0.000
	Counties in metropolitan areas of less than 250 thousand population vs Others	3.187	0.074	0.355	0.551	1.314	0.252
	Nonmetropolitan counties adjacent to a metropolitan area vs Nonmetropolitan County not adjacent to a metropolitan area	21.335	0.000	21.435	0.000	22.933	0.000
	Nonmetropolitan counties adjacent to a metropolitan area vs Others	0.529	0.467	0.090	0.764	0.022	0.882
	Nonmetropolitan counties not adjacent to a metropolitan area vs Others	0.031	0.860	1.436	0.231	0.617	0.432
	Primary site						
	Right upper lobe vs Right middle lobe	162.922	0.000	80.685	0.000	116.572	0.000
	Right upper lobe vs Right lower lobe	54.723	0.000	68.757	0.000	64.783	0.000
	Right upper lobe vs Left upper lobe	168.685	0.000	76.857	0.000	122.258	0.000
	Right upper lobe vs Left lower lobe	19.496	0.000	15.767	0.000	19.963	0.000
	Right upper lobe vs Main bronchus	10,216.526	0.000	10,257.262	0.000	10,769.433	0.000
	Right upper lobe vs Overlapping lesion of lung	595.338	0.000	829.226	0.000	770.682	0.000
	Right upper lobe vs Lung, NOS	37,093.583	0.000	36,323.045	0.000	38,235.231	0.000
	Right upper lobe vs Others	699.934	0.000	612.111	0.000	668.653	0.000
	Right middle lobe vs Right lower lobe	263.986	0.000	173.472	0.000	217.803	0.000
	Right middle lobe vs Left upper lobe	383.715	0.000	183.845	0.000	276.207	0.000
	Right middle lobe vs Left lower lobe	203.992	0.000	112.926	0.000	158.356	0.000
	Right middle lobe vs Main bronchus	6,517.198	0.000	5,704.728	0.000	6,423.992	0.000
	Right middle lobe vs Overlapping lesion of lung	779.740	0.000	877.108	0.000	882.311	0.000
	Right middle lobe vs Lung, NOS	13,575.417	0.000	11,318.686	0.000	13,058.521	0.000
	Right middle lobe vs Others	827.004	0.000	682.774	0.000	765.542	0.000
	Right lower lobe vs Left upper lobe	13.780	0.000	0.580	0.446	2.000	0.157
	Right lower lobe vs Left lower lobe	4.529	0.033	10.831	0.001	6.940	0.008
	Right lower lobe vs Main bronchus	7,741.953	0.000	7,473.661	0.000	8,027.688	0.000

Right lower lobe vs Overlapping lesion of lung	446.655	0.000	621.232	0.000	581.078	0.000
Right lower lobe vs Lung, NOS	23,928.595	0.000	22,385.509	0.000	24,235.716	0.000
Right lower lobe vs Others	609.686	0.000	513.797	0.000	571.712	0.000
Left upper lobe vs Left lower lobe	33.598	0.000	8.632	0.003	17.905	0.000
Left upper lobe vs Main bronchus	8,554.529	0.000	8,966.598	0.000	9,271.170	0.000
Left upper lobe vs Overlapping lesion of lung	419.865	0.000	684.012	0.000	599.494	0.000
Left upper lobe vs Lung, NOS	30,093.214	0.000	30,515.243	0.000	31,760.602	0.000
Left upper lobe vs Others	604.525	0.000	551.023	0.000	591.460	0.000
Left lower lobe vs Main bronchus	7,605.617	0.000	7,473.549	0.000	7,956.885	0.000
Left lower lobe vs Overlapping lesion of lung	487.337	0.000	692.059	0.000	636.294	0.000
Left lower lobe vs Lung, NOS	21,655.850	0.000	20,479.488	0.000	22,098.264	0.000
Left lower lobe vs Others	639.715	0.000	558.856	0.000	611.053	0.000
Main bronchus vs Overlapping lesion of lung	574.941	0.000	374.213	0.000	491.592	0.000
Main bronchus vs Lung, NOS	482.626	0.000	590.283	0.000	555.427	0.000
Main bronchus vs Others	1.595	0.207	8.097	0.004	5.825	0.016
Overlapping lesion of lung vs Lung, NOS	1,416.129	0.000	1,047.110	0.000	1,270.005	0.000
Overlapping lesion of lung vs Others	122.072	0.000	55.546	0.000	83.040	0.000
Lung, NOS vs Others	52.256	0.000	91.285	0.000	79.609	0.000
Right upper lobe vs Other single lobes	71.499	0.000	53.158	0.000	66.958	0.000
Right middle lobe vs Other single lobes	284.671	0.000	149.788	0.000	212.357	0.000
Right lower lobe vs Other single lobes	21.601	0.000	43.991	0.000	32.919	0.000
Left upper lobe vs Other single lobes	174.418	0.000	57.640	0.000	108.889	0.000
Left lower lobe vs Other single lobes	0.963	0.326	1.070	0.301	1.432	0.231
Main bronchus vs Single lobes	11,026.346	0.000	11,283.718	0.000	11,727.875	0.000
Overlapping lesion of lung vs Single lobes	547.887	0.000	786.542	0.000	722.280	0.000
Lung, NOS vs Single lobes	50,039.338	0.000	51,295.080	0.000	52,602.027	0.000
Histologic type (ICD-O-3)						
Neoplasia, NAS vs Epithelial neoplasms, NAS	3,757.214	0.000	7,408.176	0.000	5,986.605	0.000
Neoplasia, NAS vs Squamous cell neoplasms	20,217.196	0.000	27,516.738	0.000	25,146.774	0.000
Neoplasia, NAS vs Adenoma and adenocarcinomas	35,445.959	0.000	40,577.637	0.000	39,259.802	0.000
Neoplasia, NAS vs Cystic, mucinous and serous neoplasms	6,149.905	0.000	6,029.979	0.000	6,450.057	0.000
Neoplasia, NAS vs Acinous cell neoplasm	11,950.640	0.000	10,107.204	0.000	11,760.036	0.000
Neoplasia, NAS vs Complex epithelial neoplasms	4,939.508	0.000	5,491.534	0.000	5,632.441	0.000
Neoplasia, NAS vs Others	1,961.725	0.000	1,547.515	0.000	1,799.985	0.000
Epithelial neoplasms, NAS vs Squamous cell neoplasms	18,051.629	0.000	18,642.122	0.000	19,723.395	0.000
Epithelial neoplasms, NAS vs Adenoma and adenocarcinomas	52,956.139	0.000	43,604.909	0.000	49,887.906	0.000
Epithelial neoplasms, NAS vs Cystic, mucinous and serous neoplasms	3,920.902	0.000	2,832.710	0.000	3,530.938	0.000

(Continued)

Table 2 (Continued).

Comparison Type	Comparative Factor	Log Rank (Mantel-Cox)		Breslow (Generalized Wilcoxon)		Tarone-Ware	
		Chi Square	Sig.	Chi Square	Sig.	Chi Square	Sig.
	Epithelial neoplasms, NAS vs Acinous cell neoplasm	9,902.939	0.000	8,306.628	0.000	9,832.557	0.000
	Epithelial neoplasms, NAS vs Complex epithelial neoplasms	2,880.374	0.000	2,512.595	0.000	2,904.016	0.000
	Neoplasia, NAS vs Complex epithelial neoplasms	4,939.508	0.000	5,491.534	0.000	5,632.441	0.000
	Epithelial neoplasms, NAS vs Others	1,183.182	0.000	575.683	0.000	841.398	0.000
	Squamous cell neoplasms vs Adenoma and adenocarcinomas	4,324.050	0.000	2,002.280	0.000	2,974.305	0.000
	Squamous cell neoplasms vs Cystic, mucinous and serous neoplasms	526.311	0.000	232.401	0.000	355.225	0.000
	Squamous cell neoplasms vs Acinous cell neoplasm	5,171.203	0.000	4,982.770	0.000	5,383.737	0.000
	Squamous cell neoplasms vs Complex epithelial neoplasms	246.850	0.000	171.523	0.000	210.048	0.000
	Squamous cell neoplasms vs Others	211.562	0.000	15.811	0.000	64.762	0.000
	Adenoma and adenocarcinomas vs Cystic, mucinous and serous neoplasms	9,479	0.002	4,511	0.034	6,611	0.010
	Adenoma and adenocarcinomas vs Acinous cell neoplasm	3,429.157	0.000	3,748.082	0.000	3,805.019	0.000
	Adenoma and adenocarcinomas vs Complex epithelial neoplasms	14,960	0.000	0.000	0.991	2,697	0.101
	Adenoma and adenocarcinomas vs Others	10,571	0.001	7,914	0.005	0.424	0.515
	Cystic, mucinous and serous neoplasms vs Acinous cell neoplasm	2,508.321	0.000	3,023.062	0.000	2,957.332	0.000
	Cystic, mucinous and serous neoplasms vs Complex epithelial neoplasms	24,420	0.000	2,074	0.150	8,732	0.003
	Cystic, mucinous and serous neoplasms vs Others	0.961	0.327	12,862	0.000	3,988	0.046
	Acinous cell neoplasm vs Complex epithelial neoplasms	2,915.827	0.000	3,292.872	0.000	3,306.154	0.000
	Acinous cell neoplasm vs Others	1,432.131	0.000	2,382.199	0.000	2,110.827	0.000
	Complex epithelial neoplasms vs Others	20,792	0.000	6,543	0.011	0.027	0.871
	Summary stage						
	Distant vs Localized	189,234.197	0.000	157,689.763	0.000	180,494.909	0.000
	Distant vs Regional	95,182.979	0.000	89,552.783	0.000	97,474.996	0.000
	Distant vs Unknown/unstaged	2,281.394	0.000	1,319.592	0.000	1,873.692	0.000
	Localized vs Regional	22,646.800	0.000	24,779.500	0.000	25,260.467	0.000
	Localized vs Unknown/unstaged	54,328.909	0.000	60,221.013	0.000	59,752.077	0.000
	Regional vs Unknown/unstaged	15,840.215	0.000	19,402.780	0.000	18,494.477	0.000

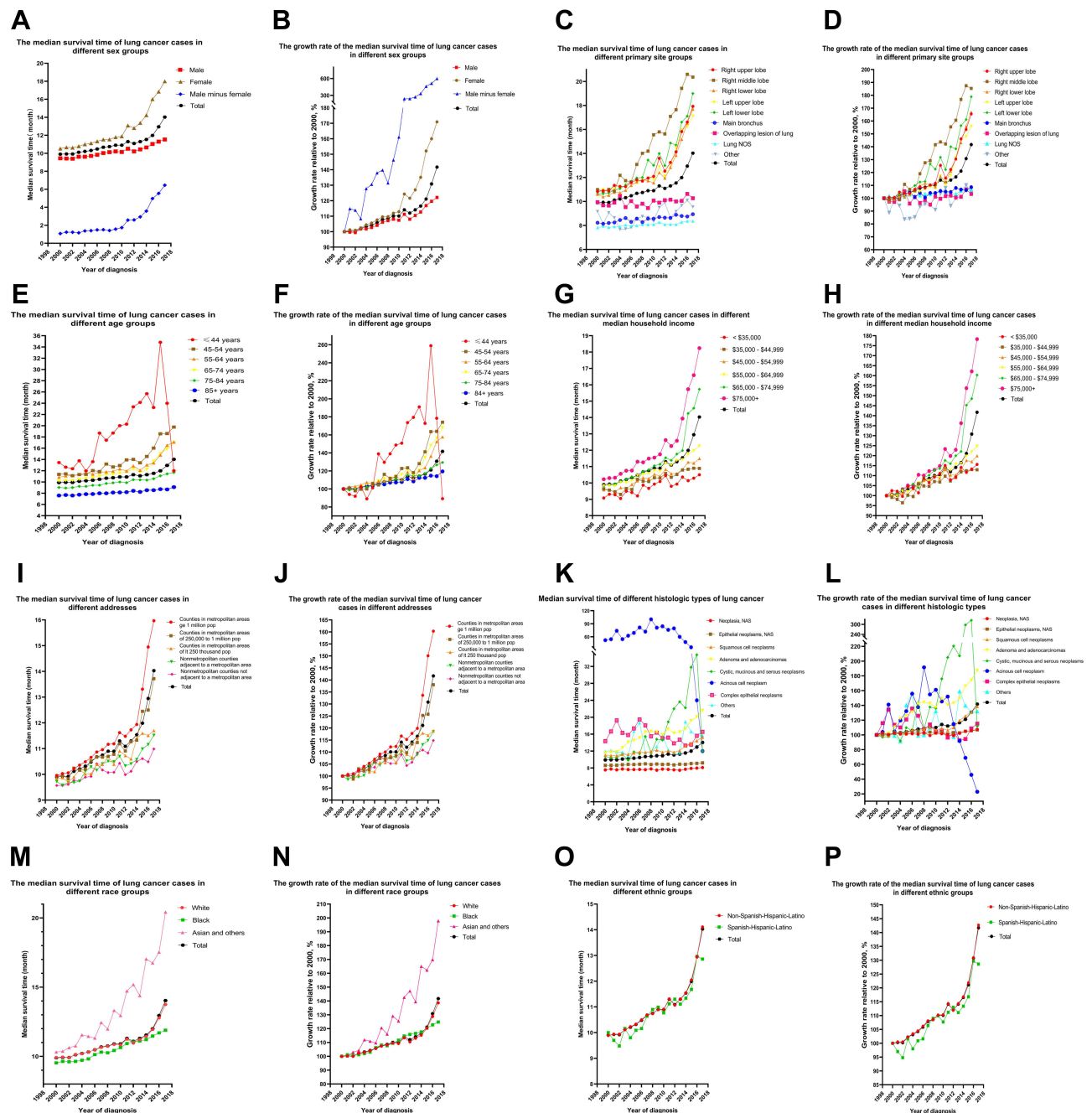


Figure 1 Median survival time. Survival and its growth rate in lung cancer patients from 2000 to 2017. (A and B) According to sex. (C and D) According to primary site. (E and F) According to age. (G and H) According to median household income (inflation adjusted to 2019). (I and J) According to address. (K and L) According to histologic type. (M and N) According to race. (O and P) According to ethnic group.

57,432.600, and Tarone-Ware was 59,443.510, with $P < 0.001$ for all (Table 2). The specific values of univariate and multivariate hazard ratios (HRs) for different primary sites were shown in Table 3.

Age

Younger patients had a longer median survival time (Figure 1E and F), but survival time was almost equal

between the 55–64 and 65–74 age groups, and the changes were synchronous (Tables S6 and S7). The sudden decrease in the median survival time of patients with lung cancer diagnosed in 2016 and 2017 in the group less than or equal to 44 years may be related to the small number of patients at onset and cannot be counted in the changing trend that the median survival time of patients with lung cancer diagnosed in the group less than or equal

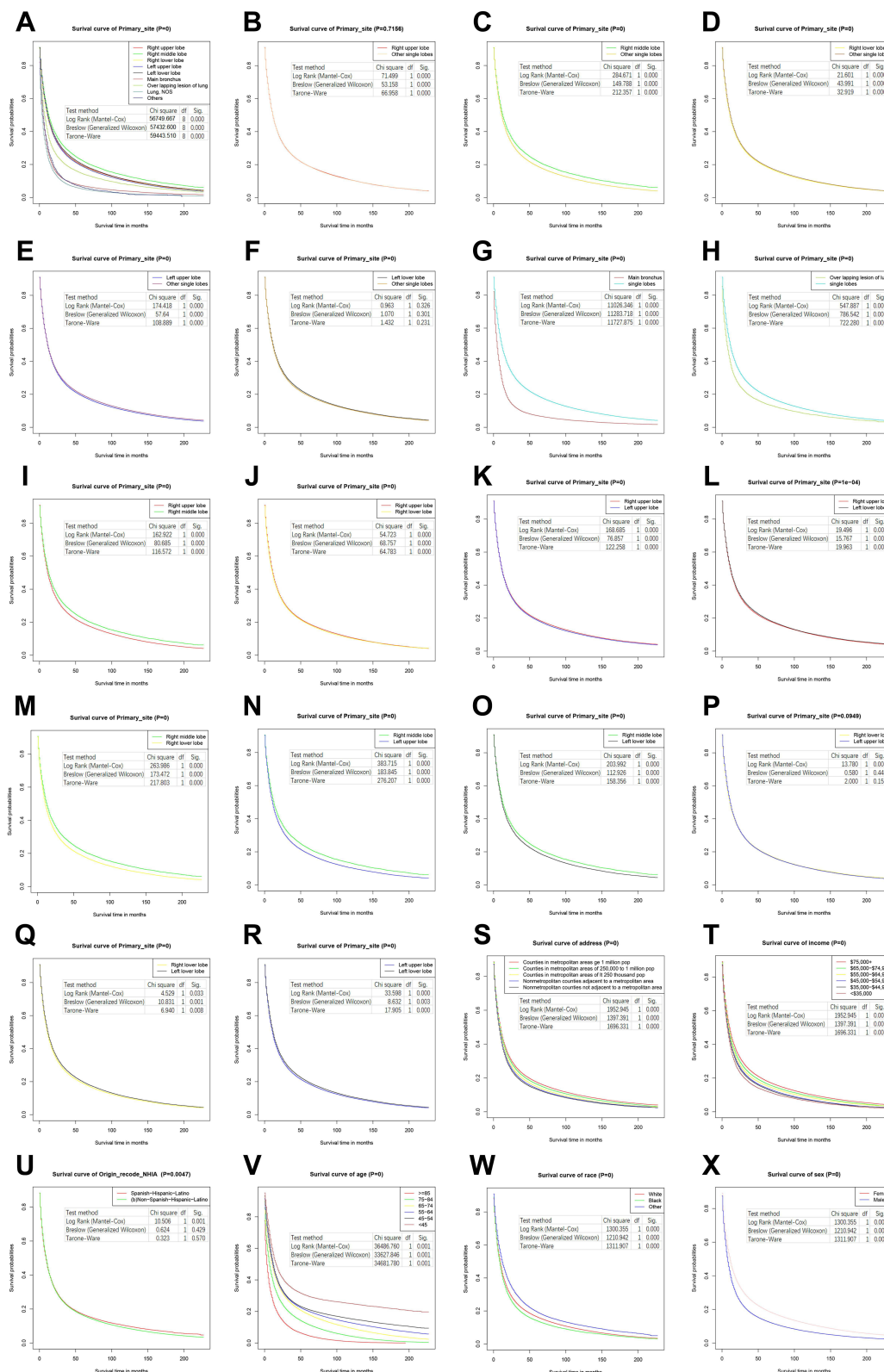


Figure 2 Kaplan-Meier survival curves of lung cancer patients according to primary site and demographics. (A) All primary site groups. (B) Right upper lobe. (C) Right middle lobe. (D) Right lower lobe. (E) Left upper lobe. (F) Left lower lobe. (G) Main bronchus. (H) Overlapping lesion of lung. (I) Right upper lobe and right middle lobe. (J) Right upper lobe and right lower lobe. (K) Right upper lobe and left upper lobe. (L) Right upper lobe and left lower lobe. (M) Middle lobe and right lower lobe. (N) Right middle lobe and left upper lobe. (O) Middle lobe and left lower lobe. (P) Right lower lobe and left lower lobe. (Q) Right lower lobe and left lower lobe. (R) Left upper lobe and left lower lobe. (S) Address groups. (T) Income groups. (U) Ethnic groups. (V) Age groups. (W) Race groups. (X) Sex groups.

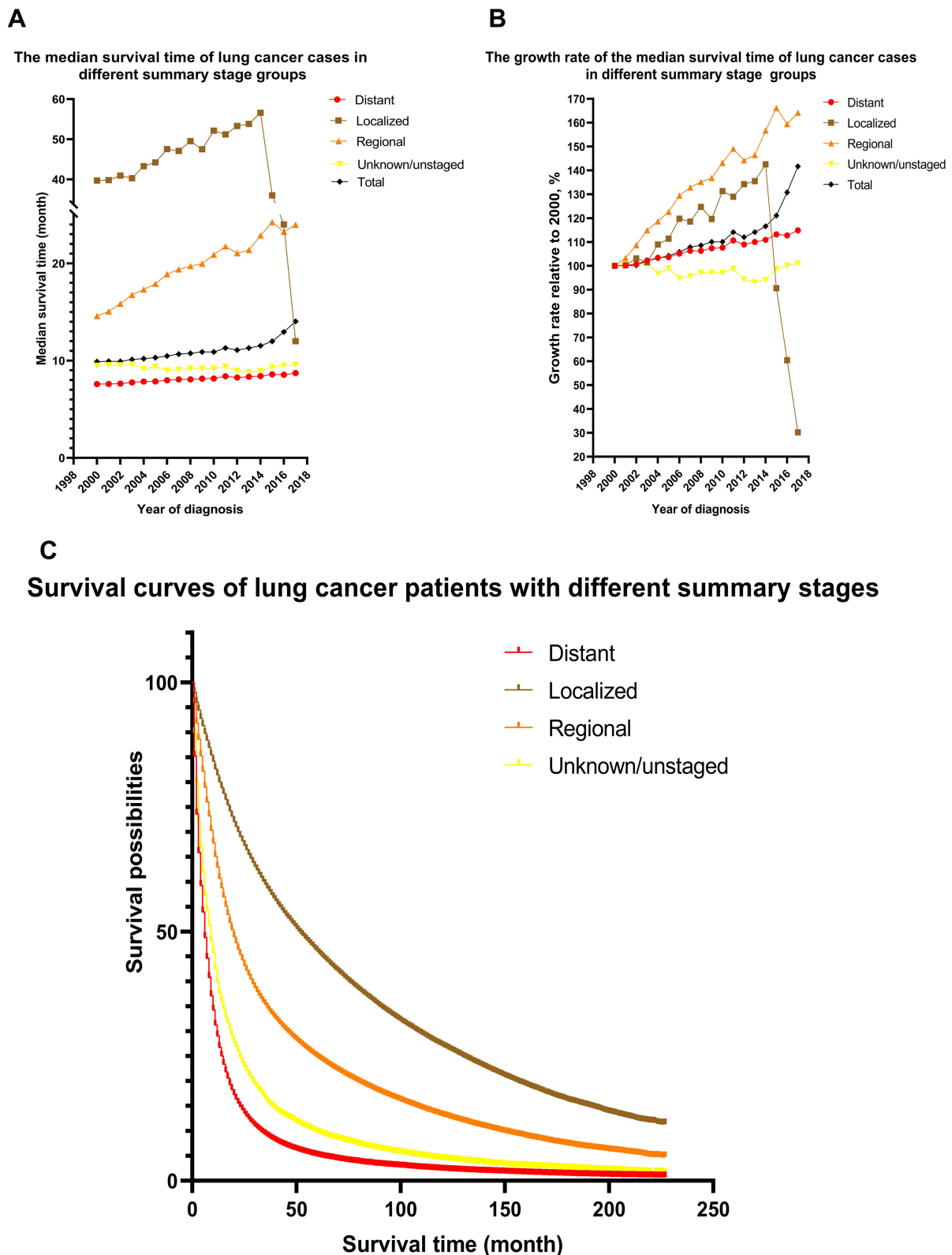


Figure 3 Survival curves of different summary stages and changes in median survival time of lung cancer patients from 2000 to 2017. **(A)** Median survival time of lung cancer patients at different summary stages from 2000 to 2017. **(B)** Increase in median survival time of lung cancer patients at different summary stages from 2000 to 2017. **(C)** Kaplan–Meier survival curves for different summary stages.

Table 3 Univariate and Multivariate Cox Proportional Hazards Analysis of Lung Cancer Based on SEER Database

Types of Cox Analysis	Comparing Factors	B	SE	Wald	df	Sig.	HR	95.0% HR, CI	
								Lower	Upper
Univariate	Primary site			51,359.75	8	0.000			
	Right middle lobe vs Right upper lobe	-0.075	0.006	152.810	1	0.000	0.927	0.916	0.939
	Right lower lobe vs Right upper lobe	0.027	0.004	49.306	1	0.000	1.027	1.019	1.035
	Left upper lobe vs Right upper lobe	0.041	0.003	151.521	1	0.000	1.042	1.035	1.048
	Left lower lobe vs Right upper lobe	0.017	0.004	16.670	1	0.000	1.017	1.009	1.025
	Main bronchus vs Right upper lobe	0.528	0.005	9,373.596	1	0.000	1.696	1.678	1.714
	Overlapping lesion of lung vs Right upper lobe	0.247	0.010	557.362	1	0.000	1.280	1.254	1.306
	Lung, NOS vs Right upper lobe	0.654	0.004	34,847.930	1	0.000	1.923	1.910	1.937
	Others (a) vs Right upper lobe	0.511	0.020	626.507	1	0.000	1.666	1.601	1.734
	Sex								
	Male vs Female	0.215	0.002	8,886.971	1	0.000	1.240	1.234	1.245
	Age			33,386.410	5	0.000			
	45–54 years vs < 45 years	0.277	0.010	724.156	1	0.000	1.319	1.293	1.346
	55–64 years vs < 45 years	0.343	0.010	1,225.613	1	0.000	1.409	1.382	1.436
	65–74 years vs < 45 years	0.426	0.010	1,941.140	1	0.000	1.532	1.503	1.561
	75–84 years vs < 45 years	0.658	0.010	4,590.031	1	0.000	1.931	1.894	1.968
	85+ years vs < 45 years	1.001	0.010	9,588.206	1	0.000	2.722	2.668	2.777
	Race			1,222.947	2	0.000			
	Black vs White	0.059	0.004	263.022	1	0.000	1.061	1.053	1.068
	Others (b) vs White	-0.144	0.005	867.837	1	0.000	0.865	0.857	0.874
	Origin recode NHIA								
	Non-Spanish-Hispanic-Latino vs Spanish-Hispanic-Latino	0.016	0.005	9.888	1	0.002	1.016	1.006	1.027
	Median household income inflation adj to 2019			2,931.738	6	0.000			
	\$35,000–\$44,999 vs <\$35,000	-0.054	0.009	38.994	1	0.000	0.948	0.932	0.964
	\$45,000–\$54,999 vs <\$35,000	-0.072	0.008	78.900	1	0.000	0.930	0.915	0.945
	\$55,000–\$64,999 vs <\$35,000	-0.119	0.008	220.252	1	0.000	0.888	0.874	0.902
	\$65,000–\$74,999 vs <\$35,000	-0.163	0.008	407.928	1	0.000	0.850	0.836	0.863
	\$75,000+ vs <\$35,000	-0.219	0.008	756.831	1	0.000	0.803	0.790	0.816
	Others (c) vs <\$35,000	-0.173	0.123	1.967	1	0.161	0.841	0.661	1.071
	Rural-Urban Continuum			1,835.107	5	0.000			
	Counties in metropolitan areas of 250,000 to 1 million pop vs Counties in metropolitan areas of greater than 1 million pop	0.036	0.003	146.527	1	0.000	1.037	1.031	1.043
	Counties in metropolitan areas of less than 250 thousand pop vs Counties in metropolitan areas of greater than 1 million pop	0.087	0.004	462.909	1	0.000	1.091	1.083	1.100

	Nonmetropolitan counties adjacent to a metropolitan area vs Counties in metropolitan areas of greater than 1 million pop	0.118	0.004	848.592	1	0.000	1.126	1.117	1.135
	Nonmetropolitan counties not adjacent to a metropolitan vs Counties in metropolitan areas of greater than 1 million pop	0.144	0.005	946.941	1	0.000	1.155	1.144	1.166
	Others (d) vs Counties in metropolitan areas of greater than 1 million pop	0.139	0.030	21.202	1	0.000	1.149	1.083	1.220
	Histologic type (ICD-O-3)			74,262.360	7	0.000			
	Epithelial neoplasms, NAS vs Neoplasia, NAS	-0.296	0.005	3,638.861	1	0.000	0.744	0.737	0.751
	Squamous cell neoplasms vs Neoplasia, NAS	-0.700	0.005	18,147.780	1	0.000	0.497	0.492	0.502
	Adenoma and adenocarcinomas vs Neoplasia, NAS	-0.900	0.005	33,303.950	1	0.000	0.406	0.403	0.410
	Cystic, mucinous and serous neoplasms vs Neoplasia, NAS	-0.933	0.011	6,687.317	1	0.000	0.393	0.385	0.402
	Acinous cell neoplasm vs Neoplasia, NAS	-2.005	0.021	9,539.132	1	0.000	0.135	0.129	0.140
	Complex epithelial neoplasms vs Neoplasia, NAS	-0.859	0.012	5,433.430	1	0.000	0.424	0.414	0.433
	Others (e) vs Neoplasia, NAS	-0.962	0.020	2,265.927	1	0.000	0.382	0.367	0.398
	Year of diagnosis			7,025.014	17	0.000			
	2001 vs 2000	-0.006	0.007	0.709	1	0.400	0.994	0.982	1.007
	2002 vs 2000	-0.006	0.007	0.912	1	0.339	0.994	0.981	1.007
	2003 vs 2000	-0.022	0.007	11.283	1	0.001	0.978	0.966	0.991
	2004 vs 2000	-0.038	0.007	33.250	1	0.000	0.963	0.951	0.975
	2005 vs 2000	-0.054	0.007	68.099	1	0.000	0.947	0.935	0.960
	2006 vs 2000	-0.077	0.007	136.769	1	0.000	0.926	0.914	0.938
	2007 vs 2000	-0.088	0.007	181.709	1	0.000	0.915	0.904	0.927
	2008 vs 2000	-0.104	0.007	252.221	1	0.000	0.901	0.889	0.913
	2009 vs 2000	-0.117	0.007	315.202	1	0.000	0.890	0.878	0.901
	2010 vs 2000	-0.131	0.007	388.059	1	0.000	0.877	0.866	0.889
	2011 vs 2000	-0.162	0.007	586.987	1	0.000	0.850	0.839	0.861
	2012 vs 2000	-0.156	0.007	540.690	1	0.000	0.855	0.844	0.867
	2013 vs 2000	-0.182	0.007	724.595	1	0.000	0.833	0.822	0.844
	2014 vs 2000	-0.220	0.007	1,029.316	1	0.000	0.803	0.792	0.814
	2015 vs 2000	-0.271	0.007	1,512.721	1	0.000	0.762	0.752	0.773
	2016 vs 2000	-0.311	0.007	1,876.193	1	0.000	0.733	0.722	0.743
	2017 vs 2000	-0.348	0.008	2,105.528	1	0.000	0.706	0.696	0.717
	Summary stage			205,903.400	3	0			
	Localized vs Distant	-1.426	0.004	165,939.800	1	0	0.240	0.239	0.242
	Regional vs Distant	-0.884	0.003	90,444.560	1	0	0.413	0.411	0.415
	Unknown/unstaged vs Distant	-0.256	0.005	2,733.579	1	0	0.774	0.767	0.782
	Primary Site			30,355.820	8	0.000			
	Right middle lobe vs Right upper lobe	-0.045	0.006	55.071	1	0.000	0.956	0.944	0.967
	Right lower lobe vs Right upper lobe	0.038	0.004	100.117	1	0.000	1.039	1.031	1.047
	Left upper lobe vs Right upper lobe	0.028	0.003	71.195	1	0.000	1.028	1.022	1.035
Multivariate									

(Continued)

Table 3 (Continued).

Types of Cox Analysis	Comparing Factors	B	SE	Wald	df	Sig.	HR	95.0% HR, CI	
								Lower	Upper
	Left lower lobe vs Right upper lobe	0.031	0.004	55.730	1	0.000	1.031	1.023	1.040
	Main bronchus vs Right upper lobe	0.446	0.005	6,583.468	1	0.000	1.562	1.545	1.579
	Overlapping lesion of lung vs Right upper lobe	0.257	0.010	603.009	1	0.000	1.293	1.267	1.320
	Lung, NOS vs Right upper lobe	0.519	0.004	20,830.791	1	0.000	1.681	1.669	1.693
	Others (f) vs Right upper lobe	0.424	0.020	431.055	1	0.000	1.528	1.468	1.590
	Sex								
	Male vs Female	0.197	0.002	7,283.054	1	0.000	1.217	1.212	1.223
	Age								
	45–54 years vs < 45 years	0.261	0.010	639.066	1	0.000	1.299	1.272	1.325
	55–64 years vs < 45 years	0.348	0.010	1,254.460	1	0.000	1.417	1.389	1.444
	65–74 years vs < 45 years	0.459	0.010	2,223.302	1	0.000	1.582	1.552	1.613
	75–84 years vs < 45 years	0.688	0.010	4,960.363	1	0.000	1.990	1.952	2.029
	85+ years vs < 45 years	0.960	0.010	8,635.988	1	0.000	2.611	2.559	2.665
	Race								
	Black vs White	0.095	0.004	642.820	1	0.000	1.099	1.091	1.108
	Others (g) vs White	–0.062	0.005	153.648	1	0.000	0.939	0.930	0.949
	Origin recode NHIA								
	Non-Spanish-Hispanic-Latino vs Spanish-Hispanic-Latino	0.018	0.005	12.181	1	0.000	1.018	1.008	1.029
	Median household income inflation adj to 2019								
	\$35,000–\$44,999 vs <\$35,000	–0.055	0.009	37.947	1	0.000	0.946	0.930	0.963
	\$45,000–\$54,999 vs <\$35,000	–0.082	0.009	87.256	1	0.000	0.921	0.905	0.937
	\$55,000–\$64,999 vs <\$35,000	–0.126	0.009	194.220	1	0.000	0.881	0.866	0.897
	\$65,000–\$74,999 vs <\$35,000	–0.165	0.009	316.049	1	0.000	0.848	0.833	0.864
	\$75,000+ vs <\$35,000	–0.203	0.009	479.380	1	0.000	0.816	0.802	0.831
	Others (h) vs <\$35,000	–0.773	0.127	36.796	1	0.000	0.462	0.360	0.593
	Rural-Urban Continuum								
	Counties in metropolitan areas of 250,000 to 1 million pop vs Counties in metropolitan areas of greater than 1 million pop	0.013	0.003	19.031	1	0.000	1.014	1.007	1.020
	Counties in metropolitan areas of less than 250 thousand pop vs Counties in metropolitan areas of greater than 1 million pop	0.001	0.004	0.068	1	0.795	1.001	0.992	1.010
	Nonmetropolitan counties adjacent to a metropolitan area vs Counties in metropolitan areas of greater than 1 million pop	–0.005	0.005	0.897	1	0.344	0.995	0.986	1.005
	Nonmetropolitan counties not adjacent to a metropolitan vs Counties in metropolitan areas of greater than 1 million pop	0.008	0.006	1.923	1	0.166	1.008	0.997	1.020
	Others (i) vs Counties in metropolitan areas of greater than 1 million pop	0.243	0.032	59.247	1	0.000	1.275	1.199	1.357
	Histologic type ICDO3								
	Epithelial neoplasms, NAS vs Neoplasia, NAS	–0.053	0.005	106.351	1	0.000	0.949	0.939	0.958

Squamous cell neoplasms vs Neoplasia, NAS	-0.428	0.005	6,132.065	1	0.000	0.652	0.645	0.659
Adenoma and adenocarcinomas vs Neoplasia, NAS	-0.557	0.005	11,534.349	1	0.000	0.573	0.567	0.579
Cystic, mucinous and serous neoplasms vs Neoplasia, NAS	-0.578	0.012	2,506.946	1	0.000	0.561	0.549	0.574
Acinous cell neoplasm vs Neoplasia, NAS	-1.553	0.021	5,656.729	1	0.000	0.212	0.203	0.220
Complex epithelial neoplasms vs Neoplasia, NAS	-0.533	0.012	2,045.116	1	0.000	0.587	0.574	0.601
Others (i) vs Neoplasia, NAS	-0.619	0.020	928.675	1	0.000	0.539	0.518	0.560
Year of diagnosis			2,414.036	17	0.000			
2001 vs 2000	-0.010	0.007	2.319	1	0.128	0.990	0.977	1.003
2002 vs 2000	-0.014	0.007	4.348	1	0.037	0.986	0.974	0.999
2003 vs 2000	-0.034	0.007	27.497	1	0.000	0.966	0.954	0.979
2004 vs 2000	-0.050	0.007	58.507	1	0.000	0.951	0.939	0.963
2005 vs 2000	-0.061	0.007	86.634	1	0.000	0.941	0.929	0.953
2006 vs 2000	-0.079	0.007	142.858	1	0.000	0.924	0.913	0.936
2007 vs 2000	-0.083	0.007	159.809	1	0.000	0.920	0.908	0.932
2008 vs 2000	-0.092	0.007	193.962	1	0.000	0.912	0.900	0.924
2009 vs 2000	-0.099	0.007	223.976	1	0.000	0.906	0.894	0.918
2010 vs 2000	-0.100	0.007	224.238	1	0.000	0.905	0.893	0.917
2011 vs 2000	-0.110	0.007	267.803	1	0.000	0.896	0.884	0.907
2012 vs 2000	-0.100	0.007	218.197	1	0.000	0.905	0.893	0.917
2013 vs 2000	-0.115	0.007	283.473	1	0.000	0.891	0.880	0.903
2014 vs 2000	-0.141	0.007	418.512	1	0.000	0.868	0.857	0.880
2015 vs 2000	-0.176	0.007	631.345	1	0.000	0.838	0.827	0.850
2016 vs 2000	-0.200	0.007	762.693	1	0.000	0.819	0.808	0.831
2017 vs 2000	-0.231	0.008	918.224	1	0.000	0.794	0.782	0.806
Summary stage			184,737.000	3	0.000			
Localized vs Distant	-1.385	0.004	149,948.100	1	0.000	0.250	0.248	0.252
Regional vs Distant	-0.854	0.003	82,171.650	1	0.000	0.426	0.423	0.428
Unknown/unstaged vs Distant	-0.533	0.005	11,191.940	1	0.000	0.587	0.581	0.593

Notes: (a) Others included Only one side - side unspecified, Bilateral, single primary and Paired site, but no information concerning laterality. (b) Others included Asian or Pacific Islander and American Indian/Alaska Native. (c) Others included unknown/missing/no match/Not 1990–2018. (d) Others included Unknown/missing/no match (Alaska or Hawaii - Entire State) and Unknown/missing/no match/Not 1990–2018. (e) Others included all the histological types of lung cancer except the above seven types. (f) Others included Only one side - side unspecified, Bilateral, single primary and Paired site, but no information concerning laterality. (g) Others included Asian or Pacific Islander and American Indian/Alaska Native (h) Others included unknown/missing/no match/Not 1990–2018 (i) Others included Unknown/missing/no match (Alaska or Hawaii - Entire State) and Unknown/missing/no match/Not 1990–2018. (j) Others included all the histological types of lung cancer except the above seven types.

to 44 years increased overall. The specific values of the 3-year, 5-year, and 10-year survival rates of lung cancer patients of different ages were shown in [Table 1](#). The log rank (Mantel-Cox) for the overall comparison was 36,486.760, the Breslow (generalized Wilcoxon) was 33,627.846, and Tarone-Ware was 34,681.780, $P < 0.001$ for all ([Table 2](#)). The specific values of univariate and multivariate hazard ratios (HRs) for different ages were shown in [Table 3](#).

Median Household Income

A longer median survival time was seen in patients with higher incomes ([Figure 1G and H](#)) and [Table S8](#)). The median survival time of the \$75,000 + group (18.24 months) was 7.740 months longer than the \$35,000 group (10.500 months). The median survival times of the \$35,000–\$44,999, \$45,000–\$54,999, \$55,000–\$64,999 and \$65,000–\$74,999 groups were 10.890 months, 11.490 months, 12.260 months, and 15.730 months, respectively. The fastest increase in median survival time was 78.30% and 60.35% for the \$75,000+ and \$65,000–\$74,999 groups, respectively ([Table S9](#)). The specific values of the 3-year, 5-year, and 10-year survival rates of lung cancer patients of different incomes were shown in [Table 1](#). The log rank (Mantel-Cox) for the overall comparison was 3,119.588, the Breslow (generalized Wilcoxon) was 2,577.577, and Tarone-Ware was 2,934.977, $P < 0.001$ for all ([Table 2](#)). The specific values of univariate and multivariate hazard ratios (HRs) for different median household incomes were shown in [Table 3](#).

Address

A longer survival time was seen in a metropolitan population ([Figure 1I and J](#)) and [Table S9](#)). Survival in metropolitan areas of 1 million (15.970 months) exceeded 14.030 months (all lung cancer patients), while in metropolitan areas of 1 million this was 13.720 months. Times in other areas were: metropolitan areas of 250,000 (11.700 months), nonmetropolitan counties adjacent to a metropolitan area (11.520 months), and the nonmetropolitan counties not adjacent to a metropolitan area group (10.990 months) had less survival time than 14.030 months ([Table S10](#)). As can be seen from [Table S10](#), the fastest increases in median survival time were 60.34% and 38.03% for metropolitan areas of 1 million and metropolitan areas of 1 million, respectively ([Table S11](#)). The specific values of the 3-year, 5-year, and 10-year survival rates of lung cancer patients of different addresses were

shown in [Table 1](#). The log rank (Mantel-Cox) for the overall comparison was 1,952.945, the Breslow (generalized Wilcoxon) was 1,397.391, and Tarone-Ware was 1,696.331, all $P < 0.001$ ([Table 2](#)). The specific values of univariate and multivariate hazard ratios (HRs) for different addresses were shown in [Table 3](#).

Histologic Type ICD-O-3

Median survival time of lung cancer patients in the adenocarcinoma group (Diagnosed 2017) was significantly higher than all other patients, followed by the complex epithelial neoplasms and squamous cell neoplasms groups. ([Figure 1K and L](#)) and [Table S12](#)). The number of patients in the Adenoma and adenocarcinomas group diagnosed in 2017 increased by 87.35% compared to 2000. Survival time in the Squamous cell neoplasms group (15.270 months) was longer than 14.030 months ([Figure 1K and L](#)) and [Table S12](#)), and the number of patients diagnosed in 2017 increased by 38.44% compared to 2000. Median survival time in the other groups was as follows: Neoplasia, NAS (8.100 months), Epithelial neoplasms, NAS (9.200 months) and Cystic, mucinous and serous neoplasms (12.000 months). Each was shorter than 14.030 months ([Table S12](#) and [S13](#)). The specific values of the 3-year, 5-year, and 10-year survival rates of lung cancer patients of different histologic types were shown in [Table 1](#).

The log rank (Mantel-Cox) for the overall comparison was 82,913.123, the Breslow (generalized Wilcoxon) was 79,928.300, and Tarone-Ware was 84,548.100, all $P < 0.001$ ([Table 2](#)). The specific values of univariate and multivariate hazard ratios (HRs) for different histologic types were shown in [Table 3](#).

Race

Median survival time of Asian and other races diagnosed in 2017 was 97.87% higher than in 2000 ([Figure 1M and N](#)), and median survival time of White patients increased by 38.61%. In contrast, Black patients only had a 24.77% increase, which is below average ([Table S15](#)). Among lung cancer patients diagnosed in 2017, median survival was 13.750 months for White patients, 11.890 months for Black patients, and 20.420 months for Asian and other patients ([Table S14](#)). The 3 -, 5 -, and 10-year survival rates for White, Black, Asian and other races were, in order: 19.00%, 14.00%, 8.00%; 17.00%, 12.00%, 7.00%; 23.00%, 17.00%, 11.00% ([Table 1](#)).

The log rank (Mantel-Cox) for the overall comparison was 1,300.355, the Breslow (generalized Wilcoxon) was

1,210.942, and Tarone-Ware was 1,311.907, all $P < 0.001$ (Table 2). Univariate HRs compared with White for Black, Asian and other races were, in order: 1.061 (1.053–1.068) and 0.865 (0.857–0.874), $P < 0.001$. Multivariate HRs were, in order: 1.099 (1.091–1.108), 0.939 (0.930–0.949), all $P < 0.001$ (Table 3). The specific values of univariate and multivariate hazard ratios (HRs) for different races were shown in Table 3.

Origin Recode the National Health Insurance Authority

Median survival time was 14.110 months for Non-Spanish-Hispanic-Latino patients diagnosed in 2017 and 12.860 months for Spanish-Hispanic-Latino patients (Figure 1O and P) and Table S16). Compared to patients diagnosed in 2000, survival in Non-Spanish-Hispanic-Latinos increased by 42.67% and in Spanish-Hispanic-Latinos by 28.60% (Table S17). The 3-, 5-, and 10-year survival rates for Non-Spanish-Hispanic-Latinos and Spanish-Hispanic-Latinos were, in order: 19.00%, 14.00%, 8.00%; 20.00%, 15.00%, 9.00% (Table 1).

The log rank (Mantel-Cox) for the pairwise and overall comparisons was 10.506, the Breslow (generalized Wilcoxon) was 0.624, and Tarone-Ware was 0.323. P values were < 0.001 , 0.429, and 0.570, respectively (Table 2). Univariate HR compared with Spanish-Hispanic-Latino for Non-Spanish-Hispanic-Latino was 1.016 (1.006–1.027), $P = 0.002$. Multivariate HR was 1.018 (1.008–1.029), $P < 0.001$ (Table 3).

Summary Stage

The survival rates of lung cancer patients at different summary stages vary considerably, as detailed in Table 1. The survival difference of lung cancer patients with different summary stages was statistically significant (Table 2). The hrs of lung cancer patients with different summary stages differed significantly (Table 3). The survival curves and median survival times of lung cancer patients with different summary stages are shown in Figure 3.

Discussion

According to Howlader and Forjaz,¹ lung cancer mortality rate in the US has decreased significantly recently. Although lung cancer incidence has been described in multiple papers,^{9–12} studies with large samples, multiple sub items, multiple statistical analysis methods, and statistical details by year of diagnosis are not common¹³ and the

data are mostly outdated.^{14–17} Therefore, we took advantage of the new data published by SEER on April 15, 2021, which allowed a detailed analysis of the survival of lung cancer patients in the US. After an in-depth study of 922,317 patients, we have several novel findings. The median survival time of all lung cancer patients diagnosed in 2017 (14.030 months) increased by 41.72% compared with 2000 (9.900 months).

Women's median survival time and 3-year, 5-year, and 10-year survival rates were more significant and growing faster than men's. Pilleron et al¹⁸ also found that gender was one of the most important factors influencing lung cancer survival time. The prognosis of female patients undergoing lobectomy/segmentectomy was significantly better than in male patients.¹⁹ Part of the reason may be that men have a higher smoking rate,²⁰ and the pathobiology of adenocarcinoma in women may differ from that in men.²¹

The median survival time of patients with a single lobe primary site was the longest where this was in the right middle lobe, followed by the left upper lobe, right upper lobe, right lower lobe, and the shortest in left lower lobe. The rapidly increasing survival time may be due to the increase in early diagnosis of lung cancer²² and improved thoracoscopic lobectomy and segmentectomy techniques.²³ In contrast, median survival rates where the primary site was in the main bronchus and over lapping lung did not significantly increase. These are independent predictors of lung cancer metastasis and worse outcomes.²⁴

Although younger patients had a longer median survival time, interestingly, median survival time was almost the same in the 55–64 and 65–74 groups. This may be because there is little difference in the physical condition²⁵ between the two age groups. The median survival time in those over 75 was significantly reduced, which may be related to the decline of the patient's physical fitness or the increased likelihood of severe complications, which are associated with poor survival.²⁶

Median survival time was longer for patients with higher incomes and there was also an association between family disposable income and survival.²⁷ Low-income patients with lung cancer may have delays in diagnosis and treatment, requiring social intervention and care.²⁸ Increased healthcare costs in the public sector were associated with lower cancer mortality.²⁹

The farther the patient's address is from a metropolitan area, the shorter the median survival time. In metropolitan areas with a population of more than 1 million, median survival time exceeded that of all other lung cancer

patients, which may be related to the availability and timeliness of access to good medical care in these areas. The HR was highest in nonmetropolitan counties not adjacent to metropolitan areas. Singh and Siahpush found a widening life expectancy gap between urban and rural areas for lung cancer patients in the US between 1969–2009,³⁰ and our results found that this gap has widened even further over the last decade. Routine tracking of lung cancer excess deaths through urban-rural county classification may help public health authorities and policy makers identify and monitor public health concerns and focus interventions to reduce potential excess deaths in these areas.⁸

Median survival time of lung cancer patients in the adenocarcinoma group (Diagnosed 2017) was significantly higher than all other patients, followed by the complex epithelial neoplasms and squamous cell neoplasms groups. Median survival time in the adenocarcinoma group was 6.35 months longer than in squamous cell carcinoma. This may be related to the improvement of minimally invasive surgery,³¹ chemotherapy,³² immunotherapy,^{33,34} molecular targeted therapy³⁴ or other treatments for lung adenocarcinoma. The Epithelial neoplasms, NAS group was one of the worst groups, containing mainly large and small cell lung cancer. Although there are some new treatments,^{35–38} survival time has not improved significantly. The acinous cell neoplasm group had the longest median survival of lung cancer histology.

The median survival times and rates of Asian, Pacific Islanders and Native American Indians/Alaskans were significantly higher than of White and Black people, and the fastest growth rate was about 97.87%. In contrast, the growth rate in White people was only about 38.61% and in Black people was only about 24.76%. This may be due to different access to health care and the provision of recommended treatment.³⁹ Efforts to ensure that all patients with lung cancer receive timely and appropriate treatment should reduce differences in survival between races.⁴⁰ Median survival time was 14.110 months for Non-Spanish-Hispanic-Latino lung cancer patients (an increase of 42.67%) and 12.860 months for Spanish-Hispanic-Latino (an increase of only 28.60%). The univariate HR of non-Hispanic Latinos was higher than in Hispanic Latinos, which is contrary to a previous study⁴¹ but may be due to a difference in sample size. According to Soneji et al⁴² narrowing racial differences in lung cancer survival rates depends not only on equal opportunities for surgical

resection, but also on better management and treatment of smoking-related complications and diseases.⁴²

The later the year of diagnosis, the longer the median survival time and the lower the risk ratio. This showed that in the past 20 years, the treatment effect in the US has improved. The reason for the survival time of localized lung cancer patients is greater than that of Distant patients. This fully shows that early detection and early treatment are very important in the treatment of lung cancer.

Our study provides detailed insight into the relationship between patients' sex, primary site, age, income, residential address, histological type, race, ethnicity, and survival thanks to the large sample size. However, we acknowledge that if patient data from other countries can be integrated, our study would be more representative. Incidence of lung cancer was not analyzed in detail so this could be further studied in subsequent papers. The SEER database still has some shortcomings, such as not collecting information on "smoking".

Conclusions

After analyzing the data of 922,317 patients with lung cancer in the recently-published SEER database, we found large differences in survival time by gender, race and ethnicity, age, income, address, histological type, primary site and summary stage. This difference has grown in recent years. Government and society need to further strengthen policies to improve trends. We should increase the frequency and precision of lung cancer screening in the future.

Abbreviations

HR, Hazard Ratio; ICD-O-3, International Classification of Disease for Oncology-3; NCI, The National Cancer Institute; SEER, The surveillance, epidemiology, and end results.

Ethics Approval and Informed Consent

Since SEER is an open database and all the data extracted from SEER are nonhuman studies, there is no need to obtain ethical approval from the Ethics Committee of the Second Affiliated Hospital of Nanchang University. Data published by the SEER database is publicly available and identifiable and therefore does not require patient informed consent. Acknowledgment

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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