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Analysis of Suicide Risk Factors in Adult US Patients with Squamous Cell Carcinoma Based on the SEER Database

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Short title: Analysis of Suicide RF in Adult US SCC Patients.

Ethical approval:

The SEER database is a tumor-related database developed by the National Cancer Institute of the United States, providing research data for researchers free of charge. All patients participating in the study received the ethical approval sought by the National Cancer Institute.

Consent for publication:

Consent for publication was obtained from all participants.

Availability of data and materials:

We obtained permission to access the database after signing and submitting the SEER Research Data Agreement form via email. The data that support the findings of this study are available from SEER database but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of SEER database.

Author Contributions:

All authors had full access to all of the data in the study.

Haohui Yu, and Jun Lyu take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Jun Lyu, Haohui Yu.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Haohui Yu, Shengru Tao, Wenli She, Min Liu.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Haohui Yu, Yayun Wu, Wenli She.

Administrative, technical, or material support: Jun Lyu, Shengru Tao.

All authors contributed to writing of the manuscript and approved the final version.

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Abstract

Objectives: The purpose of this study was to determine the risk factors for suicide in patients with squamous cell carcinoma (SCC) in the US.

Setting: Patients with SCC diagnosed between 1975 and 2017 from the Surveillance, Epidemiology, and End Results (SEER) database were selected for this study.

Participants: This study included 415,268 patients with SCC older than 20 years who were diagnosed between 1975 and 2017.

Primary and secondary outcome measures: The general population included in data from the US Centers for Disease Control and Prevention was used to calculate the suicide rate and standardized mortality rate (SMR) of SCC patients. Univariate and multivariate Cox regression analyses were used to identify risk factors for suicide in patients with SCC.

Results: There were 415,268 SCC patients registered in the SEER database, among which 1,157 cases of suicide were found, comprising a total of 2,289,772 person-years. The suicide rate for patients with SCC was 50.53 per 100,000 person-years, and the SMR was 4.13 (95% confidence interval [CI]=3.90–4.38). The Cox regression analyses showed that the factors related to a high risk of suicide among patients with SCC included being male (vs female: hazard ratio [HR]=5.36, 95% CI=4.51–6.38, P<0.001), older at the diagnosis (70–79 vs ≤39 years: HR=1.46, 95% CI=1.09–2.08, P=0.012; ≥80 vs ≤39 years: HR=1.48, 95% CI=1.05–2.08, P=0.025), and white (vs black, HR=2.97, 95% CI=2.20–4.02, P<0.001), and primary cancer (vs nonprimary cancer: HR=1.33, 95% CI=1.17–1.50, P<0.001).

Conclusions: The suicide rate among patients with SCC in the US had decreased over the past few decades, but it remains higher than that in the general population. Being male, older at the diagnosis, and white, and having a higher histological grade are risk factors for suicide in patients.

Strengths and limitations of this study

Our study had several strengths:

1) This study found that the suicide rate of patients with SCC in the US has decreased over the past few decades, but it remains higher than that in the general population.

2) The independent risk factors for suicide in patients with SCC included being male, older at the diagnosis, and white, and having a higher histological grade and not receiving surgery.

Our study had several limitations.

1) Some potentially important information that could impact suicidal behaviors is missing for patients with SCC in the SEER database, such as marital status, religious beliefs, education level, medication status, and psychological factors. The lack of this information might have biased the present research results.

2) Our study only included data on patients with SCC living in certain parts of the US. Future studies should therefore include patients with SCC in more countries and regions in order to accurately identify the factors affecting the risk of suicide in SCC patients worldwide.

Background

The World Health Organization has reported that the number of cancer deaths worldwide is increasing, with cancer now being the third-most-common cause of deaths worldwide.[1] There were about 18.1 million new cancer patients and about 9.6 million deaths worldwide in 2018.[2] Previous studies have shown that patients with depression and cancers with a poor prognosis have a high risk of suicide.[3] Suicide is influenced by many factors,[4] and the World Health Organization has also reported that the number of suicides worldwide is increasing, with approximately 800,000 suicide deaths each year.[5–7] According to data released by the US Centers for Disease Control and Prevention, suicide is one of the common causes of death in the US.[8] The suicide rate in the general US population was 14.78 per 100,000 people in 2018, which was higher than in other countries.[8] Multiple studies have shown that the suicide rate is higher in cancer patients than in the general US population.[9–12] In particular, the suicide rate of patients with head and neck cancer was more than three times higher than that in the general US population.[13] Cancer patients face enormous financial pressures and physical burdens. The poor prognosis of cancer is often accompanied by long-term mental and psychological problems, and often leads to death.[7] The increasing incidence of cancer has resulted in mental and psychological problems gradually becoming a major complication experienced by cancer patients.[14] The resulting fear of a cancer prognosis, depression, and other psychological problems have gradually increased the risk of suicide.[4] Therefore, it is of great importance to identify the risk factors for suicide in cancer patients in order to control suicidality in this population. Some studies have found male sex, white race, marital status, type of cancer, and other factors to be strongly correlated with the suicide risk of patients with some types of cancer.[9–13]

Squamous cell carcinoma (SCC) refers to a malignant tumor derived from the squamous epithelium. This is the general term for a class of tumors that include multiple cancers occurring in the squamous epithelium covering tissues and organs, and which are more common in the skin, mouth, esophagus, cervix, and vagina.[15–17] According to a report by the US Centers for Disease Control and Prevention, the number of deaths from malignant tumors in the US in 2018 was second only to that due to cardiovascular disease, and suicide has become the second leading cause of death among US residents aged 10 to 34 years.[8] The number of deaths due to SCC in the US is increasing. GuoPei Yu et al. investigated the causes of death in patients with oral and oropharyngeal SCC in the US,[18] but did not conduct in-depth studies on the causes of suicide. Therefore, the purpose of this study was to identify potential risk factors associated with suicide in US SCC patients by analyzing data in the US Surveillance, Epidemiology, and End Results (SEER) database.

Method

Data source

All patients with SCC in this study were selected from the SEER database (http://seer.cancer.gov). This database covers about 30% of the US population and provides researchers with a large amount of research data, including on patient demographics, cancer incidence, and survival data.[19] We used SEER*Stat software (version 8.3.6) to identify US patients with SCC who were added to the database from 1975 to 2017. We obtained permission to access the database after signing and submitting the SEER Research Data Agreement form via email.

Patient and Public Involvement:

All patients were selected from the SEER database. No patient involved.

Inclusion and exclusion criteria for the study population

This study applied screening criteria for the research objectives based on histological type codes in ICD-O-3. We used morphology codes 8050/0–8084/3 to identify patients with SCC in the SEER database. The collected patients were divided into the following three groups based on morphology codes: papillary carcinoma (PC, codes 8050/3–8060/0), SCC (codes 8070/2–8078/3), and other carcinomas (OC, codes 8080/2–8084/3). The cause of death of "Suicide and Self-Inflicted Injury" was searched for in order to identify cases of suicide. The exclusion criteria for study subjects included being younger than 20 years, unknown follow-up time, unknown age, and no diagnosis or microscopy data. The information collected by all patients with SCC includes sex, age, year of diagnosis, race, histological grade, cancer type, survival time, surgery status, radiotherapy status, chemotherapy status, cause of death, and area of residence. This study collected 415,268 patients with SCC, which included 1,157 who suicided. The screening procedure for patients with SCC is shown in eFigure 1 in the Supplement.

Statistical analysis

This study divided the SCC patients collected from the SEER database into the following three groups in order to perform basic data comparisons: suicided group, nonsuicide death group, and alive group. We analyzed the age distributions in these three groups of patients from 0 to 85 years and the year of diagnosis distribution of patients from 1975 to 2017. The chi-square test was used to compare the suicide rates among patients in each group. The SMR for suicide in each group was based on the total population of the US from 1981 to 2017, using data obtained from the Web-Based Injury Statistics Query and Reporting System of the Centers for Disease Control and Prevention (https://www.cdc.gov/injury/wisqars/fatal.html). The 95% confidence interval (CI) of the SMR for suicide was approximated using the method of Byar.[20] Univariate and multivariate Cox regression analyses were subsequently used to generate the hazard ratio (HR), and the 95% CI combined with the HR were used to identify potential risk factors for suicide. All statistical analyses was performed using R software (version 3.6.3, http://www.r-project.org/). All tests were two-sided, and the significance criterion was set as P<0.05.

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Results

Patient baseline characteristics

The 415,268 identified US patients with SCC in the SEER database from 1975 to 2017 included 248,816 males (59.9%). These patients comprised 1,157 (0.3%) in the suicided group, 322,384 (77.6%) in the not-suicide-death group, and 91,727 (22.1%) in the alive group. Most of them were older than 60 years (66.3%), white (81.7%), non-Latin American (95.7%), non-Hispanic white (77.6%), and lived in urban areas (56.2%). The age distributions of the suicided, not-suicide-death, alive, and dead patients are shown in eFigure 2 in the Supplement. The basic statistics of each group of SCC patients are presented in Table 1.

Table 1. Baseline characteristics of squamous cell carcinoma patients (1975-2017)

Variables	Overall N(%)	Suicidal death N(%)	Nonsuicidal death N(%)	Alive N(%)
Patients	415268	1157(0.3%)	322384(77.6%)	91727(22.1%)
Year of dignosis				
1975-1984	90334(21.8%)	341(29.5%)	85435(26.5%)	4558(5.0%)
1985-1994	98947(23.8%)	335(29.0%)	88294(27.4%)	10318(11.2%)
1995-2004	94368(22.7%)	253(21.8%)	75490(23.4%)	18625(20.3%)
2005-2017	131619(31.7%)	228(19.7%)	73165(22.7%)	58226(63.5%)
Sex				
Female	166452(40.1%)	159(13.7%)	118262(36.7%)	48031(52.4%)
Male	248816(59.9%)	998(86.3%)	204122(63.3%)	43696(47.6%)
Age at diagnosis				
≤39	22031(5.3%)	67(5.8%)	6211(1.9%)	15753(17.2%)
40-49	36569(8.8%)	114(9.9%)	20570(6.4%)	15885(17.3%)
50-59	81389(19.6%)	246(21.3%)	58737(18.2%)	22406(24.4%)
60-69	120016(28.9%)	360(31.1%)	98541(30.6%)	21115(23.0%)
70-79	104931(25.3%)	282(24.3%)	92561(28.7%)	12088(13.2%)
≥80	50332(12.1%)	88(7.6%)	45764(14.2%)	4480(4.9%)
Race				
Black	50022(12.0%)	45(3.9%)	42014(13.0%)	7963(8.7%)
White	339376(81.7%)	1067(92.2%)	263117(81.6%)	75192(82.0%)
Other	24658(5.9%)	45(3.9%)	16979(5.3%)	7634(8.3%)
Unknown	1212(0.3%)	0	274(0.1%)	938(1.0%)
Race Latino				
Latino	18018(4.3%)	27(2.3%)	11338(3.5%)	6653(7.3%)
Non-Latino	397250(95.7%)	1130(97.7%)	311046(96.5%)	85074(92.7%)
Race Hispanic				
Hispanic	18018(4.3%)	27(2.3%)	11338(3.5%)	6653(7.3%)
Non-Hispanic White	322235(77.6%)	1040(89.9%)	252268(78.2%)	68927(75.1%)

Variables	Overall N(%)	Suicidal death N(%)	Nonsuicidal death N(%)	Alive N(%)
Non-Hispanic Americacn/Indian Native	2137(0.5%)	3(0.3%)	1485(0.5%)	649(0.7%)
Non-Hispanic Asian	22123(5.3%)	42(3.6%)	15253(4.7%)	6828(7.4%)
Non-Hispanic Black	49711(12.0%)	45(3.9%)	41828(13.0%)	7866(8.6%)
Non-Hispanic Unknown Race	1044(0.3%)	0	240(0.1%)	804(0.9%)
Grade				
Grade I	43008(10.4%)	134(11.6%)	31492(9.8%)	11382(12.4%)
Grade II	121959(29.4%)	398(34.4%)	94991(29.5%)	26570(29.0%)_
Grade III	108530(26.0%)	271(23.4%)	89299(27.7%)	18960(20.7%)
Grade IV	6169(1.5%)	20(1.7%)	5198(1.6%)	951(1.0%)
Unknown	135602(32.7%)	334(28.9%)	101404(31.5%)	33864(36.9%)
Surgery performed				
No	207029(49.9%)	494(42.7%)	175871(54.5%)	30664(33.4%)
Yes	197252(47.5%)	643(55.6%)	135928(42.2%)	60681(66.2%)
Unkonwn	10987(2.6%)	20(1.7%)	10585(3.3%)	382(0.4%)
Primary diaeases				
No	127948(30.8%)	362(31.3%)	102800(31.9%)	24786(27.0%)
Yes	287320(69.2%)	795(68.7%)	219584(68.1%)	66941(73.0%)
Household income				
<$50,000	28804(6.9%)	61(5.3%)	19661(6.1%)	9082(9.9%)
$50,000 - $74,999	137290(33.1%)	331(28.6%)	95873(29.7%)	41094(44.8%)
$75,000+	109556(26.4%)	237(20.5%)	76605(23.8%)	3271(35.7%)
Unkonwn	139610(33.6%)	528(45.6%)	130245(40.4%)	8837(9.6%)
Living area#				
Large city	159750(38.5%)	371(32.0%)	112206(34.8%)	47173(51.4%)
Medium city	56207(13.5%)	110(9.5%)	37366(11.6%)	18731(20.4%)
Small city	17605(4.2%)	46(4.0%)	12032(3.7%)	5527(6.0%)
Suburbs	19322(4.7%)	45(3.9%)	13706(4.3%)	5571(6.1%)
Rural	18652(4.5%)	47(4.1%)	13419(4.1%)	5186(5.7%)
Unkonwn	143732(34.6%)	538(46.5%)	133655(41.5%)	9539(10.4%)
Radiotherapy				
No/Unknown	188695(45.4%)	544(47.0%)	146075(45.3%)	42076(45.9%)
Yes	226573(54.6%)	613(53.0%)	176309(54.7%)	49651(54.1%)
Chemotherapy				
No/Unknown	298396(71.9%)	835(72.2%)	231140(71.7%)	66421(72.4%)
Yes	116872(28.1%)	322(27.8%)	91244(28.3%)	25306(27.6%)

#**Large city**,Counties in metropolitan areas ge 1 million pop; **Medium city**, Counties in metropolitan areas of 250,000 to 1 million pop; **Small city**, Counties in metropolitan areas of lt 250 thousand pop; **Suburbs**, Nonmetropolitan counties adjacent to a metropolitan area; **Rural**, Nonmetropolitan counties not adjacent to a metropolitan area; **Unknown**, Unknown/missing/no match/Not 1990-2017.

Patient distributions according to year

We found that most of the US patients with SCC who suicided were males. The number of suicided patients declined each year from 1975 to 2017. The alive patients mostly appeared during 2014–2017, while the number and percentage of dead patients gradually decreased. The total number of alive patients was similar from 1975 to 2000, while it decreased significantly from 2000 to 2017. The distributions of the numbers of suicided, not-suicide-death, and alive patients with SCC from 1975 to 2017 are shown in eFigure 3 in the Supplement. The survival time of patients showed a right-skewed distribution, mostly concentrated at 0–12 months, and around 2017 (eFigure 4 in the Supplement). We defined the patient suicide rate as the ratio of the number of suicides per year to the total number of patients in the same year. We found that the suicide rate of patients showed a downward trend from 1975 to 2017, and was higher for males, histological grade IV, white race, and urban residents. The distribution of the patient suicide rates is shown in Figure 1.

Figure 1

Suicide rates and SMRs

The observations from 1975 to 2017 comprised a total of 2,289,772 person-years, with a suicide rate for patients with SCC of 50.53 per 100,000 person-years. According to the report of the US Centers for Disease Control and Prevention, the average suicide rate of the general US population was 12.24 per 100,000 years from 1981 to 2017.[8] We calculated that the SMR of US SCC patients was 4.13 (95% CI=3.90–4.38). The suicide rate was higher in patients with SCC than in the general US population, with the main contributing factors being male (SMR=4.61, 95% CI=4.34–4.92), white (SMR=4.01, 95% CI=3.77–4.26), Hispanic (SMR=4.17, 95% CI=2.96–6.55), non-Hispanic white (SMR=4.28, 95% CI=4.02–4.55), age at diagnosis, histological grade, and histological classification. However, the suicide rates among non-Hispanic and native Indian Americans (SMR=1.59, 95% CI=0.30–4.38) and PC patients (SMR=1.10, 95% CI=0.83–1.46) did not differ from those in the general population. The suicide rates and SMRs of US SCC patients are presented in Table 2.

Table 2. Suicide rates and SMRs among squamous cell carcinoma patients

Variables	Suicidal death	Person-years	Suicide rate per 100 000 person-years	p	SMR &	95%CI
Patients	1157	2289772	50.53	<0.001***	4.13	(3.90, 4.38)
Year of dignosis						
1975-1984	341	625950	54.48	<0.001***	4.45	(3.97, 4.92)
1985-1994	335	672752	49.80	<0.001***	4.07	(3.66, 4.55)
1995-2004	253	588512	42.99	<0.001***	3.51	(3.09, 3.97)
2005-2017	228	402558	56.64	<0.001***	4.63	(4.07, 5.3)
Sex						

Variables	Suicidal death	Person-years	Suicide rate per 100 000 person-years	p	SMR &	95%CI
Female	159	1186008	13.41	<0.001***	2.61	(2.22, 3.04)
Male	998	1103764	90.42	<0.001***	4.61	(4.34, 4.92)
Age at diagnosis						
≤39	67	383965	17.45	0.006**	2.06	(1.57, 2.58)
40-49	114	374125	30.47	<0.001***	1.77	(1.47, 2.14)
50-59	246	535626	45.93	<0.001***	2.55	(2.25, 2.9)
60-69	360	551128	65.32	<0.001***	4.49	(4.05, 4.99)
70-79	282	338607	83.28	<0.001***	5.45	(4.81, 6.09)
≥80	88	106321	82.77	<0.001***	4.55	(3.71, 5.71)
Race						
Black	45	207006	21.74	<0.001***	3.99	(2.98, 5.47)
Other	45	152299	29.55	<0.001***	4.21	(2.98, 5.47)
Unknown	0	9908	0.00	0.271	-	-
White	1067	1920671	55.55	<0.001***	4.01	(3.77, 4.26)
Race Latino						
Non-Latino	1130	2172603	52.01	<0.001***	4.25	(4.00, 4.5)
Latino	27	117169	23.04	<0.001***	1.88	(1.27, 2.81)
Race Hispanic						
Hispanic	27	117169	23.04	<0.001***	4.17	(2.96, 6.55)
Non-Hispanic Americacn/Indian Native	3	14066	21.33	0.276	1.59	(0.30, 4.38)
Non-Hispanic Asian	42	135956	30.89	<0.001***	2.30	(1.68, 3.15)
Non-Hispanic Black	45	205387	21.91	<0.001***	1.63	(1.17, 2.15)
Non-Hispanic Unknown Race	0	9218	0	0.288	-	-
Non-Hispanic White	1040	1808088	57.52	<0.001***	4.28	(4.02, 4.55)
Grade						
Grade I	134	336671	39.80	<0.001***	3.25	(2.74, 3.87)
Grade II	398	612369	64.99	<0.001***	5.31	(4.8, 5.85)
Grade III	271	432004	62.73	<0.001***	5.13	(4.52, 5.76)
Grade IV	20	26183	76.38	<0.001***	6.24	(4.07, 10.30)
Unknown	334	882545	37.85	<0.001***	3.09	(2.77, 3.44)
Surgery performed						
No	494	589965	83.73	<0.001***	6.84	(6.27, 7.49)
Yes	643	1662394	38.68	<0.001***	3.16	(2.93, 3.42)
Unkonwn	20	37412	53.46	<0.001***	4.37	(2.44, 6.18)
Primary diaeases						
No	362	798353	45.34	<0.001***	3.70	(3.32, 4.09)
Yes	795	1491419	53.30	<0.001***	4.35	(4.05, 4.66)
Household income						
<$50,000	61	112076	54.43	<0.001***	4.45	(3.33, 5.6)
$50,000 - $74,999	331	650167	50.91	<0.001***	4.16	(3.7, 4.61)

Variables	Suicidal death	Person-years	Suicide rate per 100 000 person-years	p	SMR &	95%CI
$75,000+	237	566038	41.87	<0.001***	3.42	(3.01, 3.9)
Unkonwn	528	961490	54.91	<0.001***	4.49	(4.1, 4.87)
Living area#						
Large city	371	750776	49.42	<0.001***	4.24	(3.8, 4.67)
Medium city	110	271574	40.50	<0.001***	3.47	(2.83, 4.14)
Small city	46	90809	50.66	<0.001***	4.34	(3.06, 5.58)
Suburbs	45	95676	47.03	<0.001***	3.02	(2.19, 4.01)
Rural	47	89864	52.30	<0.001***	3.36	(2.47, 4.46)
Unkonwn	538	991072	54.28	<0.001***	3.49	(3.20, 3.80)
Radiotherapy						
No/Unknown	544	1039336	52.34	<0.001***	4.28	(3.93, 4.66)
Yes	613	1250436	49.02	<0.001***	4.01	(3.7, 4.34)
Chemotherapy						
No/Unknown	835	1638816	50.95	<0.001***	4.16	(3.88, 4.45)
Yes	322	650956	49.47	<0.001***	4.04	(3.6, 4.49)

#**Large city**,Counties in metropolitan areas ge 1 million pop;   **Medium city**, Counties in metropolitan areas of 250,000 to 1 million pop;   **Small city**, Counties in metropolitan areas of lt 250 thousand pop;   **Suburbs**, Nonmetropolitan counties adjacent to a metropolitan area;   **Rural**, Nonmetropolitan counties not adjacent to a metropolitan area;   **Unknown**, Unknown/missing/no match/Not 1990-2017.

&**SMR**, standardized mortality ratio: Compared with the suicide rates of the general US population based on the Centers for Disease Control and Prevention's Web‐based Injury Statistics Query and Reporting System (1981‐2017).

* P<0.05, ** P<0.01,   *** P<0.001.

We subsequently analyzed the changes in the SMR of suicided patients from 1975 to 2017. Because the US Centers for Disease Control and Prevention did not provide data on the suicide rate of the general population from 1975 to 1980, we used the suicide rate of the population from 1981 to 1983 to adjust the suicide rate of patients with SCC between 1975 and 1980.8 It was found that the suicide SMR of US SCC patients fluctuated between 3 and 6, and was higher among those who suicided between 2011 and 2017. The changes in the SMR for suicide in US SCC patients are shown in Figure 2.

Figure 2

Factors associated with suicide

Univariate analyses showed that the factors associated with a high risk of suicide in patients with SCC were being male (vs female: HR=6.00, 95% CI=5.07–7.11, P<0.001), older at the diagnosis (40–49 vs ≤39 years: HR=1.60, 95% CI=1.19–2.18, P<0.001; 50–59 vs ≤39 years: HR=2.22, 95% CI=1.69–2.92, P<0.001; 60–69 vs ≤39 years: HR=2.90, 95% CI=2.21– 3.79, P<0.001; 70–79 vs ≤39 years: HR=3.35,

95% CI=2.54–4.43, P<0.001; ≥80 vs ≤39 years: HR=2.92, 95% CI=2.10–4.06, P<0.001), and white (vs black, HR=2.77, 95% CI=2.05–3.73, P<0.001), having a higher histological grade (grade II vs grade I: HR=1.45, 95% CI=1.19–1.77, P<0.001; grade III vs grade I: HR=1.34, 95% CI=1.09–1.65, P=0.006; grade IV vs grade I: HR=1.70, 95% CI=1.06–2.71, P=0.028) and primary cancer (vs nonprimary cancer: HR=1.17, 95% CI=1.03–1.32, P=0.013), and the histological classification (SCC vs PC: HR=3.33, 95% CI=2.51–4.42, P<0.001; OC vs PC: HR=3.76, 95% CI=2.11–6.70, P<0.001). The factors associated with a lower risk of patient suicide were the year of diagnosis (1995–2004 vs 1975–1984: HR=0.71, 95% CI=0.60–0.83, P<0.001; 2005–2017 vs 1975–1984: HR=0.69, 95% CI=0.58–0.82, P<0.001), being Latino (vs non-Latin American: HR=0.46, 95% CI=0.32–0.68, P<0.001), and receiving surgery (vs no surgery: HR=0.59, 95% CI=0.52–0.66, P<0.001). Multivariate Cox regression analyses showed that the factors related to a high risk of suicide in patients with SCC were being male (vs female: HR=5.36, 95% CI=4.51–6.38, P<0.001), older at the diagnosis (70–79 vs ≤39 years: HR=1.46, 95% CI=1.09–2.08, P=0.012; ≥80 vs ≤39 years: HR=1.48, 95% CI=1.05–2.08, P=0.025), and white (vs black: HR=2.97, 95% CI=2.20–4.02, P<0.001), having a higher histological grade (grade II vs grade I: HR=1.54, 95% CI=1.26–1.87, P<0.001; grade III vs grade I: HR=1.42, 95% CI=1.15–1.76, P<0.001; grade IV vs grade I: HR=1.65, 95% CI=1.03–2.66, P=0.039) and primary cancer (vs nonprimary cancer: HR=1.33, 95% CI=1.17–1.50, P<0.001), and the histological classification (SCC vs PC: HR=1.95, 95% CI=1.45–2.62, P<0.001; OC vs PC: HR=2.21, 95% CI=1.22–3.99, P=0.009). The factors associated with a low risk of patient suicide were being Latino (vs non-Latin American: HR=0.58, 95% CI=0.40–0.85, P<0.001), receiving surgery (vs no surgery: HR=0.65, 95% CI=0.57–0.74, P<0.001), and having a higher family income (US$ 75,000 + vs <US$ 50,000: HR=0.71, 95% CI=0.51–0.99, P=0.047). The risk factors related to suicide in US SCC patients are listed in Table 3. A Cox survival regression analysis showed that male patients with SCC had a higher risk of suicide than did female patients with SCC (eFigure 5 in the Supplement).

Table 3. Univariable and multivariable analysis for suicide of leukemia patients

Variables	Univariable analysis		Multivariable analysis	
	HR(95%CI)	P	HR(95%CI)	P
Year of dignosis				
1975-1984	Reference		Reference	
1985-1994	0.89(0.76-1.04)	0.132	1.04(0.87-1.24)	0.68
1995-2004	0.71(0.60-0.83)	<0.001***	0.97(0.74-1.28)	0.853
2005-2017	0.69(0.58-0.82)	<0.001***	0.78(0.59-1.03)	0.078
Sex				
Female	Reference		Reference	
Male	6.00(5.07-7.11)	<0.001***	5.36(4.51-6.38)	<0.001***
Age at diagnosis				
≤39	Reference		Reference	

Variables	Univariable analysis		Multivariable analysis	
	HR(95%CI)	*P*	HR(95%CI)	*P*
40-49	1.61(1.19-2.18)	0.002**	0.93(0.68-1.27)	0.656
50-59	2.22(1.69-2.92)	<0.001***	0.97(0.72-1.29)	0.814
60-69	2.90(2.21-3.79)	<0.001***	1.20(0.90-1.59)	0.21
70-79	3.35(2.54-4.43)	<0.001***	1.46(1.09-2.08)	0.012**
≥80	2.92(2.10-4.06)	<0.001***	1.48(1.05-2.08)	0.025*
Race				
Black	Reference		Reference	
White	2.77(2.05-3.73)	<0.001***	2.97(2.20-4.02)	<0.001***
Other	1.53(1.01-2.31)	0.044*	1.84(1.20-2.82)	0.005**
Unknown	-	-	-	-
Race Latino				
Non-Latino	Reference		Reference	
Latino	0.46(0.32-0.68)	<0.001***	0.58(0.40-0.85)	<0.001***
Grade				
Grade I	Reference		Reference	
Grade II	1.45(1.19-1.77)	<0.001***	1.54(1.26-1.87)	<0.001***
Grade III	1.34(1.09-1.65)	0.006**	1.42(1.15-1.76)	<0.001***
Grade IV	1.70(1.06-2.71)	0.028*	1.65(1.03-2.66)	0.039*
Unknown	0.96(0.79-1.18)	0.723	1.28(1.04-1.57)	0.018*
Surgery performed				
No	Reference		Reference	
Yes	0.59(0.52-0.66)	<0.001***	0.65(0.57-0.74)	<0.001***
Unkonwn	0.70(0.45-1.10)	0.121	0.54(0.35-0.85)	0.008**
Primary diaeases				
No	Reference		Reference	
Yes	1.17(1.03-1.32)	0.013*	1.33(1.17-1.50)	<0.001***
Household income				
<$50,000	Reference		Reference	
$50,000-$74,999	1.00(0.76-1.32)	0.993	0.93(0.69-1.26)	0.629
$75,000+	0.85(0.64-1.13)	0.254	0.71(0.51-0.99)	0.047*
Unkonwn	1.31(1.01-1.72)	0.044*	1.01(0.49-2.11)	0.976
Living area#				
Large city	Reference		Reference	
Medium city	0.82(0.66-1.01)	0.067	0.79(0.63-0.98)	0.032*
Small city	1.05(0.77-1.42)	0.772	0.85(0.62-1.17)	0.326
Suburbs	0.96(0.71-1.31)	0.808	0.73(0.53-1.01)	0.058
Rural	1.06(0.78-1.44)	0.699	0.79(0.56-1.11)	0.169
Unkonwn	1.33(1.17-1.53)	<0.001***	1.00(0.52-1.92)	0.992
Radiotherapy				
No/Unknown	Reference		Reference	

Variables	Univariable analysis		Multivariable analysis	
	HR(95%CI)	*P*	HR(95%CI)	*P*
Yes	0.94(0.84-1.05)	0.280	0.95(0.84-1.07)	0.381
Chemotherapy				
No/Unknown	Reference		Reference	
Yes	0.98(0.86-1.12)	0.772	0.98(0.85-1.12)	0.750

[#]**Large city**, Counties in metropolitan areas ge 1 million pop;　**Medium city**, Counties in metropolitan areas of 250,000 to 1 million pop;　**Small city**, Counties in metropolitan areas of lt 250 thousand pop;　**Suburbs**, Nonmetropolitan counties adjacent to a metropolitan area;　**Rural**, Nonmetropolitan counties not adjacent to a metropolitan area;　**Unknown**, Unknown/missing/no match/Not 1990-2017.

* P<0.05, ** P<0.01,　*** P<0.001.

Discussion

This study found that the suicide rate of patients with SCC in the US was higher than that in the general population,[8] which is similar to the results of previous studies of the suicide rates of cancer patients in the US[11,21,22] and many other countries, including the UK, Italy, Estonia, Sweden, and Denmark.[3,23–26] Our analyses revealed that the factors associated with a high risk of suicide in SCC patients include being male, older at the diagnosis, and white, and having a higher histological grade and not receiving surgery.

Males accounted for 59.9% of the US patients with SCC in this study. The number of patients who suicided or died of another cause was higher for males than females in each year from 1975 to 2017, with male suicided patients accounting for 86.2% of the total (Table 1, eFigure 2, and eFigure 3 in the Supplement). The death rate during each year of the analysis was also higher for males than for females (eFigure 3 in the Supplement). Further analysis showed that the suicide rate for patients with SCC in the US was 90.42 per 100,000 person-years among males (SMR=4.61, 95% CI=4.34–4.92) and 13.41 per 100,000 person-years among females (SMR=2.61, 95% CI=2.22–3.04) (Table 1). The risk of suicide was markedly higher in male than female patients (HR=6.00, 95% CI=5.07–7.11) (Table 3). Other studies have also found that male cancer patients are a high-risk group for suicide, which may be related to male patients suffering more social pressures, family burdens, and their own psychological problems.[18,27,28]

Most of the patients with SCC were older than 50 years (85.7%). Males aged 55-79 years predominated among patients who suicided or died of another cause, while females younger than 75 years predominated among alive patients (eFigure 2 in the Supplement). Compared with patients younger than 39 years, elderly patients exhibited a higher suicide rate (HR>2.5, P<0.001) (Table 3). Table 2 indicates that the suicide rate of the patients gradually increased with age. Previous studies have also found the suicide rate to be significantly higher in elderly cancer patients than in the general population.[9,21] The high rate of suicide among elderly SCC cancer patients could be related to various factors, including more concomitant diseases, lower disease resistance, lower quality of life, loneliness, and depression.[10,29–31]

Our analysis of the changes in the suicide SMR of SCC patients from 1975 to 2017 revealed that this fluctuated between 3 and 6, peaking between 2011 and 2017 at SMR>5 (Figure 2). However, the suicide rate of patients decreased over time (Figure 1). The sudden increase in the SMR after 2011 could have been due to their mortality rate before 2010 exceeding 70%, whereas the alive patients were mainly distributed after 2011 (eFigure 3 in the Supplement). At the same time, we found that the maximum survival time of patients with SCC was 515 months from 1975 to 2017, while the survival time of most patients was shorter than 12 months, and it was mainly distributed from 2011 to 2017 (eFigure 4 in the Supplement). Therefore, the total number of patient years decreased from 2011 to 2017 (eFigure 3 in the Supplement), resulting in a high value for the suicide SMR during this period.

The Cox regression analyses showed that race was a risk factor for suicide in

patients with SCC. Compared with black patients, white patients had an approximately threefold higher risk of suicide (HR=2.97, 95% CI=2.20–4.02, P<0.001) (Table 3). Meanwhile, the suicide rate of white Americans decreased over time, and that of black Americans remained at a low level. However, the suicide rates of other races fluctuated markedly (Figure 1), which might have been due to the relatively small proportion of other races in the analyzed population. It can be concluded that white Americans with SCC are a high-risk group for suicide, which is consistent with previous findings for other cancer patients in the US.[30–32] The variations in suicide rates between different racial groups of SCC patients in the US might be related to variations in culture, religious beliefs, quality of life, mental health, and economic conditions.[28,30,33]

We also found that patients with SCC of different histological grades had different suicide rates, with this being highest in grade IV (SMR=6.24, 95% CI=4.07-10.30) (Table 2). The suicide risk of patients with histological grades higher than grade I increased to varying degrees (overall HR>1.40) (Table 3). Although the suicide rate of patients with different histological grades trended downward each year, the annual suicide rate of grade IV patients fluctuated greatly (Figure 1), which might be related to their small proportion (1.5%). We subsequently classified the US SCC patients based on morphology codes into PC, SCC, and OC, which revealed that SCC constituted the highest proportion of patients in the US (93.0%). Compared with PC patients, the suicide risks in SCC and OC patients were 1.95-fold (95% CI=1.45–2.62, P<0.001) and 2.21-fold (95% CI=2.21–3.99, P<0.001) higher, respectively (Table 3). The risk of suicide was higher in patients with primary cancer than in those with nonprimary cancer (HR=1.33, 95% CI=1.17–1.50, P<0.001) (Table 3). Different types of cancer are generally associated with different rates of disease progression and different prognoses, with a higher degree of malignancy associated with faster disease progression and a worse prognosis.[30] Studies have found that cancers with poor prognoses are often accompanied by serious psychological problems such as loneliness and depression, which in turn increase the risk of suicide.[29,34] Similarly, the present patients who did receive surgery had a lower suicide risk (HR=0.65, 95% CI=0.57–0.74, P<0.001) (Table 3), which might be related to the better prognosis of patients after they receive surgery. The above results indicate that patients with SCC with a higher histological grade and degree of malignancy are at high risk of suicide.

Multiple studies have found cancer patients to be more likely to have depression and other psychological problems than the general population, and also have a higher risk of suicide.[29,30,35] Suicide is one cause of death in cancer patients that is potentially preventable.[36] Suicide is a complex behavior and is affected by many factors, including psychological factors, religious beliefs, and family support. Our results showed that compared with the general population,[37,38] patients with SCC in the US have a higher suicide rate. Being male, white, and older at the diagnosis, and having a higher histological grade were found to be factors contributing to a high risk of suicide. Preventing and reducing suicide in patients with SCC requires a greater focus on high-risk populations and the risk of depression being identified in psychiatric assessments of patients with SCC, such as using the Baker Depression

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Scale.[39] Actively improving the treatment plan and quality of life of cancer patients, and strengthening the care and communication of people at a high risk of cancer could reduce the psychological burden of these patients and so reduce their risk of suicide.[40]

Strength and limitation

This study was subject to some limitations. Suicide is a risk behavior of an individual in which various means are employed to end life under the influence of various factors. Some potentially important information that could impact suicidal behaviors is missing for patients with SCC in the SEER database, such as marital status, religious beliefs, education level, medication status, and psychological factors. The lack of this information might have biased the present research results. Moreover, our study only included data on patients with SCC living in certain parts of the US. Future studies should therefore include patients with SCC in more countries and regions in order to accurately identify the factors affecting the risk of suicide in SCC patients worldwide. In addition, this study was subject to some of the limitations inherent in retrospective research.

Conclusions

This study found that the suicide rate of patients with SCC in the US has decreased over the past few decades, but it remains higher than that in the general population. The independent risk factors for suicide in patients with SCC included being male, older at the diagnosis, and white, and having a higher histological grade and not receiving surgery. Clinicians can use the findings of this research to evaluate the suicide risk in individual patients with SCC. Effective intervention measures should be applied to the identified high-risk population in order to reduce their suicide rate.

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Statements：

Contributorship statement:

None.

Competing interests:

None.

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Data sharing statement:

The datasets generated and analyzed during the current study are available in the

SEER database repository (https://seer.cancer.gov) .

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Figure legends

Figure 1. The distribution of suicide rate in patients with squamous cell carcinoma.

Figure 2. Standardized mortality ratio of suicide for squamous cell carcinoma patients
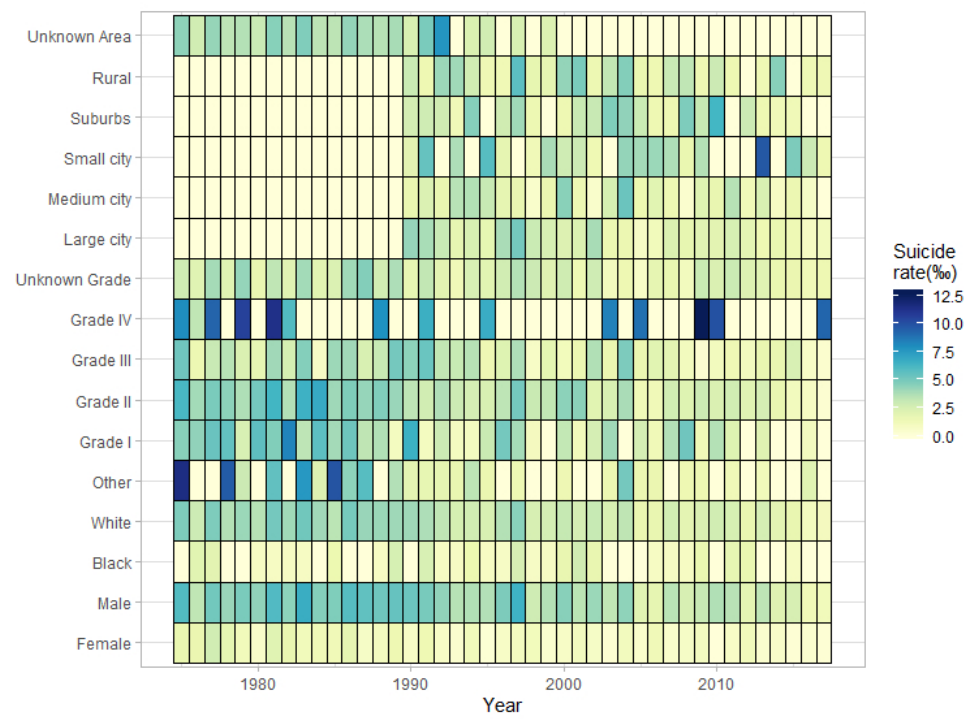
(1975–2017).

Figure 1. The distribution of suicide rate in patients with squamous cell carcinoma.

203x147mm (96 x 96 DPI)

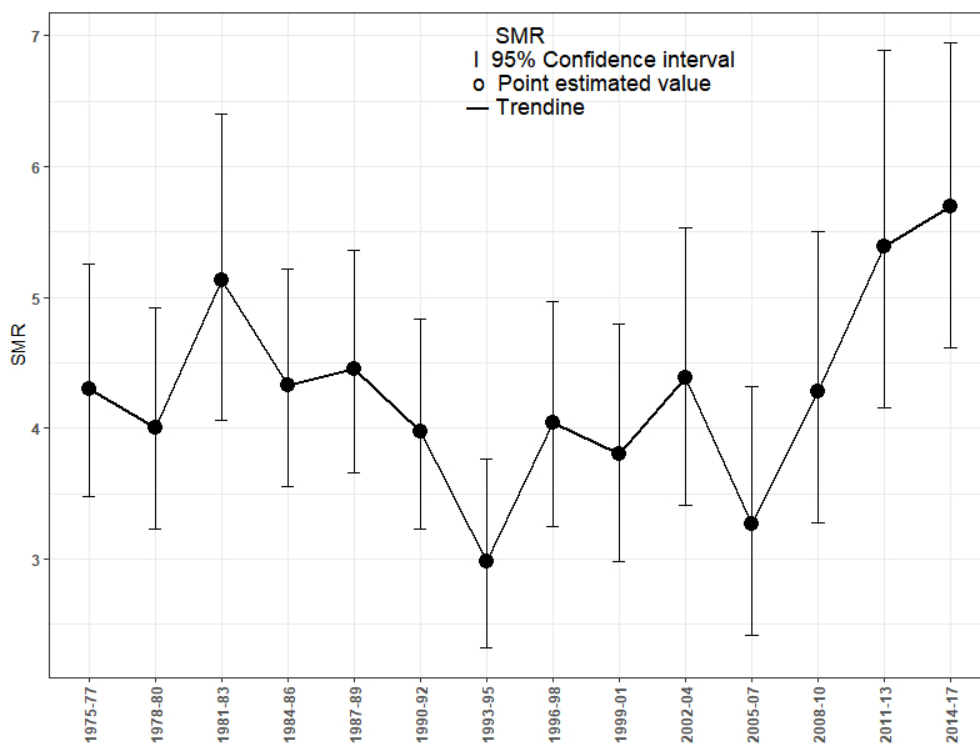Figure 2. Standardized mortality ratio of suicide for squamous cell carcinoma patients (1975–2017).

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Analysis of Suicide Risk Factors in Adult US Patients with Squamous Cell Carcinoma Based on the SEER Database

Supplement Online

eFigure legends
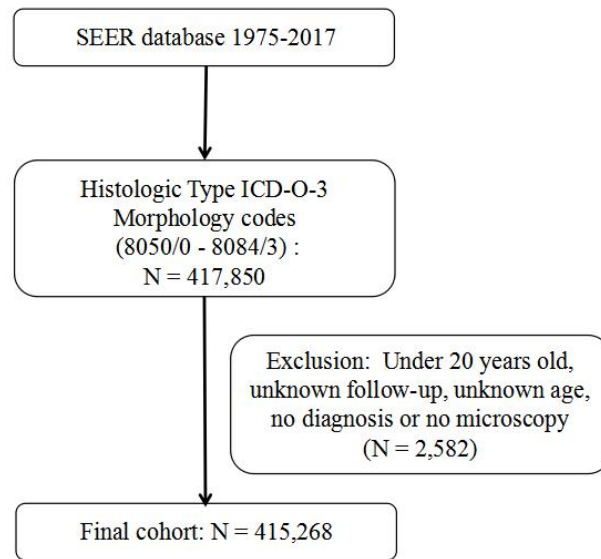
eFigure 1. The flow diagram of squamous cell carcinoma patients selection.

eFigure 2. The distribution of patients with squamous cell carcinoma by age.

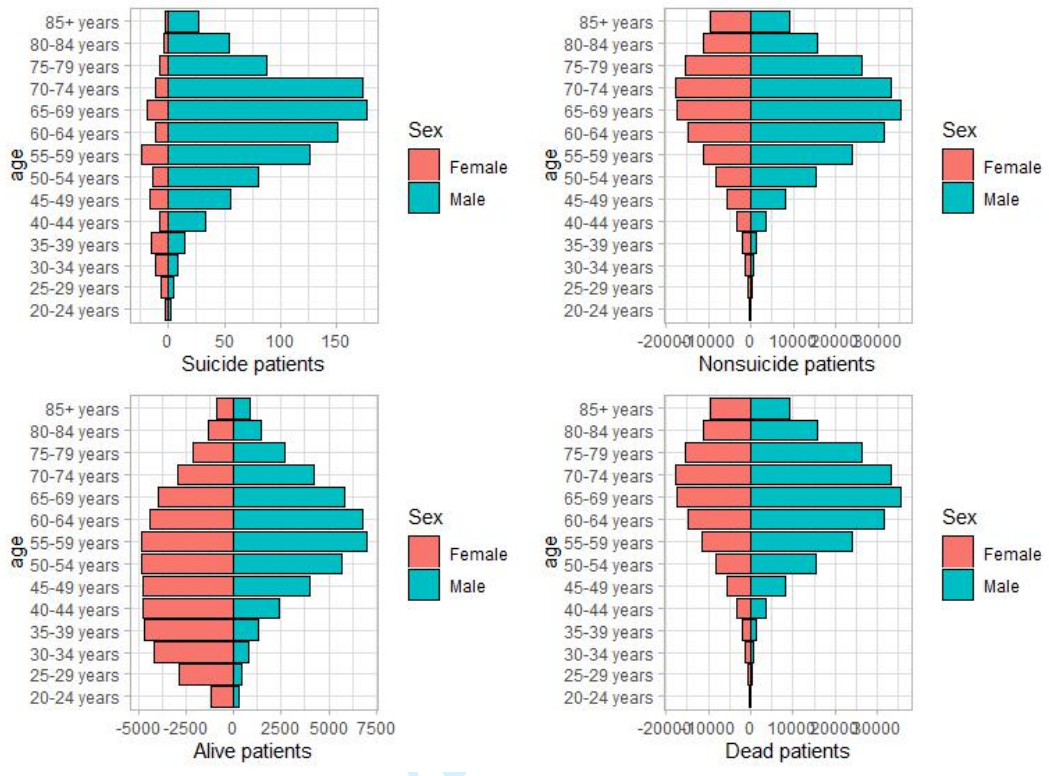eFigure 3. The distribution of patients with squamous cell carcinoma by year.

eFigure 4. The distribution of survival months of patients with squamous cell carcinoma in different years.

eFigure 5. Comparison chart of survival curves of male and female squamous cell carcinoma patients.

eFigure 1. The flow diagram of squamous cell carcinoma patients selection.

eFigure 2. The distribution of patients with squamous cell carcinoma by age.

eFigure 3. The distribution of patients with squamous cell carcinoma by year.

eFigure 4. The distribution of survival months of patients with squamous cell
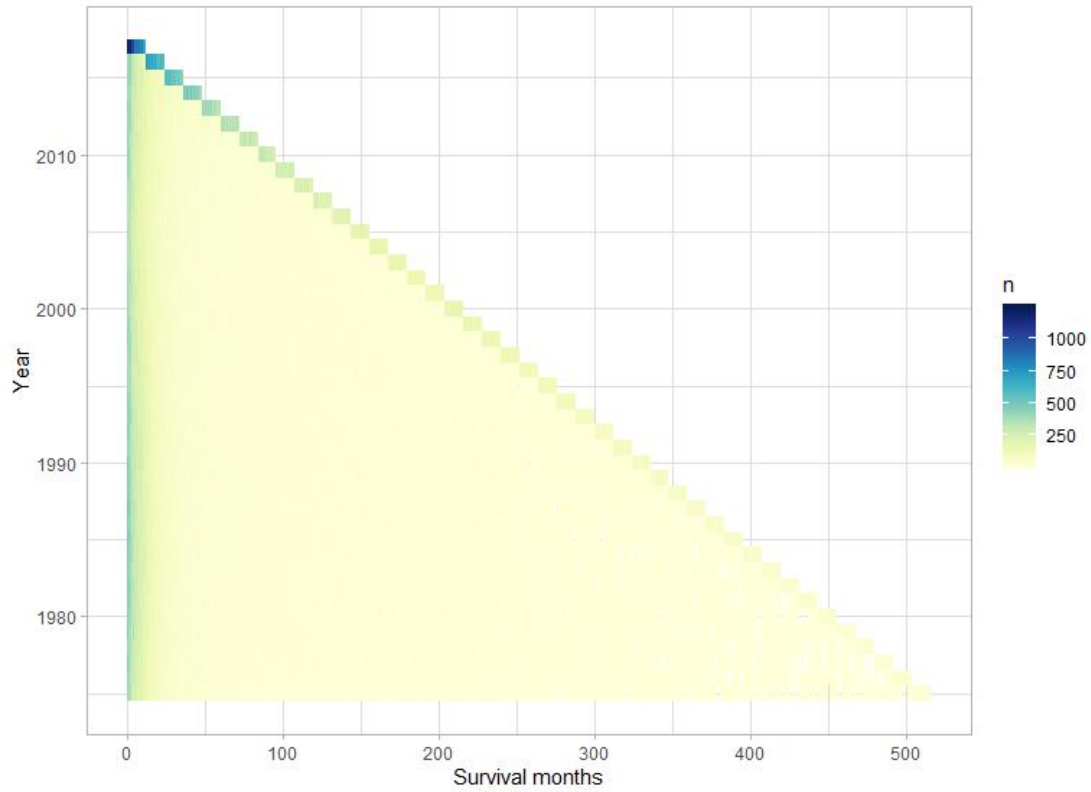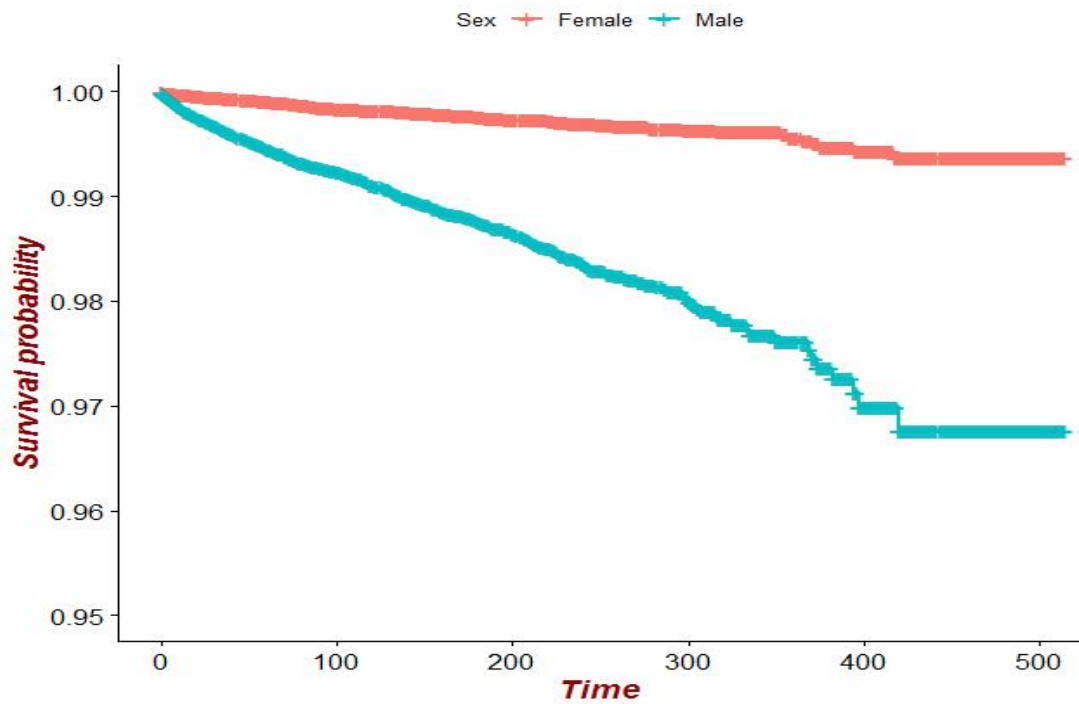
carcinoma in different years.

eFigure 5. Comparison chart of survival curves of male and female squamous cell

carcinoma patients.

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Analysis of Suicide Risk Factors in Adult US Patients with Squamous Cell Carcinoma Based on the SEER Database

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Short title: Analysis of Suicide RF in Adult US SCC Patients.

Abstract

Objectives: The purpose of this study was to determine the risk factors for suicide in patients with squamous cell carcinoma (SCC) in the US.

Setting: Patients with SCC diagnosed between 1975 and 2017 from the Surveillance, Epidemiology, and End Results (SEER) database were selected for this study.

Participants: This study included patients with SCC older than 20 years who were diagnosed between 1975 and 2017.

Primary and secondary outcome measures: The general population included in data from the US Centers for Disease Control and Prevention were used to calculate the suicide rate and standardized mortality rate (SMR) of SCC patients. Univariate and multivariate Cox regression analyses were used to identify risk factors for suicide in patients with SCC.

Results: There were 415,268 SCC patients registered in the SEER database, among which 1,157 cases of suicide were found, comprising a total of 2,289,772 person-years. The suicide rate for patients with SCC was 50.53 per 100,000 person-years, and the SMR was 4.13 (95% confidence interval [CI]=3.90–4.38). The Cox regression analyses showed that the factors related to a high risk of suicide among patients with SCC included being male (vs female: hazard ratio [HR]=5.36, 95% CI=4.51–6.38, P<0.001), older at the diagnosis (70–79 vs ≤39 years: HR=1.46, 95% CI=1.09–2.08, P=0.012; ≥80 vs ≤39 years: HR=1.48, 95% CI=1.05–2.08, P=0.025), and white (vs black, HR=2.97, 95% CI=2.20–4.02, P<0.001), and surgery (vs no performed: HR=0.65, 95% CI=0.57–0.74, P<0.001).

Conclusions: Compared with the general population, patients with SCC in the United States have a higher risk of suicide. Being male, older at the diagnosis, white, and having a higher histological grade are risk factors for suicide in patients.

Strengths and limitations of this study

Our study had several strengths:

■ This study found that the suicide rate of patients with SCC in the US has decreased over the past few decades, but it remains higher than that in the general population.

■ The independent risk factors for suicide in patients with SCC included being male, older at the diagnosis, white, and having a higher histological grade and not receiving surgery.

Our study had several limitations：

■ Some potentially important information that could impact suicidal behaviors is missing for patients with SCC in the SEER database, such as religious beliefs, education level, medication status, and psychological factors. The lack of this information might have biased the present research results.

■ Our study only included data on patients with SCC living in certain parts of the US. Future studies should therefore include patients with SCC in more countries and regions in order to accurately identify the factors affecting the risk of suicide in SCC patients worldwide.

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Background

The World Health Organization has reported that the number of cancer deaths worldwide is increasing, with cancer now being the third-most-common cause of deaths worldwide.[1] There were about 18.1 million new cancer patients and about 9.6 million deaths worldwide in 2018.[2] Previous studies have shown that patients with depression and cancers with a poor prognosis have a high risk of suicide.[3] Suicide is influenced by many factors,[4] and the World Health Organization has also reported that the number of suicides worldwide is increasing, with approximately 800,000 suicide deaths each year.[5–7] According to data released by the US Centers for Disease Control and Prevention, suicide is one of the common causes of death in the US.[8] The suicide rate in the general US population was 14.78 per 100,000 people in 2018, which was higher than in other countries.[8] Multiple studies have shown that the suicide rate is higher in cancer patients than in the general US population.[9–12] In particular, the suicide rate of patients with head and neck cancer was more than three times higher than that in the general US population.[13] Cancer patients face enormous financial pressures and physical burdens. The poor prognosis of cancer is often accompanied by long-term mental and psychological problems, and often leads to death.[7] The increasing incidence of cancer has resulted in mental and psychological problems gradually becoming a major complication experienced by cancer patients.[14] The resulting fear of a cancer prognosis, depression, and other psychological problems have gradually increased the risk of suicide.[4] Therefore, it is of great importance to identify the risk factors for suicide in cancer patients in order to control suicidality in this population. Some studies have found male sex, white race, marital status, type of cancer, and other factors to be strongly correlated with the suicide risk of patients with some types of cancer.[9–13]

Squamous cell carcinoma (SCC) refers to a malignant tumor derived from the squamous epithelium. This is the general term for a class of tumors that include multiple cancers occurring in the squamous epithelium covering tissues and organs, and which are more common in the skin, mouth, esophagus, cervix, and vagina.[15–17] According to a report by the US Centers for Disease Control and Prevention, the number of deaths from malignant tumors in the US in 2018 was second only to that due to cardiovascular disease, and suicide has become the second leading cause of death among US residents aged 10 to 34 years.[8] The number of deaths due to SCC in the US is increasing. GuoPei Yu et al. investigated the causes of death in patients with oral and oropharyngeal SCC in the US,[18] but did not conduct in-depth studies on the causes of suicide. Therefore, the purpose of this study was to identify potential risk factors associated with suicide in US SCC patients by analyzing data in the US Surveillance, Epidemiology, and End Results (SEER) database.

Method

Data source

All patients with SCC in this study were selected from the SEER database (http://seer.cancer.gov). This database covers about 30% of the US population and provides researchers with a large amount of research data, including on patient demographics, cancer incidence, and survival data.[19] We used SEER*Stat software (version 8.3.6) to identify US patients with SCC who were added to the database from 1975 to 2017. We obtained permission to access the database after signing and submitting the SEER Research Data Agreement form via email.

Patient and Public Involvement:

All patients were selected from the SEER database. No patient involved.

Inclusion and exclusion criteria for the study population

This study applied screening criteria for the research objectives based on histological type codes in ICD-O-3. We used morphology codes 8050/0–8084/3 to identify patients with SCC in the SEER database. The collected patients were divided into the following three groups based on morphology codes: papillary carcinoma (PC, codes 8050/3–8060/0), SCC (codes 8070/2–8078/3), and other carcinomas (OC, codes 8080/2–8084/3). The cause of death of "Suicide and Self-Inflicted Injury" was searched for in order to identify cases of suicide. The exclusion criteria for study subjects included being younger than 20 years, unknown follow-up time, unknown age, and no diagnosis or microscopy data. The information collected by all patients with SCC includes sex, age, year of diagnosis, race, histological grade, cancer type, survival time, surgery status, radiotherapy status, chemotherapy status, cause of death, and area of residence. This study collected 415,268 patients with SCC, which included 1,157 who suicided. The screening procedure for patients with SCC is shown in eFigure 1 in the Supplement.

Statistical analysis

This study divided the SCC patients collected from the SEER database into the following three groups in order to perform basic data comparisons: suicided group, nonsuicide death group, and alive group. We analyzed the age distributions in these three groups of patients from 0 to 85 years and the year of diagnosis distribution of patients from 1975 to 2017. The chi-square test was used to compare the suicide rates among patients in each group. The SMR for suicide in each group was based on the total population of the US from 1981 to 2017, using data obtained from the Web-Based Injury Statistics Query and Reporting System of the Centers for Disease Control and Prevention (https://www.cdc.gov/injury/wisqars/fatal.html). The 95% confidence interval (CI) of the SMR for suicide was approximated using the method of Byar.[20] Univariate and multivariate Cox regression analyses were subsequently used to generate the hazard ratio (HR), and the 95% CI combined with the HR were used to identify potential risk factors for suicide. All statistical analyses was performed using R software (version 3.6.3, http://www.r-project.org/). All tests were two-sided, and the significance criterion was set as $P<0.05$.

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Results

Patient baseline characteristics

The 415,268 identified US patients with SCC in the SEER database from 1975 to 2017 included 248,816 males (59.9%). These patients comprised 1,157 (0.3%) in the suicided group, 322,384 (77.6%) in the not-suicide-death group, and 91,727 (22.1%) in the alive group. Most of them were older than 60 years (66.3%), white (81.7%), non-Latin American (95.7%), non-Hispanic white (77.6%), and lived in urban areas (56.2%). The age distributions of the suicided, not-suicide-death, alive, and dead patients are shown in eFigure 2 in the Supplement. The basic statistics of each group of SCC patients are presented in Table 1.

Table 1. Baseline characteristics of squamous cell carcinoma patients (1975-2017)

Variables	Overall N(%)	Suicidal death N(%)	Nonsuicidal death N(%)	Alive N(%)	p
Patients	415268	1157(0.3%)	322384(77.6%)	91727(22.1%)	-
Year of dignosis					
1975-1984	90334(21.8%)	341(29.5%)	85435(26.5%)	4558(5.0%)	
1985-1994	98947(23.8%)	335(29.0%)	88294(27.4%)	10318(11.2%)	<0.001
1995-2004	94368(22.7%)	253(21.8%)	75490(23.4%)	18625(20.3%)	
2005-2017	131619(31.7%)	228(19.7%)	73165(22.7%)	58226(63.5%)	
Sex					
Female	166452(40.1%)	159(13.7%)	118262(36.7%)	48031(52.4%)	<0.001
Male	248816(59.9%)	998(86.3%)	204122(63.3%)	43696(47.6%)	
Age at diagnosis					
≤39	22031(5.3%)	67(5.8%)	6211(1.9%)	15753(17.2%)	
40-49	36569(8.8%)	114(9.9%)	20570(6.4%)	15885(17.3%)	
50-59	81389(19.6%)	246(21.3%)	58737(18.2%)	22406(24.4%)	<0.001
60-69	120016(28.9%)	360(31.1%)	98541(30.6%)	21115(23.0%)	
70-79	104931(25.3%)	282(24.3%)	92561(28.7%)	12088(13.2%)	
≥80	50332(12.1%)	88(7.6%)	45764(14.2%)	4480(4.9%)	
Race					
Black	50022(12.0%)	45(3.9%)	42014(13.0%)	7963(8.7%)	
White	339376(81.7%)	1067(92.2%)	263117(81.6%)	75192(82.0%)	<0.001
Other	24658(5.9%)	45(3.9%)	16979(5.3%)	7634(8.3%)	
Unknown	1212(0.3%)	0	274(0.1%)	938(1.0%)	
Race Hispanic					
Hispanic	18018(4.3%)	27(2.3%)	11338(3.5%)	6653(7.3%)	
Non-Hispanic White	322235(77.6%)	1040(89.9%)	252268(78.2%)	68927(75.1%)	
Non-Hispanic Ameriacn/Indian Native	2137(0.5%)	3(0.3%)	1485(0.5%)	649(0.7%)	<0.001
Non-Hispanic Asian	22123(5.3%)	42(3.6%)	15253(4.7%)	6828(7.4%)	
Non-Hispanic Black	49711(12.0%)	45(3.9%)	41828(13.0%)	7866(8.6%)	

Variables	Overall N(%)	Suicidal death N(%)	Nonsuicidal death N(%)	Alive N(%)	p
Non-Hispanic Unknown Race	1044(0.3%)	0	240(0.1%)	804(0.9%)	
Grade					
Grade I	43008(10.4%)	134(11.6%)	31492(9.8%)	11382(12.4%)	
Grade II	121959(29.4%)	398(34.4%)	94991(29.5%)	26570(29.0%)_	
Grade III	108530(26.0%)	271(23.4%)	89299(27.7%)	18960(20.7%)	<0.001
Grade IV	6169(1.5%)	20(1.7%)	5198(1.6%)	951(1.0%)	
Unknown	135602(32.7%)	334(28.9%)	101404(31.5%)	33864(36.9%)	
Surgery performed					
No	207029(49.9%)	494(42.7%)	175871(54.5%)	30664(33.4%)	
Yes	197252(47.5%)	643(55.6%)	135928(42.2%)	60681(66.2%)	<0.001
Unkonwn	10987(2.6%)	20(1.7%)	10585(3.3%)	382(0.4%)	
Primary diaeases					
No	127948(30.8%)	362(31.3%)	102800(31.9%)	24786(27.0%)	<0.001
Yes	287320(69.2%)	795(68.7%)	219584(68.1%)	66941(73.0%)	
Household income					
<$50,000	28804(6.9%)	61(5.3%)	19661(6.1%)	9082(9.9%)	
$50,000 - $74,999	137290(33.1%)	331(28.6%)	95873(29.7%)	41094(44.8%)	
$75,000+	109556(26.4%)	237(20.5%)	76605(23.8%)	3271(35.7%)	<0.001
Unkonwn	139610(33.6%)	528(45.6%)	130245(40.4%)	8837(9.6%)	
Living area#					
Large city	159750(38.5%)	371(32.0%)	112206(34.8%)	47173(51.4%)	
Medium city	56207(13.5%)	110(9.5%)	37366(11.6%)	18731(20.4%)	
Small city	17605(4.2%)	46(4.0%)	12032(3.7%)	5527(6.0%)	
Suburbs	19322(4.7%)	45(3.9%)	13706(4.3%)	5571(6.1%)	<0.001
Rural	18652(4.5%)	47(4.1%)	13419(4.1%)	5186(5.7%)	
Unkonwn	143732(34.6%)	538(46.5%)	133655(41.5%)	9539(10.4%)	
Radiotherapy					
No/Unknown	188695(45.4%)	544(47.0%)	146075(45.3%)	42076(45.9%)	0.006
Yes	226573(54.6%)	613(53.0%)	176309(54.7%)	49651(54.1%)	
Chemotherapy					
No/Unknown	298396(71.9%)	835(72.2%)	231140(71.7%)	66421(72.4%)	<0.001
Yes	116872(28.1%)	322(27.8%)	91244(28.3%)	25306(27.6%)	

#**Large city**,Counties in metropolitan areas ge 1 million pop; **Medium city**, Counties in metropolitan areas of 250,000 to 1 million pop; **Small city**, Counties in metropolitan areas of lt 250 thousand pop; **Suburbs**, Nonmetropolitan counties adjacent to a metropolitan area; **Rural**, Nonmetropolitan counties not adjacent to a metropolitan area; **Unknown**, Unknown/missing/no match/Not 1990-2017.

Patient distributions according to year

We found that most of the US patients with SCC who suicided were males. The number of suicided patients declined each year from 1975 to 2017. The alive patients mostly appeared during 2014–2017, while the number and percentage of dead patients gradually decreased. The total number of alive patients was similar from 1975 to 2000, while it decreased significantly from 2000 to 2017. The distributions of the numbers of suicided, not-suicide-death, and alive patients with SCC from 1975 to 2017 are shown in eFigure 3 in the Supplement. The survival time of patients showed a right-skewed distribution, mostly concentrated at 0–12 months, and around 2017 (eFigure 4 in the Supplement). We defined the patient suicide rate as the ratio of the number of suicides per year to the total number of patients in the same year. We found that the suicide rate of patients showed a downward trend from 1975 to 2017, and was higher for males, histological grade IV, white race, and urban residents. The distribution of the patient suicide rates is shown in Figure 1.

Figure 1

Suicide rates and SMRs

The observations from 1975 to 2017 comprised a total of 2,289,772 person-years, with a suicide rate for patients with SCC of 50.53 per 100,000 person-years. According to the report of the US Centers for Disease Control and Prevention, the average suicide rate of the general US population was 12.24 per 100,000 years from 1981 to 2017.[8] We calculated that the SMR of US SCC patients was 4.13 (95% CI=3.90–4.38). The suicide rate was higher in patients with SCC than in the general US population, with the main contributing factors being male (SMR=4.61, 95% CI=4.34–4.92), white (SMR=4.01, 95% CI=3.77–4.26), Hispanic (SMR=4.17, 95% CI=2.96–6.55), non-Hispanic white (SMR=4.28, 95% CI=4.02–4.55), age at diagnosis, histological grade, and histological classification. However, the suicide rates among non-Hispanic and native Indian Americans (SMR=1.59, 95% CI=0.30–4.38) and PC patients (SMR=1.10, 95% CI=0.83–1.46) did not differ from those in the general population. The suicide rates and SMRs of US SCC patients are presented in Table 2.

Table 2. Suicide rates and SMRs among squamous cell carcinoma patients

Variables	Suicidal death	Person-years	Suicide rate per 100 000 person-years	p	SMR &	95%CI
Patients	1157	2289772	50.53	<0.001***	4.13	(3.90, 4.38)
Year of dignosis						
1975-1984	341	625950	54.48	<0.001***	4.45	(3.97, 4.92)
1985-1994	335	672752	49.80	<0.001***	4.07	(3.66, 4.55)
1995-2004	253	588512	42.99	<0.001***	3.51	(3.09, 3.97)
2005-2017	228	402558	56.64	<0.001***	4.63	(4.07, 5.3)
Sex						

Variables	Suicidal death	Person-years	Suicide rate per 100 000 person-years	p	SMR &	95%CI
Female	159	1186008	13.41	<0.001***	2.61	(2.22, 3.04)
Male	998	1103764	90.42	<0.001***	4.61	(4.34, 4.92)
Age at diagnosis						
≤39	67	383965	17.45	0.006**	2.06	(1.57, 2.58)
40-49	114	374125	30.47	<0.001***	1.77	(1.47, 2.14)
50-59	246	535626	45.93	<0.001***	2.55	(2.25, 2.9)
60-69	360	551128	65.32	<0.001***	4.49	(4.05, 4.99)
70-79	282	338607	83.28	<0.001***	5.45	(4.81, 6.09)
≥80	88	106321	82.77	<0.001***	4.55	(3.71, 5.71)
Race						
Black	45	207006	21.74	<0.001***	3.99	(2.98, 5.47)
Other	45	152299	29.55	<0.001***	4.21	(2.98, 5.47)
Unknown	0	9908	0.00	0.271	-	-
White	1067	1920671	55.55	<0.001***	4.01	(3.77, 4.26)
Race Latino						
Non-Latino	1130	2172603	52.01	<0.001***	4.25	(4.00, 4.5)
Latino	27	117169	23.04	<0.001***	1.88	(1.27, 2.81)
Race Hispanic						
Hispanic	27	117169	23.04	<0.001***	4.17	(2.96, 6.55)
Non-Hispanic Americn/Indian Native	3	14066	21.33	0.276	1.59	(0.30, 4.38)
Non-Hispanic Asian	42	135956	30.89	<0.001***	2.30	(1.68, 3.15)
Non-Hispanic Black	45	205387	21.91	<0.001***	1.63	(1.17, 2.15)
Non-Hispanic Unknown Race	0	9218	0	0.288	-	-
Non-Hispanic White	1040	1808088	57.52	<0.001***	4.28	(4.02, 4.55)
Grade						
Grade I	134	336671	39.80	<0.001***	3.25	(2.74, 3.87)
Grade II	398	612369	64.99	<0.001***	5.31	(4.8, 5.85)
Grade III	271	432004	62.73	<0.001***	5.13	(4.52, 5.76)
Grade IV	20	26183	76.38	<0.001***	6.24	(4.07, 10.30)
Unknown	334	882545	37.85	<0.001***	3.09	(2.77, 3.44)
Surgery performed						
No	494	589965	83.73	<0.001***	6.84	(6.27, 7.49)
Yes	643	1662394	38.68	<0.001***	3.16	(2.93, 3.42)
Unkonwn	20	37412	53.46	<0.001***	4.37	(2.44, 6.18)
Primary diaeases						
No	362	798353	45.34	<0.001***	3.70	(3.32, 4.09)
Yes	795	1491419	53.30	<0.001***	4.35	(4.05, 4.66)
Household income						
<$50,000	61	112076	54.43	<0.001***	4.45	(3.33, 5.6)
$50,000 - $74,999	331	650167	50.91	<0.001***	4.16	(3.7, 4.61)

Variables	Suicidal death	Person-years	Suicide rate per 100 000 person-years	p	SMR &	95%CI
$75,000+	237	566038	41.87	<0.001***	3.42	(3.01, 3.9)
Unkonwn	528	961490	54.91	<0.001***	4.49	(4.1, 4.87)
Living area#						
Large city	371	750776	49.42	<0.001***	4.24	(3.8, 4.67)
Medium city	110	271574	40.50	<0.001***	3.47	(2.83, 4.14)
Small city	46	90809	50.66	<0.001***	4.34	(3.06, 5.58)
Suburbs	45	95676	47.03	<0.001***	3.02	(2.19, 4.01)
Rural	47	89864	52.30	<0.001***	3.36	(2.47, 4.46)
Unkonwn	538	991072	54.28	<0.001***	3.49	(3.20, 3.80)
Radiotherapy						
No/Unknown	544	1039336	52.34	<0.001***	4.28	(3.93, 4.66)
Yes	613	1250436	49.02	<0.001***	4.01	(3.7, 4.34)
Chemotherapy						
No/Unknown	835	1638816	50.95	<0.001***	4.16	(3.88, 4.45)
Yes	322	650956	49.47	<0.001***	4.04	(3.6, 4.49)

#**Large city**,Counties in metropolitan areas ge 1 million pop; **Medium city**, Counties in metropolitan areas of 250,000 to 1 million pop; **Small city**, Counties in metropolitan areas of lt 250 thousand pop; **Suburbs**, Nonmetropolitan counties adjacent to a metropolitan area; **Rural**, Nonmetropolitan counties not adjacent to a metropolitan area; **Unknown**, Unknown/missing/no match/Not 1990-2017.

&**SMR**, standardized mortality ratio: Compared with the suicide rates of the general US population based on the Centers for Disease Control and Prevention's Web‐based Injury Statistics Query and Reporting System (1981‐2017).

* P<0.05, ** P<0.01, *** P<0.001.

We subsequently analyzed the changes in the SMR of suicided patients from 1975 to 2017. Because the US Centers for Disease Control and Prevention did not provide data on the suicide rate of the general population from 1975 to 1980, we used the suicide rate of the population from 1981 to 1983 to adjust the suicide rate of patients with SCC between 1975 and 1980.8 It was found that the suicide SMR of US SCC patients fluctuated between 3 and 6, and was higher among those who suicided between 2011 and 2017. The changes in the SMR for suicide in US SCC patients are shown in Figure 2.

Figure 2

There were a total of 1157 suicides among adults with SCC in the United States between 1975 and 2017. From the perspective of gender distribution, suicide patients are mainly male, accounting for about 86.3%. The median time to suicide was 27.5 months for male patients and 55 months for female patients. It showed that male patients were more likely to commit suicide than females. In terms of the distribution of cancer types, the suicide patients were mainly lung cancer (250, 21.6%), laryngeal

cancer (185, 16.0%), tongue cancer (123, 10.6%) and oral cancer (101, 8.7%). The median time to suicide in patients with various major tumors was 10.5 months for lung cancer, 44 months for laryngeal cancer, 32 months for tongue cancer, and 73 months for oral cancer. The gender distribution and median time to suicide of SCC suicide patients in the United States are shown in Figure 3.

Figure 3

Factors associated with suicide

Univariate analyses showed that the factors associated with a high risk of suicide in patients with SCC were being male (vs female: HR=6.00, 95% CI=5.07–7.11, P<0.001), older at the diagnosis (40–49 vs ≤39 years: HR=1.60, 95% CI=1.19–2.18, P<0.001; 50–59 vs ≤39 years: HR=2.22, 95% CI=1.69–2.92, P<0.001; 60–69 vs ≤39 years: HR=2.90, 95% CI=2.21– 3.79, P<0.001; 70–79 vs ≤39 years: HR=3.35, 95% CI=2.54–4.43, P<0.001; ≥80 vs ≤39 years: HR=2.92, 95% CI=2.10–4.06, P<0.001), and white (vs black, HR=2.77, 95% CI=2.05–3.73, P<0.001), having a higher histological grade (grade II vs grade I: HR=1.45, 95% CI=1.19–1.77, P<0.001; grade III vs grade I: HR=1.34, 95% CI=1.09–1.65, P=0.006; grade IV vs grade I: HR=1.70, 95% CI=1.06–2.71, P=0.028) and primary cancer (vs nonprimary cancer: HR=1.17, 95% CI=1.03–1.32, P=0.013), and the histological classification (SCC vs PC: HR=3.33, 95% CI=2.51–4.42, P<0.001; OC vs PC: HR=3.76, 95% CI=2.11–6.70, P<0.001). The factors associated with a lower risk of patient suicide were the year of diagnosis (1995–2004 vs 1975–1984: HR=0.71, 95% CI=0.60–0.83, P<0.001; 2005–2017 vs 1975–1984: HR=0.69, 95% CI=0.58–0.82, P<0.001), being Latino (vs non-Latin American: HR=0.46, 95% CI=0.32–0.68, P<0.001), and receiving surgery (vs no surgery: HR=0.59, 95% CI=0.52–0.66, P<0.001). Multivariate Cox regression analyses showed that the factors related to a high risk of suicide in patients with SCC were being male (vs female: HR=5.36, 95% CI=4.51–6.38, P<0.001), older at the diagnosis (70–79 vs ≤39 years: HR=1.46, 95% CI=1.09–2.08, P=0.012; ≥80 vs ≤39 years: HR=1.48, 95% CI=1.05–2.08, P=0.025), and white (vs black: HR=2.97, 95% CI=2.20–4.02, P<0.001), having a higher histological grade (grade II vs grade I: HR=1.54, 95% CI=1.26–1.87, P<0.001; grade III vs grade I: HR=1.42, 95% CI=1.15–1.76, P<0.001; grade IV vs grade I: HR=1.65, 95% CI=1.03–2.66, P=0.039) and primary cancer (vs nonprimary cancer: HR=1.33, 95% CI=1.17–1.50, P<0.001), and the histological classification (SCC vs PC: HR=1.95, 95% CI=1.45–2.62, P<0.001; OC vs PC: HR=2.21, 95% CI=1.22–3.99, P=0.009). The factors associated with a low risk of patient suicide were being Latino (vs non-Latin American: HR=0.58, 95% CI=0.40–0.85, P<0.001), receiving surgery (vs no surgery: HR=0.65, 95% CI=0.57–0.74, P<0.001), and having a higher family income (US$ 75,000 + vs <US$ 50,000: HR=0.71, 95% CI=0.51–0.99, P=0.047). The risk factors related to suicide in US SCC patients are listed in Table 3. A Cox survival regression analysis showed that male patients with SCC had a higher risk of suicide than did female patients with SCC (eFigure 5 in the Supplement).

Table 3. Univariable and multivariable analysis for suicide of leukemia patients

Variables	Univariable analysis		Multivariable analysis	
	HR(95%CI)	*P*	HR(95%CI)	*P*
Year of dignosis				
1975-1984	Reference		Reference	
1985-1994	0.89(0.76-1.04)	0.132	1.04(0.87-1.24)	0.68
1995-2004	0.71(0.60-0.83)	<0.001***	0.97(0.74-1.28)	0.853
2005-2017	0.69(0.58-0.82)	<0.001***	0.78(0.59-1.03)	0.078
Sex				
Female	Reference		Reference	
Male	6.00(5.07-7.11)	<0.001***	5.36(4.51-6.38)	<0.001***
Age at diagnosis				
≤39	Reference		Reference	
40-49	1.61(1.19-2.18)	0.002**	0.93(0.68-1.27)	0.656
50-59	2.22(1.69-2.92)	<0.001***	0.97(0.72-1.29)	0.814
60-69	2.90(2.21-3.79)	<0.001***	1.20(0.90-1.59)	0.21
70-79	3.35(2.54-4.43)	<0.001***	1.46(1.09-2.08)	0.012**
≥80	2.92(2.10-4.06)	<0.001***	1.48(1.05-2.08)	0.025*
Race				
Black	Reference		Reference	
White	2.77(2.05-3.73)	<0.001***	2.97(2.20-4.02)	<0.001***
Other	1.53(1.01-2.31)	0.044*	1.84(1.20-2.82)	0.005**
Unknown	-	-	-	-
Race Latino				
Non-Latino	Reference		Reference	
Latino	0.46(0.32-0.68)	<0.001***	0.58(0.40-0.85)	<0.001***
Grade				
Grade I	Reference		Reference	
Grade II	1.45(1.19-1.77)	<0.001***	1.54(1.26-1.87)	<0.001***
Grade III	1.34(1.09-1.65)	0.006**	1.42(1.15-1.76)	<0.001***
Grade IV	1.70(1.06-2.71)	0.028*	1.65(1.03-2.66)	0.039*
Unknown	0.96(0.79-1.18)	0.723	1.28(1.04-1.57)	0.018*
Surgery performed				
No	Reference		Reference	
Yes	0.59(0.52-0.66)	<0.001***	0.65(0.57-0.74)	<0.001***
Unkonwn	0.70(0.45-1.10)	0.121	0.54(0.35-0.85)	0.008**
Primary diaeases				
No	Reference		Reference	
Yes	1.17(1.03-1.32)	0.013*	1.33(1.17-1.50)	<0.001***
Household income				

Variables	Univariable analysis		Multivariable analysis	
	HR(95%CI)	*P*	HR(95%CI)	*P*
<$50,000	Reference		Reference	
$50,000-$74,999	1.00(0.76-1.32)	0.993	0.93(0.69-1.26)	0.629
$75,000+	0.85(0.64-1.13)	0.254	0.71(0.51-0.99)	0.047*
Unkonwn	1.31(1.01-1.72)	0.044*	1.01(0.49-2.11)	0.976
Living area#				
Large city	Reference		Reference	
Medium city	0.82(0.66-1.01)	0.067	0.79(0.63-0.98)	0.032*
Small city	1.05(0.77-1.42)	0.772	0.85(0.62-1.17)	0.326
Suburbs	0.96(0.71-1.31)	0.808	0.73(0.53-1.01)	0.058
Rural	1.06(0.78-1.44)	0.699	0.79(0.56-1.11)	0.169
Unkonwn	1.33(1.17-1.53)	<0.001***	1.00(0.52-1.92)	0.992
Radiotherapy				
No/Unknown	Reference		Reference	
Yes	0.94(0.84-1.05)	0.280	0.95(0.84-1.07)	0.381
Chemotherapy				
No/Unknown	Reference		Reference	
Yes	0.98(0.86-1.12)	0.772	0.98(0.85-1.12)	0.750

#**Large city**, Counties in metropolitan areas ge 1 million pop; **Medium city**, Counties in metropolitan areas of 250,000 to 1 million pop; **Small city**, Counties in metropolitan areas of lt 250 thousand pop; **Suburbs**, Nonmetropolitan counties adjacent to a metropolitan area; **Rural**, Nonmetropolitan counties not adjacent to a metropolitan area; **Unknown**, Unknown/missing/no match/Not 1990-2017.

* P<0.05, ** P<0.01, *** P<0.001.

Discussion

This study found that the suicide rate of patients with SCC in the US was higher than that in the general population,[8] which is similar to the results of previous studies of the suicide rates of cancer patients in the US[11,21,22] and many other countries, including the UK, Italy, Estonia, Sweden, and Denmark.[3,23–26] Our analyses revealed that the factors associated with a high risk of suicide in SCC patients include being male, older at the diagnosis, and white, and having a higher histological grade and not receiving surgery.

Males accounted for 59.9% of the US patients with SCC in this study. The number of patients who suicided or died of another cause was higher for males than females in each year from 1975 to 2017, with male suicided patients accounting for 86.2% of the total (Table 1, eFigure 2, and eFigure 3 in the Supplement). The death rate during each year of the analysis was also higher for males than for females (eFigure 3 in the Supplement). Further analysis showed that the suicide rate for patients with SCC in the US was 90.42 per 100,000 person-years among males (SMR=4.61, 95% CI=4.34–4.92) and 13.41 per 100,000 person-years among females (SMR=2.61, 95% CI=2.22–3.04) (Table 1). The risk of suicide was markedly higher in male than female patients (HR=6.00, 95% CI=5.07–7.11) (Table 3). Other studies have also found that male cancer patients are a high-risk group for suicide, which may be related to male patients suffering more social pressures, family burdens, and their own psychological problems.[18,27,28]

Most of the patients with SCC were older than 50 years (85.7%). Males aged 55-79 years predominated among patients who suicided or died of another cause, while females younger than 75 years predominated among alive patients (eFigure 2 in the Supplement). Compared with patients younger than 39 years, elderly patients exhibited a higher suicide rate (HR>2.5, P<0.001) (Table 3). Table 2 indicates that the suicide rate of the patients gradually increased with age. Previous studies have also found the suicide rate to be significantly higher in elderly cancer patients than in the general population.[9,21] The high rate of suicide among elderly SCC cancer patients could be related to various factors, including more concomitant diseases, lower disease resistance, lower quality of life, loneliness, and depression.[10,29–31]

Our analysis of the changes in the suicide SMR of SCC patients from 1975 to 2017 revealed that this fluctuated between 3 and 6, peaking between 2011 and 2017 at SMR>5 (Figure 2). However, the suicide rate of patients decreased over time (Figure 1). The sudden increase in the SMR after 2011 could have been due to their mortality rate before 2010 exceeding 70%, whereas the alive patients were mainly distributed after 2011 (eFigure 3 in the Supplement). At the same time, we found that the maximum survival time of patients with SCC was 515 months from 1975 to 2017, while the survival time of most patients was shorter than 12 months, and it was mainly distributed from 2011 to 2017 (eFigure 4 in the Supplement). Therefore, the total number of patient years decreased from 2011 to 2017 (eFigure 3 in the Supplement), resulting in a high value for the suicide SMR during this period.

The Cox regression analyses showed that race was a risk factor for suicide in

patients with SCC. Compared with black patients, white patients had an approximately threefold higher risk of suicide (HR=2.97, 95% CI=2.20–4.02, P<0.001) (Table 3). Meanwhile, the suicide rate of white Americans decreased over time, and that of black Americans remained at a low level. However, the suicide rates of other races fluctuated markedly (Figure 1), which might have been due to the relatively small proportion of other races in the analyzed population. It can be concluded that white Americans with SCC are a high-risk group for suicide, which is consistent with previous findings for other cancer patients in the US.[30–32] The variations in suicide rates between different racial groups of SCC patients in the US might be related to variations in culture, religious beliefs, quality of life, mental health, and economic conditions.[28,30,33]

We also found that patients with SCC of different histological grades had different suicide rates, with this being highest in grade IV (SMR=6.24, 95% CI=4.07-10.30) (Table 2). The suicide risk of patients with histological grades higher than grade I increased to varying degrees (overall HR>1.40) (Table 3). Although the suicide rate of patients with different histological grades trended downward each year, the annual suicide rate of grade IV patients fluctuated greatly (Figure 1), which might be related to their small proportion (1.5%). We subsequently classified the US SCC patients based on morphology codes into PC, SCC, and OC, which revealed that SCC constituted the highest proportion of patients in the US (93.0%). Compared with PC patients, the suicide risks in SCC and OC patients were 1.95-fold (95% CI=1.45–2.62, P<0.001) and 2.21-fold (95% CI=2.21–3.99, P<0.001) higher, respectively (Table 3). The risk of suicide was higher in patients with primary cancer than in those with nonprimary cancer (HR=1.33, 95% CI=1.17–1.50, P<0.001) (Table 3). Different types of cancer are generally associated with different rates of disease progression and different prognoses, with a higher degree of malignancy associated with faster disease progression and a worse prognosis.[30] Studies have found that cancers with poor prognoses are often accompanied by serious psychological problems such as loneliness and depression, which in turn increase the risk of suicide.[29,34] Similarly, the present patients who did receive surgery had a lower suicide risk (HR=0.65, 95% CI=0.57–0.74, P<0.001) (Table 3), which might be related to the better prognosis of patients after they receive surgery. The above results indicate that patients with SCC with a higher histological grade and degree of malignancy are at high risk of suicide.

Multiple studies have found cancer patients to be more likely to have depression and other psychological problems than the general population, and also have a higher risk of suicide.[29,30,35] Suicide is one cause of death in cancer patients that is potentially preventable.[36] Suicide is a complex behavior and is affected by many factors, including psychological factors, religious beliefs, and family support. Our results showed that compared with the general population,[37,38] patients with SCC in the US have a higher suicide rate. Being male, white, and older at the diagnosis, and having a higher histological grade were found to be factors contributing to a high risk of suicide. Preventing and reducing suicide in patients with SCC requires a greater focus on high-risk populations and the risk of depression being identified in psychiatric assessments of patients with SCC, such as using the Baker Depression

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Scale.[39] Actively improving the treatment plan and quality of life of cancer patients, and strengthening the care and communication of people at a high risk of cancer could reduce the psychological burden of these patients and so reduce their risk of suicide.[40]

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Conclusions

This study found that the suicide rate of patients with SCC in the US has decreased over the past few decades. Compared with the general population, patients with SCC in the United States have a higher risk of suicide. The independent risk factors for suicide in patients with SCC included being male, older at the diagnosis, white, and having a higher histological grade and not receiving surgery. Clinicians can use the findings of this research to evaluate the suicide risk in individual patients with SCC. Effective intervention measures should be applied to the identified high-risk population in order to reduce their suicide rate.

Statements

Ethical approval:

The SEER database is a tumor-related database developed by the National Cancer Institute of the United States, providing research data for researchers free of charge. All patients participating in the study received the ethical approval sought by the National Cancer Institute.

Consent for publication:

Consent for publication was obtained from all participants.

Availability of data and materials:

We obtained permission to access the database after signing and submitting the SEER Research Data Agreement form via email. The data that support the findings of this study are available from SEER database but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of SEER database.

Competing interests:

None.

Funding:

None.

Author Contributions:

All authors had full access to all of the data in the study. Haohui Yu, and Jun Lyu take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Jun Lyu, Haohui Yu. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Haohui Yu, Shengru Tao, Wenli She, Min Liu. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: Haohui Yu, Yayun Wu, Wenli She. Administrative, technical, or material support: Jun Lyu, Shengru Tao. All authors contributed to writing of the manuscript and approved the final version.

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Figure legends

Figure 1. The distribution of suicide rate in patients with squamous cell carcinoma.

Figure 2. Standardized mortality ratio of suicide for squamous cell carcinoma patients

(1975–2017).

Figure 3. Distribution of median time to suicide for squamous cell carcinoma patients

(1975–2017).

Figure 1. The distribution of suicide rate in patients with squamous cell carcinoma.
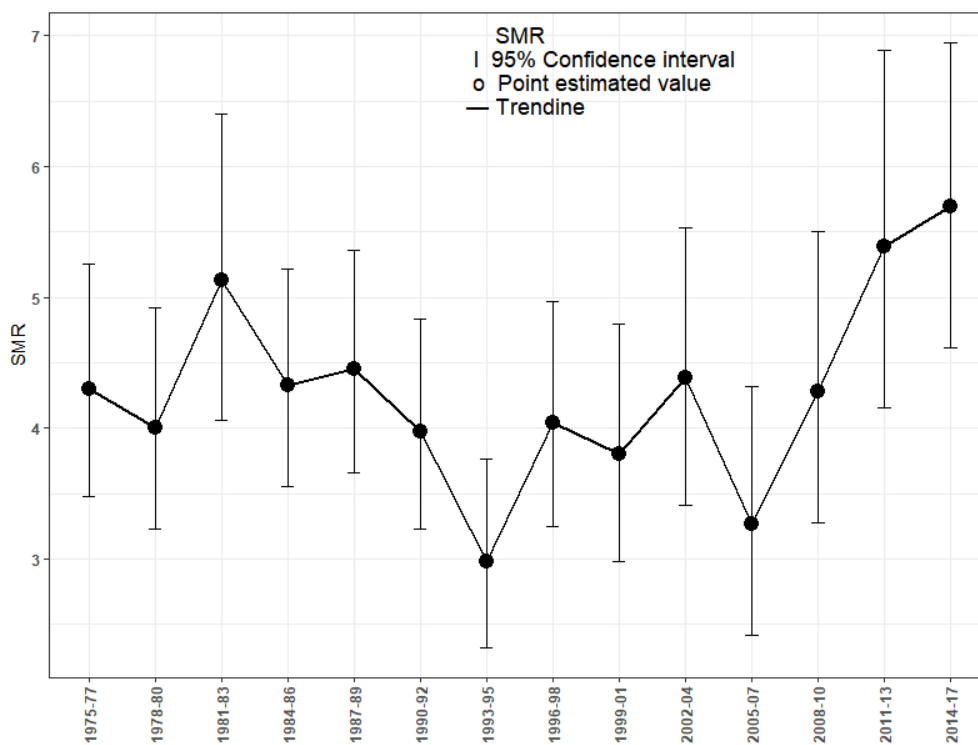
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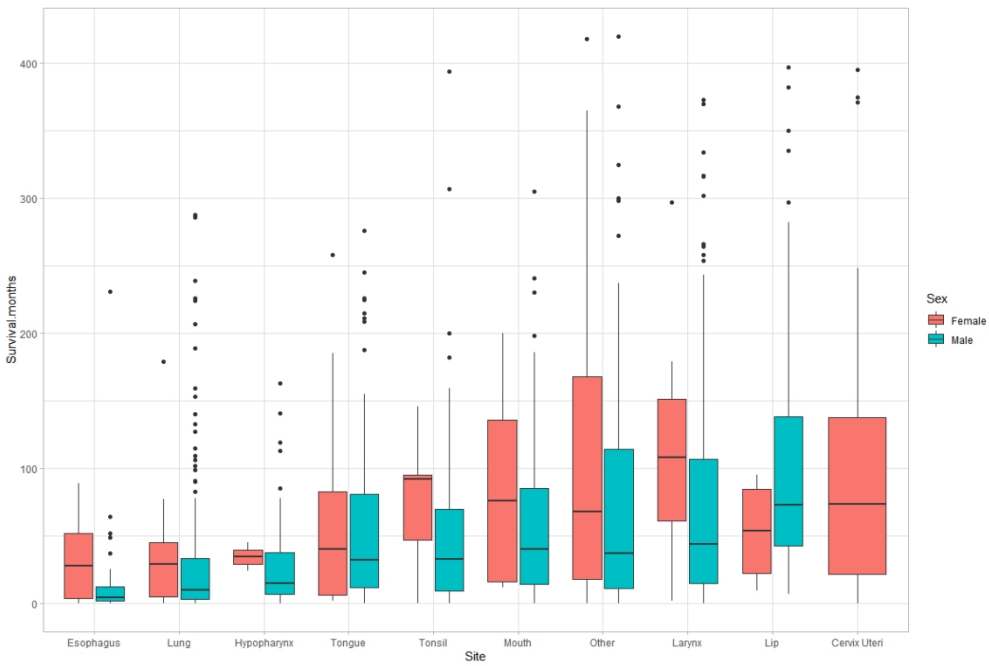
Figure 2. Standardized mortality ratio of suicide for squamous cell carcinoma patients (1975–2017).

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Distribution of median time to suicide for squamous cell carcinoma patients (1975–2017).

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Analysis of Suicide Risk Factors in Adult US Patients with Squamous Cell Carcinoma Based on the SEER Database
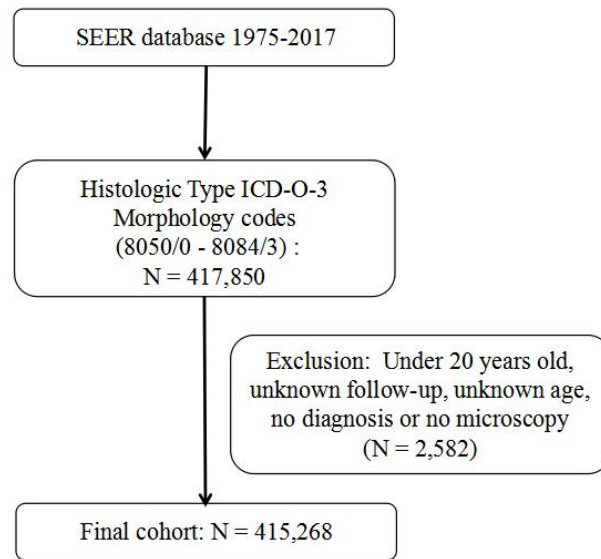
Supplement Online

eFigure legends

eFigure 1. The flow diagram of squamous cell carcinoma patients selection.

eFigure 2. The distribution of patients with squamous cell carcinoma by age.

eFigure 3. The distribution of patients with squamous cell carcinoma by year.

eFigure 4. The distribution of survival months of patients with squamous cell carcinoma in different years.

eFigure 5. Comparison chart of survival curves of male and female squamous cell carcinoma patients.

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eFigure 1. The flow diagram of squamous cell carcinoma patients selection.

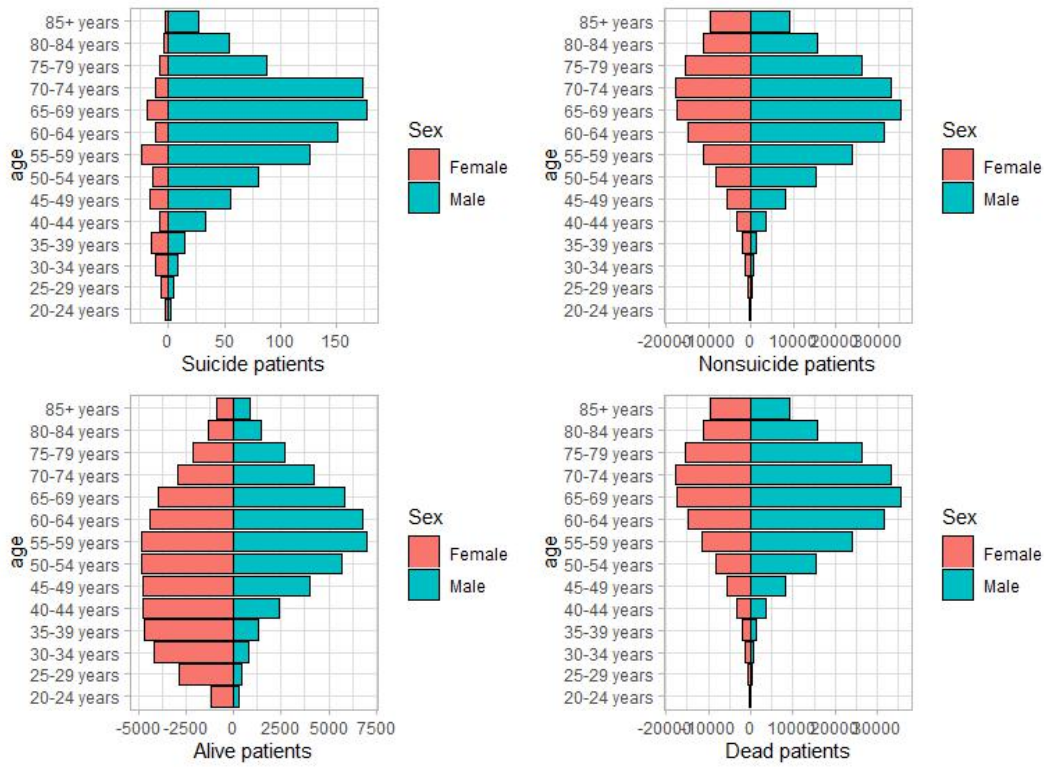eFigure 2. The distribution of patients with squamous cell carcinoma by age.

eFigure 3. The distribution of patients with squamous cell carcinoma by year.

eFigure 4. The distribution of survival months of patients with squamous cell
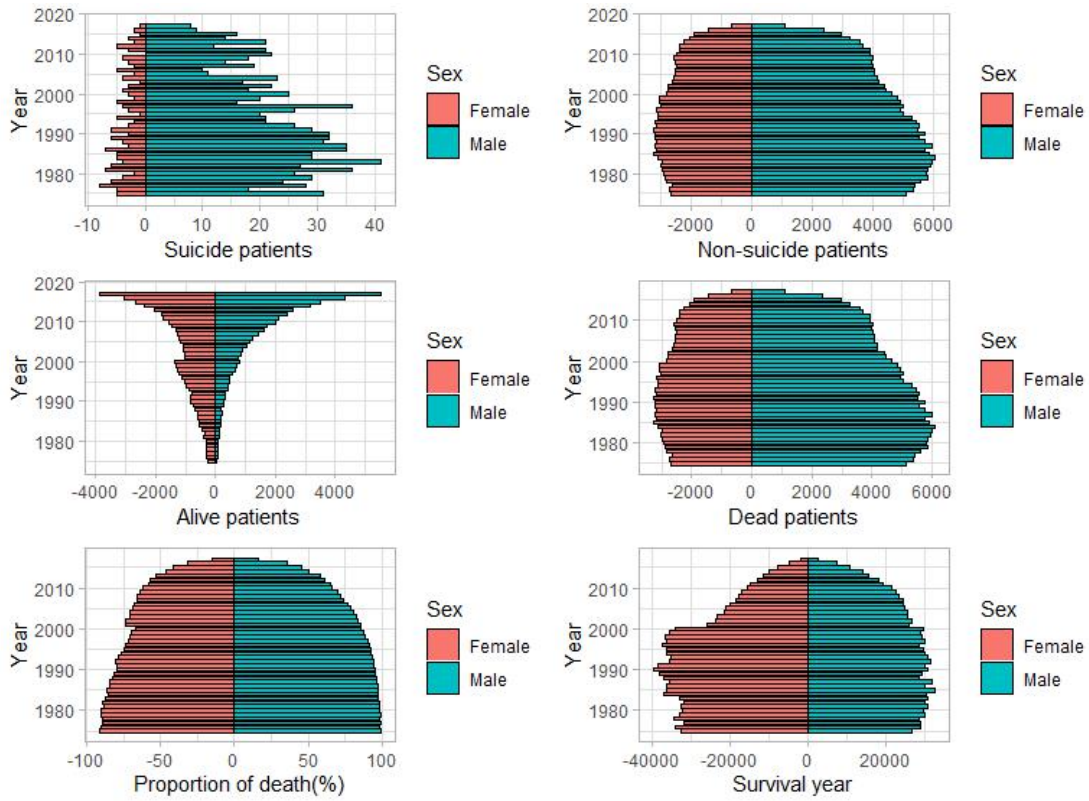
carcinoma in different years.

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eFigure 5. Comparison chart of survival curves of male and female squamous cell

carcinoma patients.

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Analysis of Suicide Risk in Adult US Patients with Squamous Cell Carcinoma: a Retrospective Study Based on the Surveillance, Epidemiology, and End Results Database

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Analysis of Suicide Risk in Adult US Patients with Squamous Cell Carcinoma: a Retrospective Study Based on the Surveillance, Epidemiology, and End Results Database

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Short title: Analysis of Suicide RF in Adult US SCC Patients.

Abstract

Objectives: The purpose of this study was to determine the risk factors for suicide in patients with squamous cell carcinoma (SCC) in the US.

Setting: Patients with SCC diagnosed between 1975 and 2017 from the Surveillance, Epidemiology, and End Results (SEER) database were selected for this study.

Participants: This study included patients with SCC older than 20 years who were diagnosed between 1975 and 2017.

Primary and secondary outcome measures: The general population included in data from the US Centers for Disease Control and Prevention were used to calculate the suicide rate and standardized mortality rate (SMR) of SCC patients. Univariate and multivariate Cox regression analyses were used to identify risk factors for suicide in patients with SCC.

Results: There were 415,268 SCC patients registered in the SEER database, among which 1,157 cases of suicide were found, comprising a total of 2,289,772 person-years. The suicide rate for patients with SCC was 50.53 per 100,000 person-years, and the SMR was 4.13 (95% confidence interval [CI]=3.90–4.38). The Cox regression analyses showed that the factors related to a high risk of suicide among patients with SCC included being male (vs female: hazard ratio [HR]=5.36, 95% CI=4.51–6.38, P<0.001), older at the diagnosis (70–79 vs ≤39 years: HR=1.46, 95% CI=1.09–2.08, P=0.012; ≥80 vs ≤39 years: HR=1.48, 95% CI=1.05–2.08, P=0.025), and white (vs black, HR=2.97, 95% CI=2.20–4.02, P<0.001), and surgery (vs not performed: HR=0.65, 95% CI=0.57–0.74, P<0.001).

Conclusions: Compared with the general population, patients with SCC in the United States have a higher risk of suicide. Being male, older at the diagnosis, white, and having a higher histological grade are risk factors for suicide in patients.

Strengths and limitations of this study

Our study had several strengths:

- This study found that the suicide rate of patients with SCC in the US has decreased over the past few decades, but it remains higher than that in the general population.
- The independent risk factors for suicide in patients with SCC included being male, older at the diagnosis, white, and having a higher histological grade and not receiving surgery.

Our study had several limitations：

- Some potentially important information that could impact suicidal behaviors is missing for patients with SCC in the SEER database, such as religious beliefs, education level, medication status, and psychological factors.
- Future studies should therefore include patients with SCC in more countries and regions in order to accurately identify the factors affecting the risk of suicide in SCC patients worldwide.

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Background

The World Health Organization has reported that the number of cancer deaths worldwide is increasing, with cancer now being the third-most-common cause of deaths worldwide.[1] There were about 18.1 million new cancer patients and about 9.6 million deaths worldwide in 2018.[2] Previous studies have shown that patients with depression and cancers with a poor prognosis have a high risk of suicide.[3] Suicide is influenced by many factors,[4] and the World Health Organization has also reported that the number of suicides worldwide is increasing, with approximately 800,000 suicide deaths each year.[5–7] According to data released by the US Centers for Disease Control and Prevention, suicide is one of the common causes of death in the US.[8] The suicide rate in the general US population was 14.78 per 100,000 people in 2018, which was higher than in other countries.[8] Multiple studies have shown that the suicide rate is higher in cancer patients than in the general US population.[9–12] In particular, the suicide rate of patients with head and neck cancer was more than three times higher than that in the general US population.[13] Cancer patients face enormous financial pressures and physical burdens. The poor prognosis of cancer is often accompanied by long-term mental and psychological problems, and often leads to death.[7] The increasing incidence of cancer has resulted in mental and psychological problems gradually becoming a major complication experienced by cancer patients.[14] The resulting fear of a cancer prognosis, depression, and other psychological problems have gradually increased the risk of suicide.[4] Therefore, it is of great importance to identify the risk factors for suicide in cancer patients in order to control suicidality in this population. Some studies have found male sex, white race, marital status, type of cancer, and other factors to be strongly correlated with the suicide risk of patients with some types of cancer.[9–13]

Squamous cell carcinoma (SCC) refers to a malignant tumor derived from the squamous epithelium. This is the general term for a class of tumors that include multiple cancers occurring in the squamous epithelium covering tissues and organs, and which are more common in the skin, mouth, esophagus, cervix, and vagina.[15–17] According to a report by the US Centers for Disease Control and Prevention, the number of deaths from malignant tumors in the US in 2018 was second only to that due to cardiovascular disease, and suicide has become the second leading cause of death among US residents aged 10 to 34 years.[8] The number of deaths due to SCC in the US is increasing. GuoPei Yu et al. investigated the causes of death in patients with oral and oropharyngeal SCC in the US,[18] but did not conduct in-depth studies on the causes of suicide. Therefore, the purpose of this study was to identify potential risk factors associated with suicide in US SCC patients by analyzing data in the US Surveillance, Epidemiology, and End Results (SEER) database.

Method

Data source

All patients with SCC in this study were selected from the SEER database (http://seer.cancer.gov). This database covers about 30% of the US population and provides researchers with a large amount of research data, including on patient demographics, cancer incidence, and survival data.[19] We used SEER*Stat software (version 8.3.6) to identify US patients with SCC who were added to the database from 1975 to 2017. We obtained permission to access the database after signing and submitting the SEER Research Data Agreement form via email.

Patient and Public Involvement:

All patients were selected from the SEER database. No patient involved.

Inclusion and exclusion criteria for the study population

This study applied screening criteria for the research objectives based on histological type codes in ICD-O-3. We used morphology codes 8050/0–8084/3 to identify patients with SCC in the SEER database. The collected patients were divided into the following three groups based on morphology codes: papillary carcinoma (PC, codes 8050/3–8060/0), SCC (codes 8070/2–8078/3), and other carcinomas (OC, codes 8080/2–8084/3). The cause of death of "Suicide and Self-Inflicted Injury" was searched for in order to identify cases of suicide. The exclusion criteria for study subjects included being younger than 20 years, unknown follow-up time, unknown age, and no diagnosis or microscopy data. The information collected by all patients with SCC includes sex, age, year of diagnosis, race, histological grade, cancer type, survival time, surgery status, radiotherapy status, chemotherapy status, cause of death, and area of residence. This study collected 415,268 patients with SCC, which included 1,157 who suicided. The screening procedure for patients with SCC is shown in eFigure 1 in the Supplement.

Statistical analysis

This study divided the SCC patients collected from the SEER database into the following three groups in order to perform basic data comparisons: suicided group, nonsuicide death group, and alive group. We analyzed the age distributions in these three groups of patients from 0 to 85 years and the year of diagnosis distribution of patients from 1975 to 2017. The chi-square test was used to compare the suicide rates among patients in each group. The SMR for suicide in each group was based on the total population of the US from 1981 to 2017, using data obtained from the Web-Based Injury Statistics Query and Reporting System of the Centers for Disease Control and Prevention (https://www.cdc.gov/injury/wisqars/fatal.html). The 95% confidence interval (CI) of the SMR for suicide was approximated using the method of Byar.[20] We set the suicide group as "1" and other groups as "0". Univariate and multivariate Cox regression analyses were subsequently used to generate the hazard ratio (HR), and the 95% CI combined with the HR were used to identify potential risk factors for suicide. All statistical analyses was performed using R software (version 3.6.3, http://www.r-project.org/). All tests were two-sided, and the significance criterion was set as $P<0.05$.

Results

Patient baseline characteristics

The 415,268 identified US patients with SCC in the SEER database from 1975 to 2017 included 248,816 males (59.9%). These patients comprised 1,157 (0.3%) in the suicided group, 322,384 (77.6%) in the not-suicide-death group, and 91,727 (22.1%) in the alive group. Most of them were older than 60 years (66.3%), white (81.7%), non-Latin American (95.7%), non-Hispanic white (77.6%), and lived in urban areas (56.2%). The age distributions of the suicided, not-suicide-death, alive, and dead patients are shown in eFigure 2 in the Supplement. The basic statistics of each group of SCC patients are presented in Table 1.

Table 1. Baseline characteristics of squamous cell carcinoma patients (1975-2017)

Variables	Overall N(%)	Suicidal death N(%)	Nonsuicidal death N(%)	Alive N(%)	p
Patients	415268	1157(0.3%)	322384(77.6%)	91727(22.1%)	-
Year of dignosis					
1975-1984	90334(21.8%)	341(29.5%)	85435(26.5%)	4558(5.0%)	
1985-1994	98947(23.8%)	335(29.0%)	88294(27.4%)	10318(11.2%)	<0.001
1995-2004	94368(22.7%)	253(21.8%)	75490(23.4%)	18625(20.3%)	
2005-2017	131619(31.7%)	228(19.7%)	73165(22.7%)	58226(63.5%)	
Sex					
Female	166452(40.1%)	159(13.7%)	118262(36.7%)	48031(52.4%)	<0.001
Male	248816(59.9%)	998(86.3%)	204122(63.3%)	43696(47.6%)	
Age at diagnosis					
≤39	22031(5.3%)	67(5.8%)	6211(1.9%)	15753(17.2%)	
40-49	36569(8.8%)	114(9.9%)	20570(6.4%)	15885(17.3%)	
50-59	81389(19.6%)	246(21.3%)	58737(18.2%)	22406(24.4%)	<0.001
60-69	120016(28.9%)	360(31.1%)	98541(30.6%)	21115(23.0%)	
70-79	104931(25.3%)	282(24.3%)	92561(28.7%)	12088(13.2%)	
≥80	50332(12.1%)	88(7.6%)	45764(14.2%)	4480(4.9%)	
Race					
Black	50022(12.0%)	45(3.9%)	42014(13.0%)	7963(8.7%)	
White	339376(81.7%)	1067(92.2%)	263117(81.6%)	75192(82.0%)	<0.001
Other	24658(5.9%)	45(3.9%)	16979(5.3%)	7634(8.3%)	
Unknown	1212(0.3%)	0	274(0.1%)	938(1.0%)	
Race Hispanic					
Hispanic	18018(4.3%)	27(2.3%)	11338(3.5%)	6653(7.3%)	
Non-Hispanic White	322235(77.6%)	1040(89.9%)	252268(78.2%)	68927(75.1%)	
Non-Hispanic Ameriacn/Indian Native	2137(0.5%)	3(0.3%)	1485(0.5%)	649(0.7%)	<0.001
Non-Hispanic Asian	22123(5.3%)	42(3.6%)	15253(4.7%)	6828(7.4%)	
Non-Hispanic Black	49711(12.0%)	45(3.9%)	41828(13.0%)	7866(8.6%)	

Variables	Overall N(%)	Suicidal death N(%)	Nonsuicidal death N(%)	Alive N(%)	p
Non-Hispanic Unknown Race	1044(0.3%)	0	240(0.1%)	804(0.9%)	
Grade					
Grade I	43008(10.4%)	134(11.6%)	31492(9.8%)	11382(12.4%)	
Grade II	121959(29.4%)	398(34.4%)	94991(29.5%)	26570(29.0%)_	
Grade III	108530(26.0%)	271(23.4%)	89299(27.7%)	18960(20.7%)	<0.001
Grade IV	6169(1.5%)	20(1.7%)	5198(1.6%)	951(1.0%)	
Unknown	135602(32.7%)	334(28.9%)	101404(31.5%)	33864(36.9%)	
Surgery performed					
No	207029(49.9%)	494(42.7%)	175871(54.5%)	30664(33.4%)	
Yes	197252(47.5%)	643(55.6%)	135928(42.2%)	60681(66.2%)	<0.001
Unkonwn	10987(2.6%)	20(1.7%)	10585(3.3%)	382(0.4%)	
Primary diaeases					
No	127948(30.8%)	362(31.3%)	102800(31.9%)	24786(27.0%)	
Yes	287320(69.2%)	795(68.7%)	219584(68.1%)	66941(73.0%)	<0.001
Household income					
<$50,000	28804(6.9%)	61(5.3%)	19661(6.1%)	9082(9.9%)	
$50,000 - $74,999	137290(33.1%)	331(28.6%)	95873(29.7%)	41094(44.8%)	
$75,000+	109556(26.4%)	237(20.5%)	76605(23.8%)	3271(35.7%)	<0.001
Unkonwn	139610(33.6%)	528(45.6%)	130245(40.4%)	8837(9.6%)	
Living area#					
Large city	159750(38.5%)	371(32.0%)	112206(34.8%)	47173(51.4%)	
Medium city	56207(13.5%)	110(9.5%)	37366(11.6%)	18731(20.4%)	
Small city	17605(4.2%)	46(4.0%)	12032(3.7%)	5527(6.0%)	
Suburbs	19322(4.7%)	45(3.9%)	13706(4.3%)	5571(6.1%)	<0.001
Rural	18652(4.5%)	47(4.1%)	13419(4.1%)	5186(5.7%)	
Unkonwn	143732(34.6%)	538(46.5%)	133655(41.5%)	9539(10.4%)	
Radiotherapy					
No/Unknown	188695(45.4%)	544(47.0%)	146075(45.3%)	42076(45.9%)	
Yes	226573(54.6%)	613(53.0%)	176309(54.7%)	49651(54.1%)	0.006
Chemotherapy					
No/Unknown	298396(71.9%)	835(72.2%)	231140(71.7%)	66421(72.4%)	
Yes	116872(28.1%)	322(27.8%)	91244(28.3%)	25306(27.6%)	<0.001

#**Large city**,Counties in metropolitan areas ge 1 million pop; **Medium city**, Counties in metropolitan areas of 250,000 to 1 million pop; **Small city**, Counties in metropolitan areas of lt 250 thousand pop; **Suburbs**, Nonmetropolitan counties adjacent to a metropolitan area; **Rural**, Nonmetropolitan counties not adjacent to a metropolitan area; **Unknown**, Unknown/missing/no match/Not 1990-2017.

Patient distributions according to year

We found that most of the US patients with SCC who suicided were males. The number of suicided patients declined each year from 1975 to 2017. The alive patients mostly appeared during 2014–2017, while the number and percentage of dead patients gradually decreased. The total number of alive patients was similar from 1975 to 2000, while it decreased significantly from 2000 to 2017. The distributions of the numbers of suicided, not-suicide-death, and alive patients with SCC from 1975 to 2017 are shown in eFigure 3 in the Supplement. The survival time of patients showed a right-skewed distribution, mostly concentrated at 0–12 months, and around 2017 (eFigure 4 in the Supplement). We defined the patient suicide rate as the ratio of the number of suicides per year to the total number of patients in the same year. We found that the suicide rate of patients showed a downward trend from 1975 to 2017, and was higher for males, histological grade IV, white race, and urban residents. The distribution of the patient suicide rates is shown in Figure 1.

Figure 1

Suicide rates and SMRs

The observations from 1975 to 2017 comprised a total of 2,289,772 person-years, with a suicide rate for patients with SCC of 50.53 per 100,000 person-years. According to the report of the US Centers for Disease Control and Prevention, the average suicide rate of the general US population was 12.24 per 100,000 years from 1981 to 2017.[8] We calculated that the SMR of US SCC patients was 4.13 (95% CI=3.90–4.38). The suicide rate was higher in patients with SCC than in the general US population, with the main contributing factors being male (SMR=4.61, 95% CI=4.34–4.92), white (SMR=4.01, 95% CI=3.77–4.26), Hispanic (SMR=4.17, 95% CI=2.96–6.55), non-Hispanic white (SMR=4.28, 95% CI=4.02–4.55), age at diagnosis, histological grade, and histological classification. However, the suicide rates among non-Hispanic and native Indian Americans (SMR=1.59, 95% CI=0.30–4.38) and PC patients (SMR=1.10, 95% CI=0.83–1.46) did not differ from those in the general population. The suicide rates and SMRs of US SCC patients are presented in Table 2.

Table 2. Suicide rates and SMRs among squamous cell carcinoma patients

Variables	Suicidal death	Person-years	Suicide rate per 100 000 person-years	p	SMR &	95%CI
Patients	1157	2289772	50.53	<0.001***	4.13	(3.90, 4.38)
Year of dignosis						
1975-1984	341	625950	54.48	<0.001***	4.45	(3.97, 4.92)
1985-1994	335	672752	49.80	<0.001***	4.07	(3.66, 4.55)
1995-2004	253	588512	42.99	<0.001***	3.51	(3.09, 3.97)
2005-2017	228	402558	56.64	<0.001***	4.63	(4.07, 5.3)
Sex						

Variables	Suicidal death	Person-years	Suicide rate per 100 000 person-years	p	SMR &	95%CI
Female	159	1186008	13.41	<0.001***	2.61	(2.22, 3.04)
Male	998	1103764	90.42	<0.001***	4.61	(4.34, 4.92)
Age at diagnosis						
≤39	67	383965	17.45	0.006**	2.06	(1.57, 2.58)
40-49	114	374125	30.47	<0.001***	1.77	(1.47, 2.14)
50-59	246	535626	45.93	<0.001***	2.55	(2.25, 2.9)
60-69	360	551128	65.32	<0.001***	4.49	(4.05, 4.99)
70-79	282	338607	83.28	<0.001***	5.45	(4.81, 6.09)
≥80	88	106321	82.77	<0.001***	4.55	(3.71, 5.71)
Race						
Black	45	207006	21.74	<0.001***	3.99	(2.98, 5.47)
Other	45	152299	29.55	<0.001***	4.21	(2.98, 5.47)
Unknown	0	9908	0.00	0.271	-	-
White	1067	1920671	55.55	<0.001***	4.01	(3.77, 4.26)
Race Latino						
Non-Latino	1130	2172603	52.01	<0.001***	4.25	(4.00, 4.5)
Latino	27	117169	23.04	<0.001***	1.88	(1.27, 2.81)
Race Hispanic						
Hispanic	27	117169	23.04	<0.001***	4.17	(2.96, 6.55)
Non-Hispanic Americacn/Indian Native	3	14066	21.33	0.276	1.59	(0.30, 4.38)
Non-Hispanic Asian	42	135956	30.89	<0.001***	2.30	(1.68, 3.15)
Non-Hispanic Black	45	205387	21.91	<0.001***	1.63	(1.17, 2.15)
Non-Hispanic Unknown Race	0	9218	0	0.288	-	-
Non-Hispanic White	1040	1808088	57.52	<0.001***	4.28	(4.02, 4.55)
Grade						
Grade I	134	336671	39.80	<0.001***	3.25	(2.74, 3.87)
Grade II	398	612369	64.99	<0.001***	5.31	(4.8, 5.85)
Grade III	271	432004	62.73	<0.001***	5.13	(4.52, 5.76)
Grade IV	20	26183	76.38	<0.001***	6.24	(4.07, 10.30)
Unknown	334	882545	37.85	<0.001***	3.09	(2.77, 3.44)
Surgery performed						
No	494	589965	83.73	<0.001***	6.84	(6.27, 7.49)
Yes	643	1662394	38.68	<0.001***	3.16	(2.93, 3.42)
Unkonwn	20	37412	53.46	<0.001***	4.37	(2.44, 6.18)
Primary diaeases						
No	362	798353	45.34	<0.001***	3.70	(3.32, 4.09)
Yes	795	1491419	53.30	<0.001***	4.35	(4.05, 4.66)
Household income						
<$50,000	61	112076	54.43	<0.001***	4.45	(3.33, 5.6)
$50,000 - $74,999	331	650167	50.91	<0.001***	4.16	(3.7, 4.61)

Variables	Suicidal death Person-years		Suicide rate per 100 000 person-years	p	SMR &	95%CI
$75,000+	237	566038	41.87	<0.001***	3.42	(3.01, 3.9)
Unkonwn	528	961490	54.91	<0.001***	4.49	(4.1, 4.87)
Living area#						
Large city	371	750776	49.42	<0.001***	4.24	(3.8, 4.67)
Medium city	110	271574	40.50	<0.001***	3.47	(2.83, 4.14)
Small city	46	90809	50.66	<0.001***	4.34	(3.06, 5.58)
Suburbs	45	95676	47.03	<0.001***	3.02	(2.19, 4.01)
Rural	47	89864	52.30	<0.001***	3.36	(2.47, 4.46)
Unkonwn	538	991072	54.28	<0.001***	3.49	(3.20, 3.80)
Radiotherapy						
No/Unknown	544	1039336	52.34	<0.001***	4.28	(3.93, 4.66)
Yes	613	1250436	49.02	<0.001***	4.01	(3.7, 4.34)
Chemotherapy						
No/Unknown	835	1638816	50.95	<0.001***	4.16	(3.88, 4.45)
Yes	322	650956	49.47	<0.001***	4.04	(3.6, 4.49)

#**Large city**,Counties in metropolitan areas ge 1 million pop; **Medium city**, Counties in metropolitan areas of 250,000 to 1 million pop; **Small city**, Counties in metropolitan areas of lt 250 thousand pop; **Suburbs**, Nonmetropolitan counties adjacent to a metropolitan area; **Rural**, Nonmetropolitan counties not adjacent to a metropolitan area; **Unknown**, Unknown/missing/no match/Not 1990-2017.

&**SMR**, standardized mortality ratio: Compared with the suicide rates of the general US population based on the Centers for Disease Control and Prevention's Web－based Injury Statistics Query and Reporting System (1981－2017).

* P<0.05, ** P<0.01, *** P<0.001.

We subsequently analyzed the changes in the SMR of suicided patients from 1975 to 2017. Because the US Centers for Disease Control and Prevention did not provide data on the suicide rate of the general population from 1975 to 1980, we used the suicide rate of the population from 1981 to 1983 to adjust the suicide rate of patients with SCC between 1975 and 1980.8 It was found that the suicide SMR of US SCC patients fluctuated between 3 and 6, and was higher among those who suicided between 2011 and 2017. The changes in the SMR for suicide in US SCC patients are shown in Figure 2.

Figure 2

There were a total of 1157 suicides among adults with SCC in the United States between 1975 and 2017. From the perspective of gender distribution, suicide patients are mainly male, accounting for about 86.3%. The median time to suicide was 27.5 months for male patients and 55 months for female patients. It showed that male patients were more likely to commit suicide than females. In terms of the distribution of cancer types, the suicide patients were mainly lung cancer (250, 21.6%), laryngeal

cancer (185, 16.0%), tongue cancer (123, 10.6%) and oral cancer (101, 8.7%). The median time to suicide in patients with various major tumors was 10.5 months for lung cancer, 44 months for laryngeal cancer, 32 months for tongue cancer, and 73 months for oral cancer. The median time of suicidal patients was 30 months, which was higher than that of non-suicidal patients. The gender distribution and median time to suicide of SCC suicide patients in the United States are shown in Figure 3.

Figure 3

Factors associated with suicide

Univariate analyses showed that the factors associated with a high risk of suicide in patients with SCC were being male (vs female: HR=6.00, 95% CI=5.07–7.11, P<0.001), older at the diagnosis (40–49 vs ≤39 years: HR=1.60, 95% CI=1.19–2.18, P<0.001; 50–59 vs ≤39 years: HR=2.22, 95% CI=1.69–2.92, P<0.001; 60–69 vs ≤39 years: HR=2.90, 95% CI=2.21– 3.79, P<0.001; 70–79 vs ≤39 years: HR=3.35, 95% CI=2.54–4.43, P<0.001; ≥80 vs ≤39 years: HR=2.92, 95% CI=2.10–4.06, P<0.001), and white (vs black, HR=2.77, 95% CI=2.05–3.73, P<0.001), having a higher histological grade (grade II vs grade I: HR=1.45, 95% CI=1.19–1.77, P<0.001; grade III vs grade I: HR=1.34, 95% CI=1.09–1.65, P=0.006; grade IV vs grade I: HR=1.70, 95% CI=1.06–2.71, P=0.028) and primary cancer (vs nonprimary cancer: HR=1.17, 95% CI=1.03–1.32, P=0.013), and the histological classification (SCC vs PC: HR=3.33, 95% CI=2.51–4.42, P<0.001; OC vs PC: HR=3.76, 95% CI=2.11– 6.70, P<0.001). The factors associated with a lower risk of patient suicide were the year of diagnosis (1995–2004 vs 1975–1984: HR=0.71, 95% CI=0.60–0.83, P<0.001; 2005–2017 vs 1975–1984: HR=0.69, 95% CI=0.58–0.82, P<0.001), being Latino (vs non-Latin American: HR=0.46, 95% CI=0.32–0.68, P<0.001), and receiving surgery (vs no surgery: HR=0.59, 95% CI=0.52–0.66, P<0.001). Multivariate Cox regression analyses showed that the factors related to a high risk of suicide in patients with SCC were being male (vs female: HR=5.36, 95% CI=4.51–6.38, P<0.001), older at the diagnosis (70–79 vs ≤39 years: HR=1.46, 95% CI=1.09–2.08, P=0.012; ≥80 vs ≤39 years: HR=1.48, 95% CI=1.05–2.08, P=0.025), and white (vs black: HR=2.97, 95% CI=2.20–4.02, P<0.001), having a higher histological grade (grade II vs grade I: HR=1.54, 95% CI=1.26–1.87, P<0.001; grade III vs grade I: HR=1.42, 95% CI=1.15– 1.76, P<0.001; grade IV vs grade I: HR=1.65, 95% CI=1.03–2.66, P=0.039) and primary cancer (vs non-primary cancer: HR=1.33, 95% CI=1.17–1.50, P<0.001), and the histological classification (SCC vs PC: HR=1.95, 95% CI=1.45–2.62, P<0.001; OC vs PC: HR=2.21, 95% CI=1.22–3.99, P=0.009). The factors associated with a low risk of patient suicide were being Latino (vs non-Latin American: HR=0.58, 95% CI=0.40–0.85, P<0.001), receiving surgery (vs not performed: HR=0.65, 95% CI=0.57–0.74, P<0.001), and having a higher family income (US$ 75,000 + vs <US$ 50,000: HR=0.71, 95% CI=0.51–0.99, P=0.047). The risk factors related to suicide in US SCC patients are listed in Table 3. A Cox survival regression analysis showed that male patients with SCC had a higher risk of suicide than did female

patients with SCC (eFigure 5 in the Supplement).

Table 3. Univariable and multivariable analysis for suicide of leukemia patients

Variables	Univariable analysis		Multivariable analysis	
	HR(95%CI)	*P*	HR(95%CI)	*P*
Year of dignosis				
1975-1984	Reference		Reference	
1985-1994	0.89(0.76-1.04)	0.132	1.04(0.87-1.24)	0.68
1995-2004	0.71(0.60-0.83)	<0.001***	0.97(0.74-1.28)	0.853
2005-2017	0.69(0.58-0.82)	<0.001***	0.78(0.59-1.03)	0.078
Sex				
Female	Reference		Reference	
Male	6.00(5.07-7.11)	<0.001***	5.36(4.51-6.38)	<0.001***
Age at diagnosis				
≤39	Reference		Reference	
40-49	1.61(1.19-2.18)	0.002**	0.93(0.68-1.27)	0.656
50-59	2.22(1.69-2.92)	<0.001***	0.97(0.72-1.29)	0.814
60-69	2.90(2.21-3.79)	<0.001***	1.20(0.90-1.59)	0.21
70-79	3.35(2.54-4.43)	<0.001***	1.46(1.09-2.08)	0.012**
≥80	2.92(2.10-4.06)	<0.001***	1.48(1.05-2.08)	0.025*
Race				
Black	Reference		Reference	
White	2.77(2.05-3.73)	<0.001***	2.97(2.20-4.02)	<0.001***
Other	1.53(1.01-2.31)	0.044*	1.84(1.20-2.82)	0.005**
Unknown	-	-	-	-
Race Latino				
Non-Latino	Reference		Reference	
Latino	0.46(0.32-0.68)	<0.001***	0.58(0.40-0.85)	<0.001***
Grade				
Grade I	Reference		Reference	
Grade II	1.45(1.19-1.77)	<0.001***	1.54(1.26-1.87)	<0.001***
Grade III	1.34(1.09-1.65)	0.006**	1.42(1.15-1.76)	<0.001***
Grade IV	1.70(1.06-2.71)	0.028*	1.65(1.03-2.66)	0.039*
Unknown	0.96(0.79-1.18)	0.723	1.28(1.04-1.57)	0.018*
Surgery performed				
No	Reference		Reference	
Yes	0.59(0.52-0.66)	<0.001***	0.65(0.57-0.74)	<0.001***
Unkonwn	0.70(0.45-1.10)	0.121	0.54(0.35-0.85)	0.008**
Primary diaeases				
No	Reference		Reference	
Yes	1.17(1.03-1.32)	0.013*	1.33(1.17-1.50)	<0.001***

Variables	Univariable analysis		Multivariable analysis	
	HR(95%CI)	*P*	HR(95%CI)	*P*
Household income				
<$50,000	Reference		Reference	
$50,000-$74,999	1.00(0.76-1.32)	0.993	0.93(0.69-1.26)	0.629
$75,000+	0.85(0.64-1.13)	0.254	0.71(0.51-0.99)	0.047*
Unkonwn	1.31(1.01-1.72)	0.044*	1.01(0.49-2.11)	0.976
Living area#				
Large city	Reference		Reference	
Medium city	0.82(0.66-1.01)	0.067	0.79(0.63-0.98)	0.032*
Small city	1.05(0.77-1.42)	0.772	0.85(0.62-1.17)	0.326
Suburbs	0.96(0.71-1.31)	0.808	0.73(0.53-1.01)	0.058
Rural	1.06(0.78-1.44)	0.699	0.79(0.56-1.11)	0.169
Unkonwn	1.33(1.17-1.53)	<0.001***	1.00(0.52-1.92)	0.992
Radiotherapy				
No/Unknown	Reference		Reference	
Yes	0.94(0.84-1.05)	0.280	0.95(0.84-1.07)	0.381
Chemotherapy				
No/Unknown	Reference		Reference	
Yes	0.98(0.86-1.12)	0.772	0.98(0.85-1.12)	0.750

#**Large city**, Counties in metropolitan areas ge 1 million pop; **Medium city**, Counties in metropolitan areas of 250,000 to 1 million pop; **Small city**, Counties in metropolitan areas of lt 250 thousand pop; **Suburbs**, Nonmetropolitan counties adjacent to a metropolitan area; **Rural**, Nonmetropolitan counties not adjacent to a metropolitan area; **Unknown**, Unknown/missing/no match/Not 1990-2017.

* P<0.05, ** P<0.01, *** P<0.001.

Discussion

This study found that the suicide rate of patients with SCC in the US was higher than that in the general population,[8] which is similar to the results of previous studies of the suicide rates of cancer patients in the US[11,21,22] and many other countries, including the UK, Italy, Estonia, Sweden, and Denmark.[3,23–26] Our analyses revealed that the factors associated with a high risk of suicide in SCC patients include being male, older at the diagnosis, and white, and having a higher histological grade and not receiving surgery.

Males accounted for 59.9% of the US patients with SCC in this study. The number of patients who suicided or died of another cause was higher for males than females in each year from 1975 to 2017, with male suicided patients accounting for 86.2% of the total (Table 1, eFigure 2, and eFigure 3 in the Supplement). The death rate during each year of the analysis was also higher for males than for females (eFigure 3 in the Supplement). Further analysis showed that the suicide rate for patients with SCC in the US was 90.42 per 100,000 person-years among males (SMR=4.61, 95% CI=4.34–4.92) and 13.41 per 100,000 person-years among females (SMR=2.61, 95% CI=2.22–3.04) (Table 1). The risk of suicide was markedly higher in male than female patients (HR=6.00, 95% CI=5.07–7.11) (Table 3). Other studies have also found that male cancer patients are a high-risk group for suicide, which may be related to male patients suffering more social pressures, family burdens, and their own psychological problems.[18,27,28]

Most of the patients with SCC were older than 50 years (85.7%). Males aged 55-79 years predominated among patients who suicided or died of another cause, while females younger than 75 years predominated among alive patients (eFigure 2 in the Supplement). Compared with patients younger than 39 years, elderly patients exhibited a higher suicide rate (HR>2.5, P<0.001) (Table 3). Table 2 indicates that the suicide rate of the patients gradually increased with age. Previous studies have also found the suicide rate to be significantly higher in elderly cancer patients than in the general population.[9,21] The high rate of suicide among elderly SCC cancer patients could be related to various factors, including more concomitant diseases, lower disease resistance, lower quality of life, loneliness, and depression.[10,29–31]

Our analysis of the changes in the suicide SMR of SCC patients from 1975 to 2017 revealed that this fluctuated between 3 and 6, peaking between 2011 and 2017 at SMR>5 (Figure 2). However, the suicide rate of patients decreased over time (Figure 1). The sudden increase in the SMR after 2011 could have been due to their mortality rate before 2010 exceeding 70%, whereas the alive patients were mainly distributed after 2011 (eFigure 3 in the Supplement). At the same time, we found that the maximum survival time of patients with SCC was 515 months from 1975 to 2017, while the survival time of most patients was shorter than 12 months, and it was mainly distributed from 2011 to 2017 (eFigure 4 in the Supplement). Therefore, the total number of patient years decreased from 2011 to 2017 (eFigure 3 in the Supplement), resulting in a high value for the suicide SMR during this period.

The Cox regression analyses showed that race was a risk factor for suicide in

patients with SCC. Compared with black patients, white patients had an approximately threefold higher risk of suicide (HR=2.97, 95% CI=2.20–4.02, P<0.001) (Table 3). Meanwhile, the suicide rate of white Americans decreased over time, and that of black Americans remained at a low level. However, the suicide rates of other races fluctuated markedly (Figure 1), which might have been due to the relatively small proportion of other races in the analyzed population. It can be concluded that white Americans with SCC are a high-risk group for suicide, which is consistent with previous findings for other cancer patients in the US.[30–32] The variations in suicide rates between different racial groups of SCC patients in the US might be related to variations in culture, religious beliefs, quality of life, mental health, and economic conditions.[28,30,33]

We also found that patients with SCC of different histological grades had different suicide rates, with this being highest in grade IV (SMR=6.24, 95% CI=4.07-10.30) (Table 2). The suicide risk of patients with histological grades higher than grade I increased to varying degrees (overall HR>1.40) (Table 3). Although the suicide rate of patients with different histological grades trended downward each year, the annual suicide rate of grade IV patients fluctuated greatly (Figure 1), which might be related to their small proportion (1.5%). We subsequently classified the US SCC patients based on morphology codes into PC, SCC, and OC, which revealed that SCC constituted the highest proportion of patients in the US (93.0%). Compared with PC patients, the suicide risks in SCC and OC patients were 1.95-fold (95% CI=1.45–2.62, P<0.001) and 2.21-fold (95% CI=2.21–3.99, P<0.001) higher, respectively (Table 3). The risk of suicide was higher in patients with primary cancer than in those with nonprimary cancer (HR=1.33, 95% CI=1.17–1.50, P<0.001) (Table 3). Different types of cancer are generally associated with different rates of disease progression and different prognoses, with a higher degree of malignancy associated with faster disease progression and a worse prognosis.[30] Studies have found that cancers with poor prognoses are often accompanied by serious psychological problems such as loneliness and depression, which in turn increase the risk of suicide.[29,34] Similarly, the present patients who did receive surgery had a lower suicide risk (HR=0.65, 95% CI=0.57–0.74, P<0.001) (Table 3), which might be related to the better prognosis of patients after they receive surgery. The above results indicate that patients with SCC with a higher histological grade and degree of malignancy are at high risk of suicide.

Multiple studies have found cancer patients to be more likely to have depression and other psychological problems than the general population, and also have a higher risk of suicide.[29,30,35] Suicide is one cause of death in cancer patients that is potentially preventable.[36] Suicide is a complex behavior and is affected by many factors, including psychological factors, religious beliefs, and family support. Our results showed that compared with the general population,[37,38] patients with SCC in the US have a higher suicide rate. Being male, white, and older at the diagnosis, and having a higher histological grade were found to be factors contributing to a high risk of suicide. Preventing and reducing suicide in patients with SCC requires a greater focus on high-risk populations and the risk of depression being identified in psychiatric assessments of patients with SCC, such as using the Baker Depression

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Scale.[39] Actively improving the treatment plan and quality of life of cancer patients, and strengthening the care and communication of people at a high risk of cancer could reduce the psychological burden of these patients and so reduce their risk of suicide.[40]

Conclusions

This study found that the suicide rate of patients with SCC in the US has decreased over the past few decades. Compared with the general population, patients with SCC in the United States have a higher risk of suicide. The independent risk factors for suicide in patients with SCC included being male, older at the diagnosis, white, and having a higher histological grade and not receiving surgery. Clinicians can use the findings of this research to evaluate the suicide risk in individual patients with SCC. Effective intervention measures should be applied to the identified high-risk population in order to reduce their suicide rate.

Statements

Ethical approval:

The SEER database is a tumor-related database developed by the National Cancer Institute of the United States, providing research data for researchers free of charge. All patients participating in the study received the ethical approval sought by the National Cancer Institute.

Consent for publication:

Consent for publication was obtained from all participants.

Availability of data and materials:

We obtained permission to access the database after signing and submitting the SEER Research Data Agreement form via email. The data that support the findings of this study are available from SEER database but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of SEER database.

Competing interests:

None.

Funding:

None.

Author Contributions:

All authors had full access to all of the data in the study. Haohui Yu, and Jun Lyu take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Jun Lyu, Haohui Yu. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Haohui Yu, Shengru Tao, Wenli She, Min Liu. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: Haohui Yu, Yayun Wu, Wenli She. Administrative, technical, or material support: Jun Lyu, Shengru Tao. All authors contributed to writing of the manuscript and approved the final version.

Acknowledgements:

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Figure legends

Figure 1. The distribution of suicide rate in patients with squamous cell carcinoma.

Figure 2. Standardized mortality ratio of suicide for squamous cell carcinoma patients (1975–2017).

Figure 3. Distribution of median time to suicide for squamous cell carcinoma patients (1975–2017).

Figure 1. The distribution of suicide rate in patients with squamous cell carcinoma.
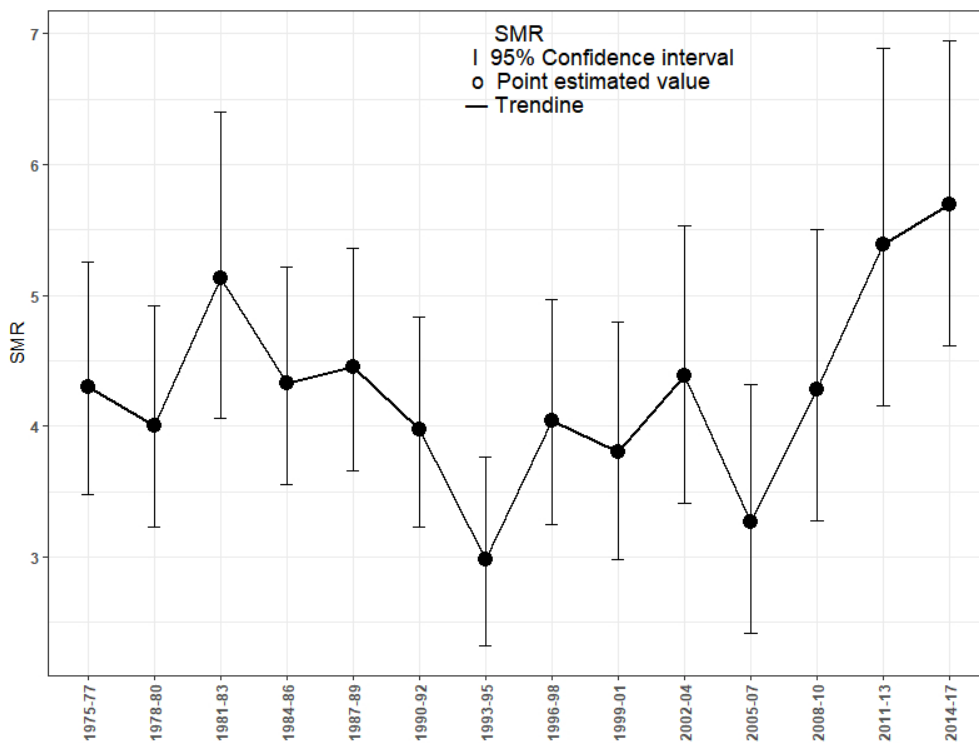
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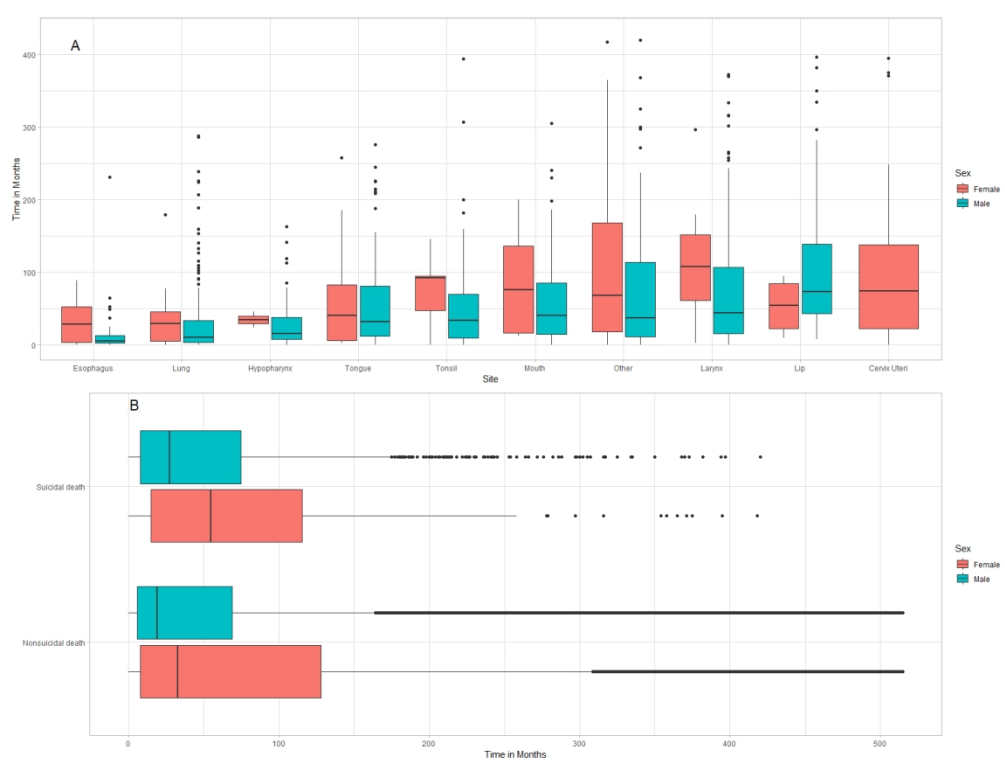
Figure 2. Standardized mortality ratio of suicide for squamous cell carcinoma patients (1975–2017).

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Distribution of median time to suicide for squamous cell carcinoma patients (1975–2017).

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Analysis of Suicide Risk in Adult US Patients with Squamous Cell Carcinoma: a Retrospective Study Based on the Surveillance, Epidemiology, and End Results Database
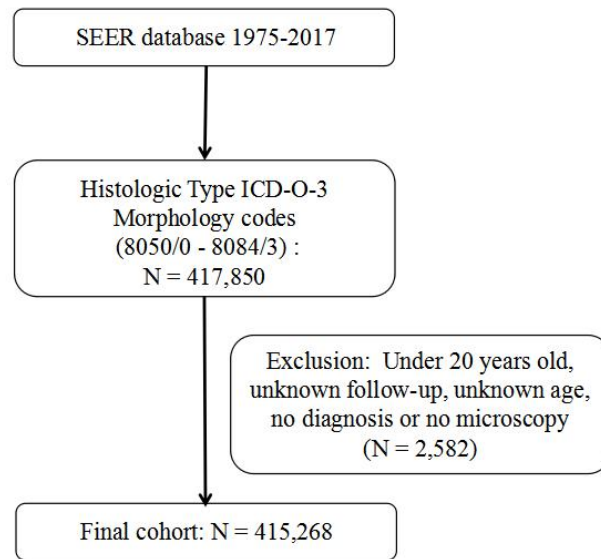
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eFigure legends

eFigure 1. The flow diagram of squamous cell carcinoma patients selection.

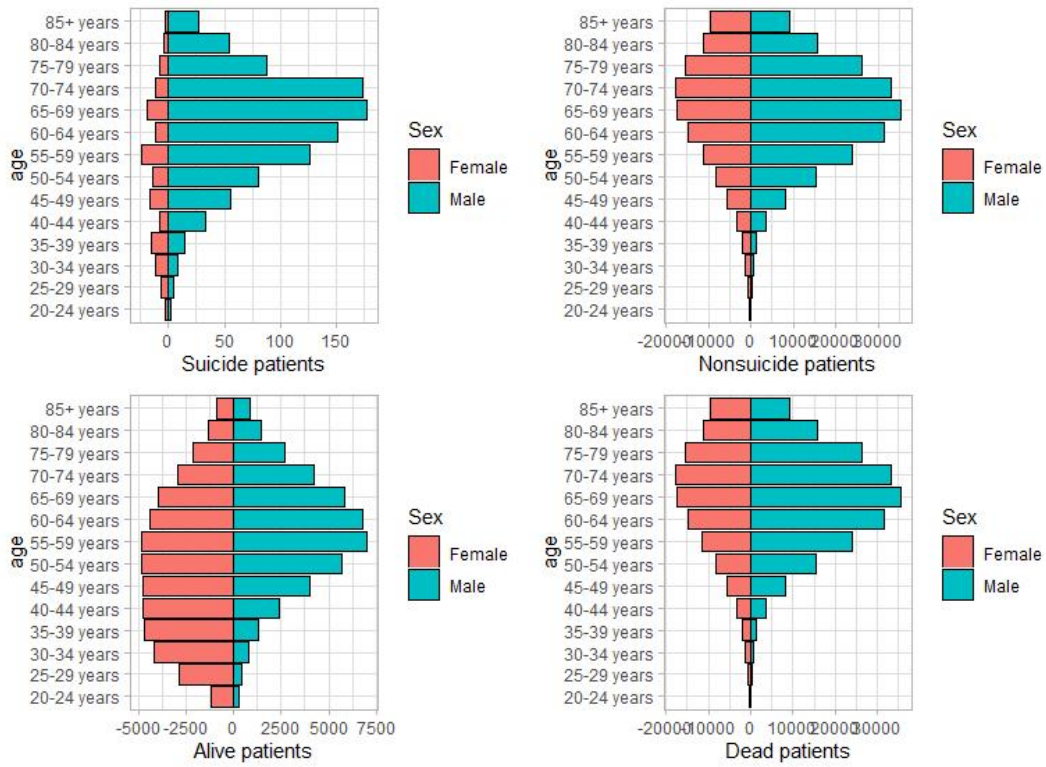eFigure 2. The distribution of patients with squamous cell carcinoma by age.

eFigure 3. The distribution of patients with squamous cell carcinoma by year.

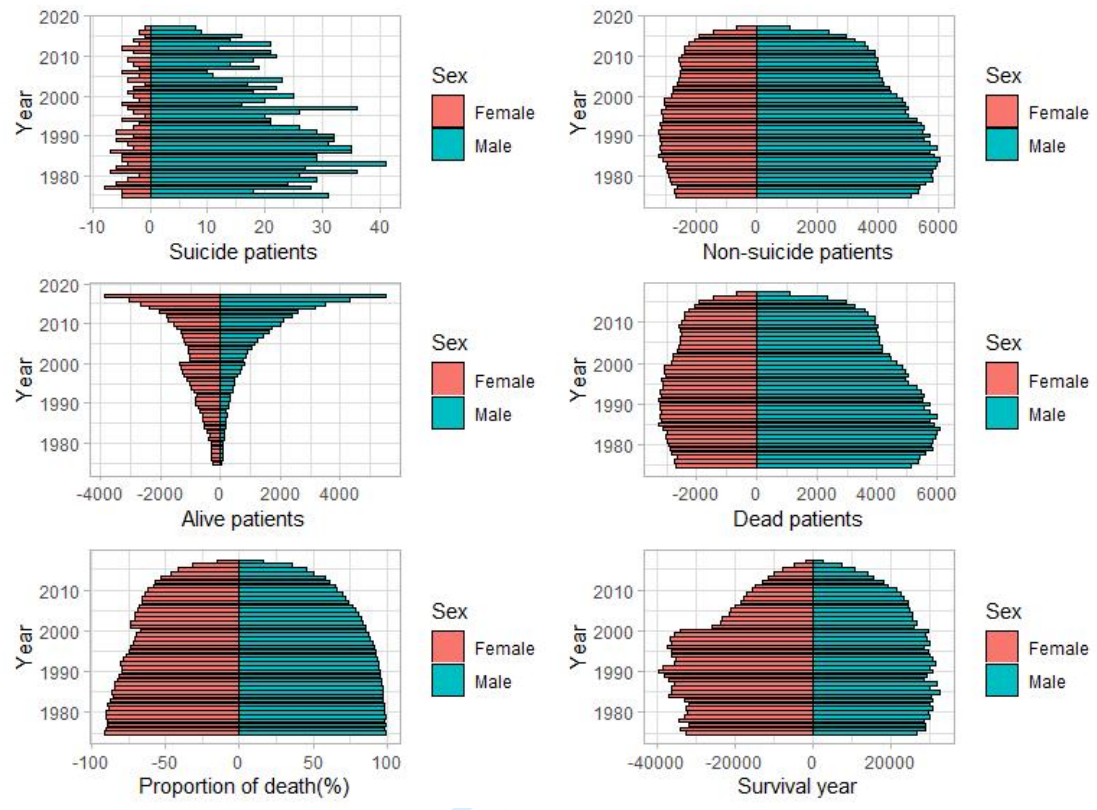eFigure 4. The distribution of survival months of patients with squamous cell carcinoma in different years.

eFigure 5. Comparison chart of survival curves of male and female squamous cell carcinoma patients.

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┌─────────────────────────────┐
│   SEER database 1975-2017   │
└─────────────────────────────┘
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┌─────────────────────────────┐
│  Histologic Type ICD-O-3    │
│     Morphology codes         │
│    (8050/0 - 8084/3) :       │
│      N = 417,850             │
└─────────────────────────────┘
                │          ┌──────────────────────────────────┐
                │          │ Exclusion:  Under 20 years old,  │
                │          │ unknown follow-up, unknown age,  │
                │          │ no diagnosis or no microscopy    │
                │          │         (N = 2,582)              │
                │          └──────────────────────────────────┘
                ▼
┌─────────────────────────────┐
│  Final cohort: N = 415,268  │
└─────────────────────────────┘
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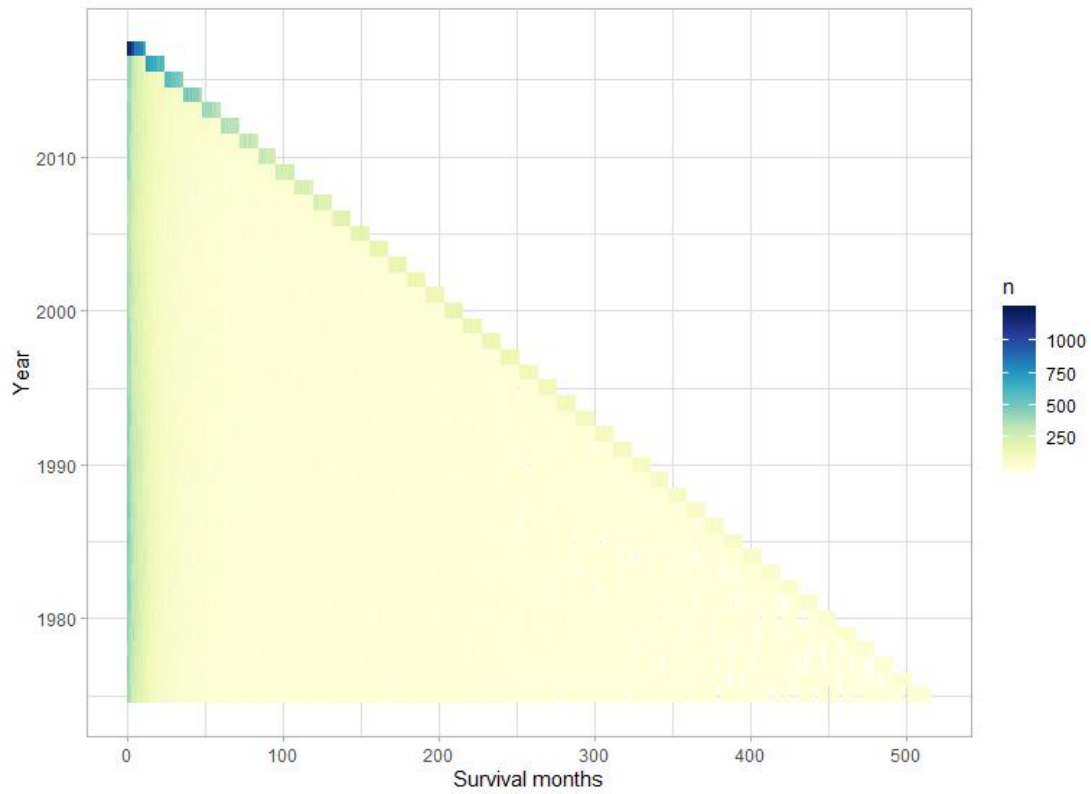
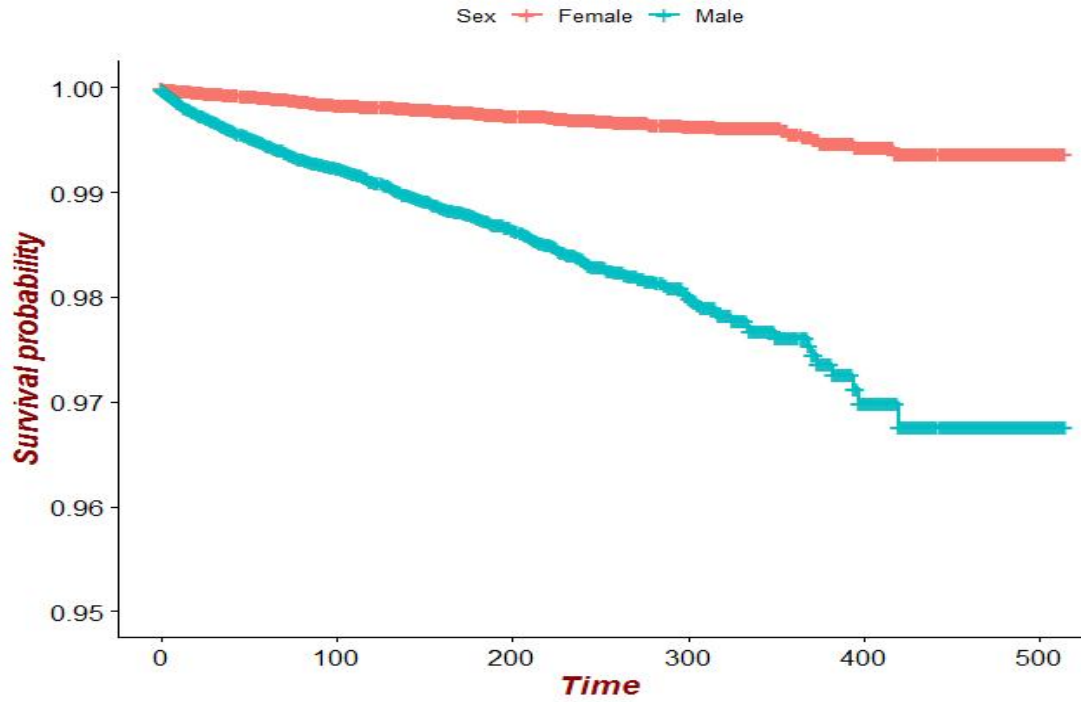eFigure 1. The flow diagram of squamous cell carcinoma patients selection.

eFigure 2. The distribution of patients with squamous cell carcinoma by age.

eFigure 3. The distribution of patients with squamous cell carcinoma by year.

eFigure 4. The distribution of survival months of patients with squamous cell

carcinoma in different years.

eFigure 5. Comparison chart of survival curves of male and female squamous cell

carcinoma patients.