

BMJ Open 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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ABSTRACT

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

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 standardised 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 1157 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% CI 3.90 to 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: HR 5.36, 95% CI 4.51 to 6.38, $p<0.001$), older at the diagnosis (70–79 vs ≤ 39 years: HR 1.46, 95% CI 1.09 to 2.08, $p=0.012$; ≥ 80 vs ≤ 39 years: HR 1.48, 95% CI 1.05 to 2.08, $p=0.025$) and white (vs black, HR 2.97, 95% CI 2.20 to 4.02, $p<0.001$) and surgery (vs not performed: HR 0.65, 95% CI 0.57 to 0.74, $p<0.001$).

Conclusions Compared with the general population, patients with SCC in the USA 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.

BACKGROUND

The WHO 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

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study found that the suicide rate of patients with squamous cell carcinoma (SCC) in the USA 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.
- ⇒ Some potentially important information that could impact suicidal behaviours is missing for patients with SCC in the Surveillance, Epidemiology and End Results 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.

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 WHO 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 USA.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 patients with cancer 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 tumour derived from the squamous epithelium. This is the general term for a class of tumours that include multiple cancers occurring in the squamous epithelium covering tissues and organs, and which are more common in the skin, mouth, oesophagus, cervix and vagina.^{15–17} According to a report by the US Centers for Disease Control and Prevention, the number of deaths from malignant tumours in the USA 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 10–34 years.⁸ The number of deaths due to SCC in the US is increasing. Yu *et al* investigated the causes of death in patients with oral and oropharyngeal SCC in the USA,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 analysing 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 (V.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 1157 who suicided. The screening procedure for patients with SCC is shown in online supplemental eFigure 1.

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, non-suicide death group and alive group. We analysed 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 χ^2 test was used to compare the suicide rates among patients in each group. The standardised mortality rate (SMR) for suicide in each group was based on the total population of the USA 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% 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 HR, and the 95% CI combined with the HR were used to identify potential risk factors for suicide. All statistical analyses were performed using R software (V.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

A total of 415 268 identified US patients with SCC in the SEER database from 1975 to 2017 included 248 816 males (59.9%). These patients comprised 1157 (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 online supplemental eFigure 2. The basic statistics of each group of SCC patients are presented in table 1.

Patient distributions according to year

We found that most of the US patients with SCC who suicided were males. The number of suicided patients

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

Variables	Overall N (%)	Suicidal death N (%)	Non-suicidal death N (%)	Alive N (%)	P value
Patients	415 268	1157 (0.3)	322 384 (77.6)	91 727 (22.1)	–
Year of diagnosis					
1975–1984	90 334 (21.8)	341 (29.5)	85 435 (26.5)	4558 (5.0)	<0.001
1985–1994	98 947 (23.8)	335 (29.0)	88 294 (27.4)	10 318 (11.2)	
1995–2004	94 368 (22.7)	253 (21.8)	75 490 (23.4)	18 625 (20.3)	
2005–2017	131 619 (31.7)	228 (19.7)	73 165 (22.7)	58 226 (63.5)	
Sex					
Female	166 452 (40.1)	159 (13.7)	118 262 (36.7)	48 031 (52.4)	<0.001
Male	248 816 (59.9)	998 (86.3)	204 122 (63.3)	43 696 (47.6)	
Age at diagnosis					
≤39	22 031 (5.3)	67 (5.8)	6211 (1.9)	15 753 (17.2)	<0.001
40–49	36 569 (8.8)	114 (9.9)	20 570 (6.4)	15 885 (17.3)	
50–59	81 389 (19.6)	246 (21.3)	58 737 (18.2)	22 406 (24.4)	
60–69	120 016 (28.9)	360 (31.1)	98 541 (30.6)	21 115 (23.0)	
70–79	104 931 (25.3)	282 (24.3)	92 561 (28.7)	12 088 (13.2)	
≥80	50 332 (12.1)	88 (7.6)	45 764 (14.2)	4480 (4.9)	
Race					
Black	50 022 (12.0)	45 (3.9)	42 014 (13.0)	7963 (8.7)	<0.001
White	339 376 (81.7)	1067 (92.2)	263 117 (81.6)	75 192 (82.0)	
Other	24 658 (5.9)	45 (3.9)	16 979 (5.3)	7634 (8.3)	
Unknown	1212 (0.3)	0	274 (0.1)	938 (1.0)	
Race Hispanic					
Hispanic	18 018 (4.3)	27 (2.3)	11 338 (3.5)	6653 (7.3)	<0.001
Non-Hispanic White	322 235 (77.6)	1040 (89.9)	252 268 (78.2)	68 927 (75.1)	
Non-Hispanic American Indian/Native	2137 (0.5)	3 (0.3)	1485 (0.5)	649 (0.7)	
Non-Hispanic Asian	22 123 (5.3)	42 (3.6)	15 253 (4.7)	6828 (7.4)	
Non-Hispanic Black	49 711 (12.0)	45 (3.9)	41 828 (13.0)	7866 (8.6)	
Non-Hispanic unknown race	1044 (0.3)	0	240 (0.1)	804 (0.9)	
Grade					
Grade I	43 008 (10.4)	134 (11.6)	31 492 (9.8)	11 382 (12.4)	<0.001
Grade II	121 959 (29.4)	398 (34.4)	94 991 (29.5)	26 570 (29.0)	
Grade III	108 530 (26.0)	271 (23.4)	89 299 (27.7)	18 960 (20.7)	
Grade IV	6169 (1.5)	20 (1.7)	5198 (1.6)	951 (1.0)	
Unknown	135 602 (32.7)	334 (28.9)	101 404 (31.5)	33 864 (36.9)	
Surgery performed					
No	207 029 (49.9)	494 (42.7)	175 871 (54.5)	30 664 (33.4)	<0.001
Yes	197 252 (47.5)	643 (55.6)	135 928 (42.2)	60 681 (66.2)	
Unknown	10 987 (2.6)	20 (1.7)	10 585 (3.3)	382 (0.4)	
Primary diseases					
No	127 948 (30.8)	362 (31.3)	102 800 (31.9)	24 786 (27.0)	<0.001
Yes	287 320 (69.2)	795 (68.7)	219 584 (68.1)	66 941 (73.0)	
Household income					
<US\$50 000	28 804 (6.9)	61 (5.3)	19 661 (6.1)	9082 (9.9)	<0.001
US\$50 000–US\$74 999	137 290 (33.1%)	331 (28.6)	95 873 (29.7)	41 094 (44.8)	
US\$75 000+	109 556 (26.4)	237 (20.5)	76 605 (23.8)	3271 (35.7)	
Unknown	139 610 (33.6)	528 (45.6)	130 245 (40.4)	8837 (9.6)	

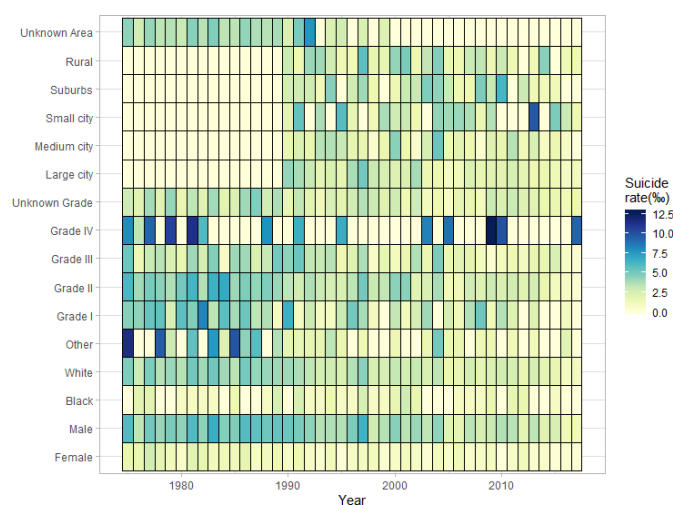
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Table 1 Continued

Variables	Overall N (%)	Suicidal death N (%)	Non-suicidal death N (%)	Alive N (%)	P value
Living area*					
Large city	159 750 (38.5)	371 (32.0)	112 206 (34.8)	47 173 (51.4)	<0.001
Medium city	56 207 (13.5)	110 (9.5)	37 366 (11.6)	18 731 (20.4)	
Small city	17 605 (4.2)	46 (4.0)	12 032 (3.7)	5527 (6.0)	
Suburbs	19 322 (4.7)	45 (3.9)	13 706 (4.3)	5571 (6.1)	
Rural	18 652 (4.5)	47 (4.1)	13 419 (4.1)	5186 (5.7)	
Unkonwn	143 732 (34.6)	538 (46.5)	133 655 (41.5)	9539 (10.4)	
Radiotherapy					
No/unknown	188 695 (45.4)	544 (47.0)	146 075 (45.3)	42 076 (45.9)	0.006
Yes	226 573 (54.6)	613 (53.0)	176 309 (54.7)	49 651 (54.1)	
Chemotherapy					
No/unknown	298 396 (71.9)	835 (72.2)	231 140 (71.7)	66 421 (72.4)	<0.001
Yes	116 872 (28.1)	322 (27.8)	91 244 (28.3)	25 306 (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, non-metropolitan counties adjacent to a metropolitan area; rural, non-metropolitan counties not adjacent to a metropolitan area; unknown, unknown/missing/no match/not 1990–2017.

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 online supplemental eFigure 3. The survival time of patients showed a right-skewed distribution, mostly concentrated at 0–12 months and around 2017 (online supplemental eFigure 4). 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.

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

The distribution of the patient suicide rates is shown in 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 to 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 to 4.92), white (SMR 4.01, 95% CI 3.77 to 4.26), Hispanic (SMR 4.17, 95% CI 2.96 to 6.55), non-Hispanic white (SMR 4.28, 95% CI 4.02 to 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 to 4.38) and PC patients (SMR 1.10, 95% CI 0.83 to 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.

We subsequently analysed 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.

Table 2 Suicide rates and SMRs among squamous cell carcinoma patients

Variables	Suicidal death	Person-years	Suicide rate per 100 000 person-years	P value	SMR	95% CI
Patients	1157	2 289 772	50.53	<0.001***	4.13	(3.90 to 4.38)
Year of diagnosis						
1975–1984	341	625 950	54.48	<0.001***	4.45	(3.97 to 4.92)
1985–1994	335	672 752	49.80	<0.001***	4.07	(3.66 to 4.55)
1995–2004	253	588 512	42.99	<0.001***	3.51	(3.09 to 3.97)
2005–2017	228	402 558	56.64	<0.001***	4.63	(4.07 to 5.3)
Sex						
Female	159	1 186 008	13.41	<0.001***	2.61	(2.22 to 3.04)
Male	998	1 103 764	90.42	<0.001***	4.61	(4.34 to 4.92)
Age at diagnosis						
≤39	67	383 965	17.45	0.006**	2.06	(1.57 to 2.58)
40–49	114	374 125	30.47	<0.001***	1.77	(1.47 to 2.14)
50–59	246	535 626	45.93	<0.001***	2.55	(2.25 to 2.9)
60–69	360	551 128	65.32	<0.001***	4.49	(4.05 to 4.99)
70–79	282	338 607	83.28	<0.001***	5.45	(4.81 to 6.09)
≥80	88	106 321	82.77	<0.001***	4.55	(3.71 to 5.71)
Race						
Black	45	207 006	21.74	<0.001***	3.99	(2.98 to 5.47)
Other	45	152 299	29.55	<0.001***	4.21	(2.98 to 5.47)
Unknown	0	9908	0.00	0.271	–	–
White	1067	1 920 671	55.55	<0.001***	4.01	(3.77 to 4.26)
Race Latino						
Non-Latino	1130	2 172 603	52.01	<0.001***	4.25	(4.00 to 4.5)
Latino	27	117 169	23.04	<0.001***	1.88	(1.27 to 2.81)
Race Hispanic						
Hispanic	27	117 169	23.04	<0.001***	4.17	(2.96 to 6.55)
Non-Hispanic American Indian/Native	3	14 066	21.33	0.276	1.59	(0.30 to 4.38)
Non-Hispanic Asian	42	135 956	30.89	<0.001***	2.30	(1.68 to 3.15)
Non-Hispanic Black	45	205 387	21.91	<0.001***	1.63	(1.17 to 2.15)
Non-Hispanic Unknown Race	0	9218	0	0.288	–	–
Non-Hispanic White	1040	1 808 088	57.52	<0.001***	4.28	(4.02 to 4.55)
Grade						
Grade I	134	336 671	39.80	<0.001***	3.25	(2.74 to 3.87)
Grade II	398	612 369	64.99	<0.001***	5.31	(4.8 to 5.85)
Grade III	271	432 004	62.73	<0.001***	5.13	(4.52 to 5.76)
Grade IV	20	26 183	76.38	<0.001***	6.24	(4.07 to 10.30)
Unknown	334	882 545	37.85	<0.001***	3.09	(2.77 to 3.44)
Surgery performed						
No	494	589 965	83.73	<0.001***	6.84	(6.27 to 7.49)
Yes	643	1 662 394	38.68	<0.001***	3.16	(2.93 to 3.42)
Unknown	20	37 412	53.46	<0.001***	4.37	(2.44 to 6.18)
Primary diseases						
No	362	798 353	45.34	<0.001***	3.70	(3.32 to 4.09)
Yes	795	1 491 419	53.30	<0.001***	4.35	(4.05 to 4.66)
Household income						
<US\$50 000	61	112 076	54.43	<0.001***	4.45	(3.33 to 5.6)

Continued

Table 2 Continued

Variables	Suicidal death	Person-years	Suicide rate per 100 000 person-years	P value	SMR	95% CI
US\$50 000–US\$74 999	331	650 167	50.91	<0.001***	4.16	(3.7 to 4.61)
US\$75 000+	237	566 038	41.87	<0.001***	3.42	(3.01 to 3.9)
Unkonwn	528	961 490	54.91	<0.001***	4.49	(4.1 to 4.87)
Living area [#]						
Large city	371	750 776	49.42	<0.001***	4.24	(3.8 to 4.67)
Medium city	110	271 574	40.50	<0.001***	3.47	(2.83 to 4.14)
Small city	46	90 809	50.66	<0.001***	4.34	(3.06 to 5.58)
Suburbs	45	95 676	47.03	<0.001***	3.02	(2.19 to 4.01)
Rural	47	89 864	52.30	<0.001***	3.36	(2.47 to 4.46)
Unkonwn	538	991 072	54.28	<0.001***	3.49	(3.20 to 3.80)
Radiotherapy						
No/unknown	544	1 039 336	52.34	<0.001***	4.28	(3.93 to 4.66)
Yes	613	1 250 436	49.02	<0.001***	4.01	(3.7 to 4.34)
Chemotherapy						
No/unknown	835	1 638 816	50.95	<0.001***	4.16	(3.88 to 4.45)
Yes	322	650 956	49.47	<0.001***	4.04	(3.6 to 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 It 250 thousand pop; suburbs, non-metropolitan counties adjacent to a metropolitan area; rural, non-metropolitan counties not adjacent to a metropolitan area; unknown, unknown/missing/no match/not 1990–2017. 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.
SMR, standardised mortality rate.

There were a total of 1157 suicides among adults with SCC in the USA 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 tumours 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 USA are shown in 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 to 7.11, p<0.001), older at the diagnosis (40–49 vs ≤39 years: HR 1.60, 95% CI 1.19 to 2.18, p<0.001; 50–59 vs ≤39 years: HR 2.22, 95% CI 1.69 to 2.92, p<0.001; 60–69 vs ≤39 years: HR 2.90, 95% CI 2.21 to 3.79, p<0.001; 70–79 vs ≤39 years: HR 3.35, 95% CI 2.54 to 4.43, p<0.001; ≥80 vs ≤39 years: HR 2.92, 95% CI 2.10 to 4.06, p<0.001) and white (vs black, HR 2.77, 95% CI 2.05 to 3.73, p<0.001), having a higher histological grade (grade II vs grade I: HR 1.45, 95% CI 1.19 to 1.77, p<0.001; grade III vs grade I: HR 1.34, 95% CI 1.09 to 1.65, p=0.006; grade IV vs grade I: HR 1.70, 95% CI 1.06 to 2.71, p=0.028) and primary cancer (vs nonprimary cancer: HR 1.17, 95% CI 1.03 to 1.32, p=0.013) and the histological classification (SCC vs PC: HR 3.33, 95% CI 2.51 to 4.42, p<0.001; OC vs PC: HR 3.76, 95% CI 2.11 to 6.70, p<0.001). The factors associated with a lower risk of patient suicide were the year of diagnosis (1995–2004

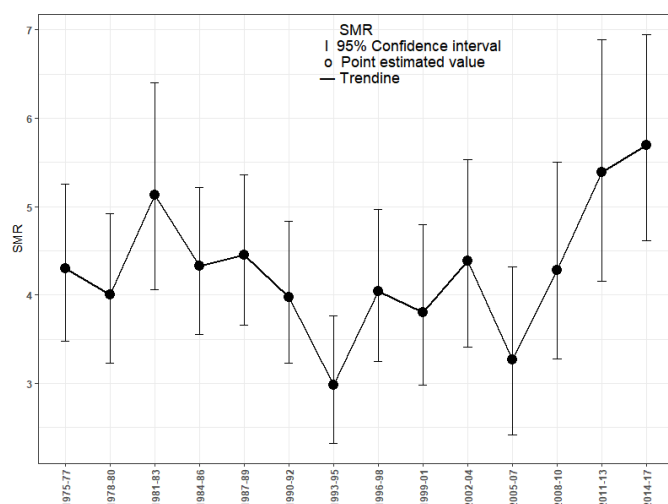


Figure 2 Standardised mortality ratio (SMR) of suicide for squamous cell carcinoma patients (1975–2017).



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

vs 1975–1984: HR 0.71, 95% CI 0.60 to 0.83, $p < 0.001$; 2005–2017 vs 1975–1984: HR 0.69, 95% CI 0.58 to 0.82, $p < 0.001$), being Latino (vs non-Latin American: HR 0.46, 95% CI 0.32 to 0.68, $p < 0.001$), and receiving surgery (vs no surgery: HR 0.59, 95% CI 0.52 to 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 to 6.38, $p < 0.001$), older at the diagnosis (70–79 vs ≤ 39 years: HR 1.46, 95% CI 1.09 to 2.08, $p = 0.012$; ≥ 80 vs ≤ 39 years: HR 1.48, 95% CI 1.05 to 2.08, $p = 0.025$) and white (vs black: HR 2.97, 95% CI 2.20 to 4.02, $p < 0.001$), having a higher histological grade (grade II vs grade I: HR 1.54, 95% CI 1.26 to 1.87, $p < 0.001$; grade III vs grade I: HR 1.42, 95% CI 1.15 to 1.76, $p < 0.001$; grade IV vs grade I: HR 1.65, 95% CI 1.03 to 2.66, $p = 0.039$) and primary cancer (vs non-primary cancer: HR 1.33, 95% CI 1.17 to 1.50, $p < 0.001$) and the histological classification (SCC vs PC: HR 1.95, 95% CI 1.45 to 2.62, $p < 0.001$; OC vs PC: HR 2.21, 95% CI 1.22 to 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 to 0.85, $p < 0.001$), receiving surgery (vs not performed: HR 0.65,

95% CI 0.57 to 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 to 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 (online supplemental eFigure 5).

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 USA^{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

Table 3 Univariable and multivariable analysis for suicide of leukaemia patients

Variables	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Year of diagnosis				
1975–1984	Reference		Reference	
1985–1994	0.89 (0.76 to 1.04)	0.132	1.04 (0.87 to 1.24)	0.68
1995–2004	0.71 (0.60 to 0.83)	<0.001***	0.97 (0.74 to 1.28)	0.853
2005–2017	0.69 (0.58 to 0.82)	<0.001***	0.78 (0.59 to 1.03)	0.078
Sex				
Female	Reference		Reference	
Male	6.00 (5.07 to 7.11)	<0.001***	5.36 (4.51 to 6.38)	<0.001***
Age at diagnosis				
≤39	Reference		Reference	
40–49	1.61 (1.19 to 2.18)	0.002**	0.93 (0.68 to 1.27)	0.656
50–59	2.22 (1.69 to 2.92)	<0.001***	0.97 (0.72 to 1.29)	0.814
60–69	2.90 (2.21 to 3.79)	<0.001***	1.20 (0.90 to 1.59)	0.21
70–79	3.35 (2.54 to 4.43)	<0.001***	1.46 (1.09 to 2.08)	0.012**
≥80	2.92 (2.10 to 4.06)	<0.001***	1.48 (1.05 to 2.08)	0.025*
Race				
Black	Reference		Reference	
White	2.77 (2.05 to 3.73)	<0.001***	2.97 (2.20 to 4.02)	<0.001***
Other	1.53 (1.01 to 2.31)	0.044*	1.84 (1.20 to 2.82)	0.005**
Unknown	–	–	–	–
Race Latino				
Non-Latino	Reference		Reference	
Latino	0.46 (0.32 to 0.68)	<0.001***	0.58 (0.40 to 0.85)	<0.001***
Grade				
Grade I	Reference		Reference	
Grade II	1.45 (1.19 to 1.77)	<0.001***	1.54 (1.26 to 1.87)	<0.001***
Grade III	1.34 (1.09 to 1.65)	0.006**	1.42 (1.15 to 1.76)	<0.001***
Grade IV	1.70 (1.06 to 2.71)	0.028*	1.65 (1.03 to 2.66)	0.039*
Unknown	0.96 (0.79 to 1.18)	0.723	1.28 (1.04 to 1.57)	0.018*
Surgery performed				
No	Reference		Reference	
Yes	0.59 (0.52 to 0.66)	<0.001***	0.65 (0.57 to 0.74)	<0.001***
Unkonwn	0.70 (0.45 to 1.10)	0.121	0.54 (0.35 to 0.85)	0.008**
Primary diaeases				
No	Reference		Reference	
Yes	1.17 (1.03 to 1.32)	0.013*	1.33 (1.17 to 1.50)	<0.001***
Household income				
<US\$50 000	Reference		Reference	
US\$50 000–US\$74 999	1.00 (0.76 to 1.32)	0.993	0.93 (0.69 to 1.26)	0.629
US\$75 000+	0.85 (0.64 to 1.13)	0.254	0.71 (0.51 to 0.99)	0.047*
Unkonwn	1.31 (1.01 to 1.72)	0.044*	1.01 (0.49 to 2.11)	0.976
Living area [#]				
Large city	Reference		Reference	
Medium city	0.82 (0.66 to 1.01)	0.067	0.79 (0.63 to 0.98)	0.032*

Continued

Table 3 Continued

Variables	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Small city	1.05 (0.77 to 1.42)	0.772	0.85 (0.62 to 1.17)	0.326
Suburbs	0.96 (0.71 to 1.31)	0.808	0.73 (0.53 to 1.01)	0.058
Rural	1.06 (0.78 to 1.44)	0.699	0.79 (0.56 to 1.11)	0.169
Unkonwn	1.33 (1.17 to 1.53)	<0.001***	1.00 (0.52 to 1.92)	0.992
Radiotherapy				
No/unknown	Reference		Reference	
Yes	0.94 (0.84 to 1.05)	0.280	0.95 (0.84 to 1.07)	0.381
Chemotherapy				
No/unknown	Reference		Reference	
Yes	0.98 (0.86 to 1.12)	0.772	0.98 (0.85 to 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, non-metropolitan counties adjacent to a metropolitan area; rural, non-metropolitan counties not adjacent to a metropolitan area; unknown, unknown/missing/no match/not 1990–2017.
*p<0.05, **p<0.01, ***p<0.001.

in each year from 1975 to 2017, with male suicided patients accounting for 86.2% of the total (table 1, online supplemental eFigures 2 and 3). The death rate during each year of the analysis was also higher for males than for females (online supplemental eFigure 3). Further analysis showed that the suicide rate for patients with SCC in the USA was 90.42 per 100 000 person-years among males (SMR 4.61, 95% CI 4.34 to 4.92) and 13.41 per 100 000 person-years among females (SMR 2.61, 95% CI 2.22 to 3.04) (table 1). The risk of suicide was markedly higher in male than female patients (HR 6.00, 95% CI 5.07 to 7.11) (table 3). Other studies have also found that male patients with cancer 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 (online supplemental eFigure 2). 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 patients with cancer 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 (online supplemental eFigure 3). 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 (online supplemental eFigure 4). Therefore, the total number of patient years decreased from 2011 to 2017 (online supplemental eFigure 3), 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 to 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 analysed 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 USA.^{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 to 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 USA (93.0%). Compared with PC patients, the suicide risks in SCC and OC patients were 1.95-fold (95% CI 1.45 to 2.62, $p<0.001$) and 2.21-fold (95% CI 2.21 to 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 to 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 to 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 patients with cancer 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 patients with cancer that is potentially preventable.³⁶ Suicide is a complex behaviour 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 USA 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 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 USA has decreased over the past few decades. Compared with the general population, patients with SCC in the USA 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.

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Contributors All authors had full access to all of the data in the study. HY and JL took responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: JL and HY. Acquisition, analysis or interpretation of data: all authors. Drafting of the manuscript: HY, S-RT, WS and ML. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: HY, YW and WS. Administrative, technical or material support: JL and S-RT. All authors contributed to writing of the manuscript and approved the final version. Professor Jun Lyu is responsible for the guarantor of the overall content of the article.

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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**

Supplement Online

eFigure legends

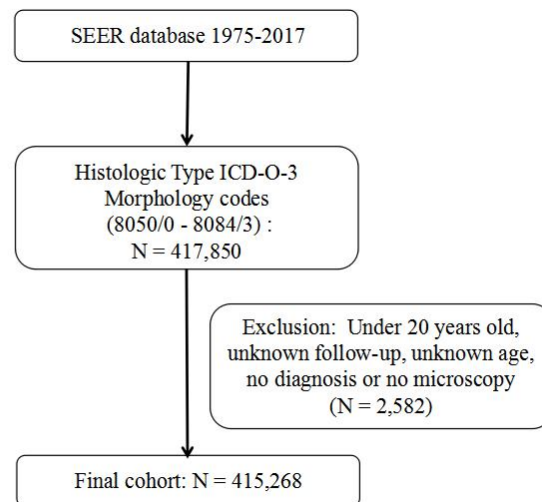
eFigure 1. The flow diagram of squamous cell carcinoma patients selection.

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

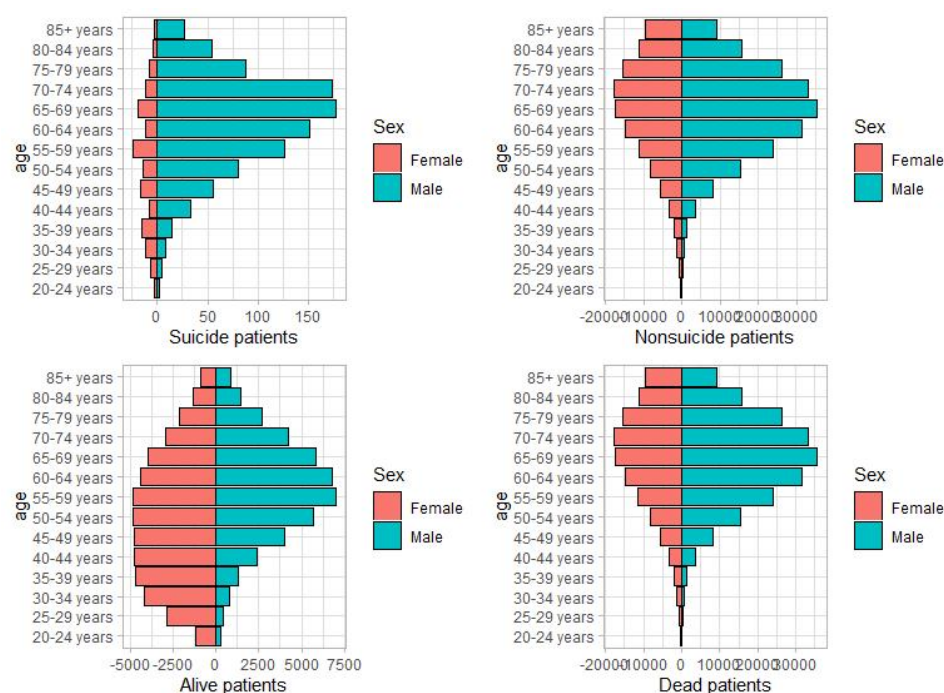
eFigure 3. The distribution of patients with squamous cell carcinoma by year.

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

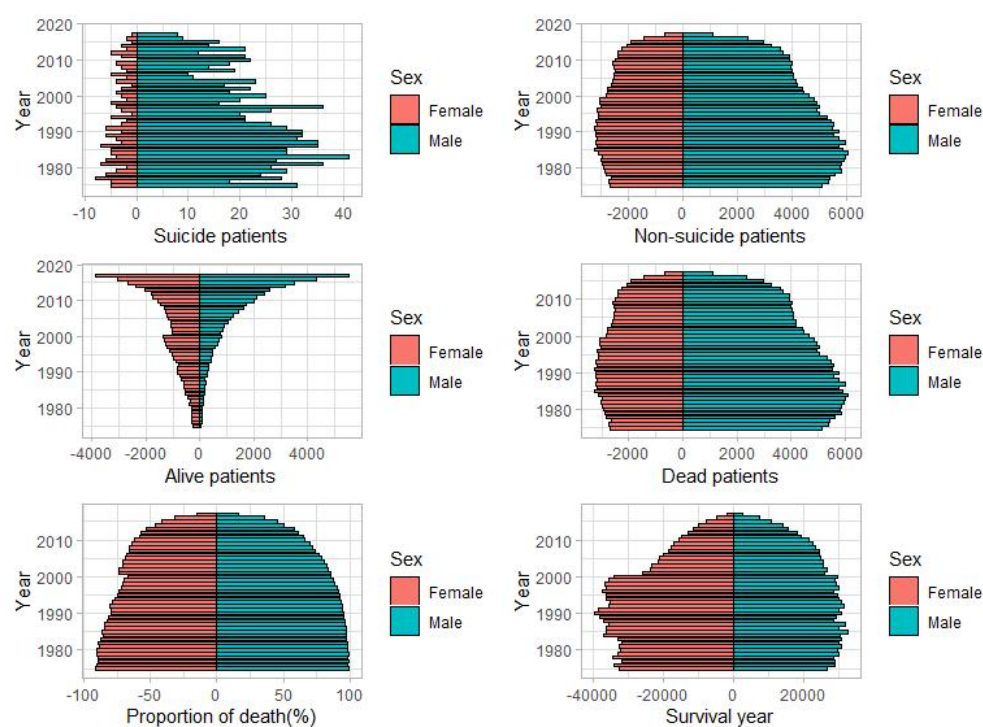
eFigure 5. Comparison chart of survival curves of male and female squamous cell carcinoma patients.



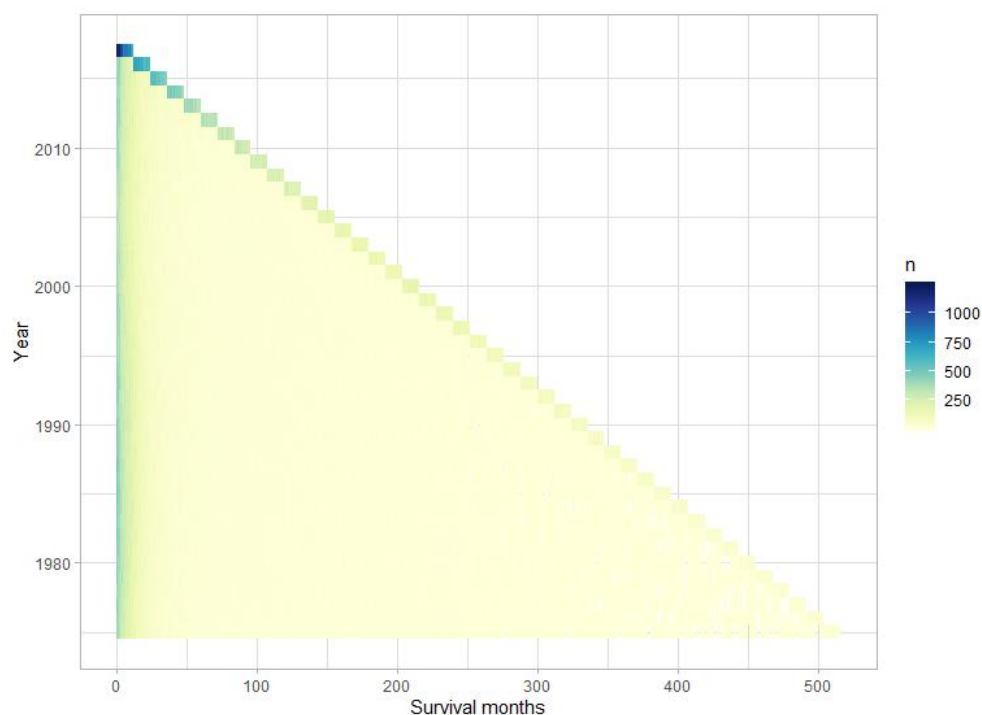
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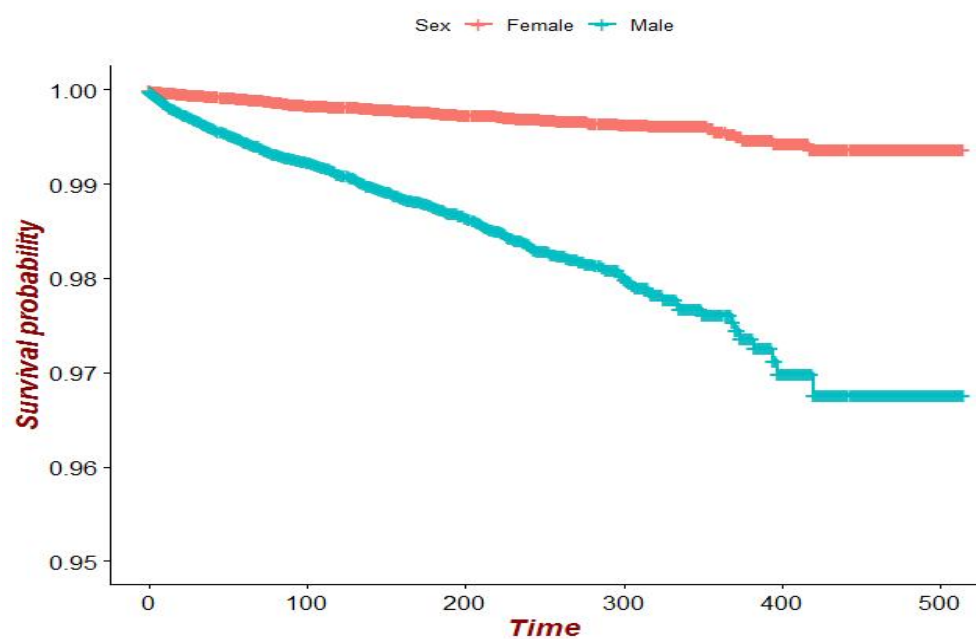
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