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 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% 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=0.025; ≥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. There were about 18.1 million new cancer patients and about 9.6 million deaths worldwide in 2018. Previous studies have shown that patients with depression and cancers with a poor prognosis have a high risk of suicide. Suicide is influenced by many factors, and the WHO has also reported that the number of suicides worldwide is increasing, with approximately 800,000 suicide deaths each year. 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. The suicide rate in the general US population was 14.78 per 100,000 people in 2018, which was higher than in other countries. Multiple studies have shown that the suicide rate is higher in cancer patients than in the general US population. 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. 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. The increasing incidence of cancer has resulted in mental and psychological problems gradually becoming a major complication experienced by cancer patients. The resulting fear of a cancer prognosis, depression and other psychological problems have gradually increased the risk of suicide. 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.

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. 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. 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, 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. 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 415268 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 $\chi^2$ 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. 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 was 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 415268 identified US patients with SCC in the SEER database from 1975 to 2017 included 248816 males (39.9%). These patients comprised 1157 (0.3%) in the suicided group, 392384 (77.6%) in the not-suicide-death group and 91727 (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                         | 415268        | 1157 (0.3)           | 322384 (77.6)            | 91727 (22.1)| –       |
| Year of diagnosis                |               |                      |                          |             |         |
| 1975–1984                        | 90334 (21.8)  | 341 (29.5)           | 85435 (26.5)             | 4558 (5.0)  | <0.001  |
| 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)| <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)| <0.001  |
| 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)  | <0.001  |
| White                            | 339376 (81.7) | 1067 (82.2)          | 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 Hispanic                    |               |                      |                          |             |         |
| Hispanic                         | 18018 (4.3)   | 27 (2.3)             | 11338 (3.5)              | 6653 (7.3)  | <0.001  |
| Non-Hispanic White               | 322235 (77.6) | 1040 (89.9)          | 252268 (78.2)            | 68927 (75.1)|         |
| Non-Hispanic American/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)| <0.001  |
| 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)| <0.001  |
| Yes                              | 197252 (47.5) | 643 (55.6)           | 135928 (42.2)            | 60681 (66.2)|         |
| Unknown                          | 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                 |               |                      |                          |             |         |
| <US$50 000                       | 28804 (6.9)   | 61 (5.3)             | 19661 (6.1)              | 9082 (9.9)  | <0.001  |
| US$50 000–US$74 999               | 137290 (33.1%)| 331 (28.6)           | 95873 (29.7)             | 41094 (44.8)|         |
| US$75 000+                       | 109556 (26.4) | 237 (20.5)           | 76605 (23.8)             | 3271 (35.7) |         |
| Unknown                          | 139610 (33.6) | 528 (45.6)           | 130245 (40.4)            | 8837 (9.6)  |         |

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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. 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 2289772 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. 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. 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           | 2289772      | 50.53                                  | <0.001*** | 4.13   | (3.90 to 4.38) |
| Year of diagnosis                             |                |              |                                        |         |        |              |
| 1975–1984                                     | 341            | 625950       | 54.48                                  | <0.001*** | 4.45   | (3.97 to 4.92) |
| 1985–1994                                     | 335            | 672752       | 49.80                                  | <0.001*** | 4.07   | (3.66 to 4.55) |
| 1995–2004                                     | 253            | 588512       | 42.99                                  | <0.001*** | 3.51   | (3.09 to 3.97) |
| 2005–2017                                     | 228            | 402558       | 56.64                                  | <0.001*** | 4.63   | (4.07 to 5.3) |
| Sex                                           |                |              |                                        |         |        |              |
| Female                                        | 159            | 1186008      | 13.41                                  | <0.001*** | 2.61   | (2.22 to 3.04) |
| Male                                          | 998            | 1103764      | 90.42                                  | <0.001*** | 4.61   | (4.34 to 4.92) |
| Age at diagnosis                              |                |              |                                        |         |        |              |
| ≤39                                           | 67             | 383965       | 17.45                                  | 0.006**  | 2.06   | (1.57 to 2.58) |
| 40–49                                         | 114            | 374125       | 30.47                                  | <0.001*** | 1.77   | (1.47 to 2.14) |
| 50–59                                         | 246            | 535626       | 45.93                                  | <0.001*** | 2.55   | (2.25 to 2.9) |
| 60–69                                         | 360            | 551128       | 65.32                                  | <0.001*** | 4.49   | (4.05 to 4.99) |
| 70–79                                         | 282            | 338607       | 83.28                                  | <0.001*** | 5.45   | (4.81 to 6.09) |
| ≥80                                           | 88             | 106321       | 82.77                                  | <0.001*** | 4.55   | (3.71 to 5.71) |
| Race                                          |                |              |                                        |         |        |              |
| Black                                         | 45             | 207006       | 21.74                                  | <0.001*** | 3.99   | (2.98 to 5.47) |
| Other                                         | 45             | 152299       | 29.55                                  | <0.001*** | 4.21   | (2.98 to 5.47) |
| Unknown                                       | 0              | 9908         | 0.00                                   | 0.271    | –      | –            |
| White                                         | 1067           | 1920671      | 55.55                                  | <0.001*** | 4.01   | (3.77 to 4.26) |
| Race Latino                                   |                |              |                                        |         |        |              |
| Non-Latino                                    | 1130           | 2172603      | 52.01                                  | <0.001*** | 4.25   | (4.00 to 4.5) |
| Latino                                        | 27             | 117169       | 23.04                                  | <0.001*** | 1.88   | (1.27 to 2.81) |
| Race Hispanic                                 |                |              |                                        |         |        |              |
| Hispanic                                      | 27             | 117169       | 23.04                                  | <0.001*** | 4.17   | (2.96 to 6.55) |
| Non-Hispanic Ameriaca/Indian Native           | 3              | 14066        | 21.33                                  | 0.276    | 1.59   | (0.30 to 4.38) |
| Non-Hispanic Asian                            | 42             | 135956       | 30.89                                  | <0.001*** | 2.30   | (1.68 to 3.15) |
| Non-Hispanic Black                           | 45             | 205387       | 21.91                                  | <0.001*** | 1.63   | (1.17 to 2.15) |
| Non-Hispanic Unknown Race                     | 0              | 9218         | 0.00                                   | 0.288    | –      | –            |
| Non-Hispanic White                            | 1040           | 1808088      | 57.52                                  | <0.001*** | 4.28   | (4.02 to 4.55) |
| Grade                                         |                |              |                                        |         |        |              |
| Grade I                                       | 134            | 336671       | 39.80                                  | <0.001*** | 3.25   | (2.74 to 3.87) |
| Grade II                                      | 398            | 612369       | 64.99                                  | <0.001*** | 5.31   | (4.8 to 5.85)  |
| Grade III                                     | 271            | 432004       | 62.73                                  | <0.001*** | 5.13   | (4.52 to 5.76) |
| Grade IV                                      | 20             | 26183        | 76.38                                  | <0.001*** | 6.24   | (4.07 to 10.30) |
| Unknown                                       | 334            | 882545       | 37.85                                  | <0.001*** | 3.09   | (2.77 to 3.44) |
| Surgery performed                             |                |              |                                        |         |        |              |
| No                                            | 494            | 589965       | 83.73                                  | <0.001*** | 6.84   | (6.27 to 7.49) |
| Yes                                           | 643            | 1662394      | 38.68                                  | <0.001*** | 3.16   | (2.93 to 3.42) |
| Unknown                                       | 20             | 37412        | 53.46                                  | <0.001*** | 4.37   | (2.44 to 6.18) |
| Primary diseases                              |                |              |                                        |         |        |              |
| No                                            | 362            | 798353       | 45.34                                  | <0.001*** | 3.70   | (3.32 to 4.09) |
| Yes                                           | 795            | 1491419      | 53.30                                  | <0.001*** | 4.35   | (4.05 to 4.66) |
| Household income                              |                |              |                                        |         |        |              |
| <US$50000                                     | 61             | 112076       | 54.43                                  | <0.001*** | 4.45   | (3.33 to 5.6)  |

Continued
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 vs 1975–2001)

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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) |
| Unknown | 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) |
| Unknown | 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 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. 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.

Figure 2  Standardised mortality ratio (SMR) of 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 USA11 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.
| 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***              |
| Unknown           | 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$50000         | Reference            |                        | Reference             |                        |
| US$50 000–US$74999| 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*                 |
| Unknown           | 1.31 (1.01 to 1.72)  | 0.044*                 | 1.01 (0.49 to 2.11)  | 0.976                  |
| Living area a     |                      |                        |                       |                        |
| Large city        | Reference            |                        | Reference             |                        |
| Medium city       | 0.82 (0.66 to 1.01)  | 0.067                  | 0.79 (0.63 to 0.98)  | 0.032*                 |
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 males than in females (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 It was also 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.9–29 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 USA might be related to variations in culture, religious beliefs, quality of life, mental health and economic conditions.28–33

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 >2.5) (table 3). 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 USA might be related to variations in culture, religious beliefs, quality of life, mental health and economic conditions.28–33
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 (95.0%). 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. 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. Similarly, the present patients who did receive surgery had a lower suicide risk (HR 0.63, 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 have 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. Suicide is one cause of death in patients with cancer that is potentially preventable. 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, 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. 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.

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.

REFERENCES

1. World Health Organization. Global health Observatory. Geneva: World Health Organization; 2018. who.int/gho/databases/en/ [Accessed 21 Jun 2018].
2. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394–424.
3. Allebeck P, Bolund C, Ringbäck G. Increased suicide rate in cancer patients. A cohort study based on the Swedish Cancer-Environment register. J Clin Epidemiol 1989;42:611–6.
4. Misono S, Weiss NS, Fann JR, et al. Incidence of suicide in persons with cancer. J Clin Oncol 2008;26:473–9.
5. Allebeck P, Bolund C. Suicides and suicide attempts in cancer patients. Psychol Med 1991;21:979–84.
6 World Health Organization. Preventing suicide: a global imperative; 2014.
7 Naghavi M, Global NM, Global Burden of Disease Self-Harm Collaborators. Global, regional, and national burden of suicide mortality 1990 to 2016: systematic analysis for the global burden of disease study 2016. BMJ 2019;364:k5560.
8 Centers for Disease Control and Prevention. Injury statistics query and reporting system. Available: https://www.cdc.gov/injury/wisqars/fatal.html.
9 Yu O, Zheng W, Zhu W, et al. Risk factors associated with suicide among kidney cancer patients: a surveillance, epidemiology, and end results analysis. Cancer Med 2019;8:5386–96.
10 Gaitanidis A, Alevizakos M, Pitiakoudis M, et al. Trends in incidence and associated risk factors of suicide mortality among breast cancer patients. Psychooncology 2018;27:1450–6.
11 Rahouma M, Kamei M, Abouraarab A, et al. Lung cancer patients have the highest malignancy-associated suicide rate in USA: a population-based analysis. Ercancermedicalsience 2018;12:859.
12 Anguiano L, Mayer DK, Piven ML, et al. A literature review of suicide in cancer patients. Cancer Nurs 2012;35:E14–26.
13 Osazuwa-Peters N, Simpson MC, Zhao L, et al. Suicide risk among cancer survivors: head and neck versus other cancers. Cancer 2018;124:4072–9.
14 Louhivuori KA, Hakama M. Risk of suicide among cancer patients. Am J Epidemiol 1979;109:59–65.
15 Waldman A, Schmuits C. Cutaneous squamous cell carcinoma. Hematol Oncol Clin North Am 2019;33:1–12.
16 Thomson PJ. Perspectives on oral squamous cell carcinoma prevention-proliferation, position, progression and prediction. J Oral Pathol Med 2018;47:803–7.
17 Kallini JR, Hamed N, Khachemoune A. Squamous cell carcinoma of the skin: epidemiology, classification, management, and novel trends. Int J Dermatol 2015;54:130–40.
18 Yu G-P, Mehta V, Branovan D, et al. Non-cancer-related deaths from suicide, cardiovascular disease, and pneumonia in patients with oral cavity and oropharyngeal squamous carcinoma. Arch Otolarangol Head Neck Surg 2012;138:25–32.
19 Yu H, Cai K, Huang Y, et al. Risk factors associated with suicide among leukemia patients: a surveillance, epidemiology, and end results analysis. Cancer Med 2020;9:9006–17.
20 Breslow NE, Day NE. Statistical methods in cancer research. Volume II—The design and analysis of cohort studies, IARC Sci Publ 1987;82:1–406.
21 Zaorsky NG, Zhang Y, Tuanquin L, et al. Suicide among cancer patients. Nat Commun 2019;10:207.
22 Shen J, Zhu M, Li S, et al. Incidence and risk factors for suicide death among Kaposi’s sarcoma patients: a surveillance, epidemiology, and end results analysis. Med Sci Monit 2020;26:e920711.
23 Henson KE, Brock R, Charnock J, et al. Risk of suicide after cancer diagnosis in England. JAMA Psychiatry 2019;76:51–60.
24 Crocetti E, Arniati S, Acaciu S, et al. High suicide mortality soon after diagnosis among cancer patients in central Italy. Br J Cancer 2014;109:2479–85.
25 Innos K, Rahu K, Rahu M, et al. Suicides among cancer patients in Estonia: a population-based study. Eur J Cancer 2003;39:2223–8.
26 Storm HH, Christensen N, Jensen OM. Suicides among Danish patients with cancer: 1971 to 1986. Cancer 1992;69:1509–12.
27 Kendall WS. Suicide and cancer: a gender-comparative study. Ann Oncol 2007;18:381–7.
28 Siracuse BL, Gorgy G, Ruskin J, et al. What is the incidence of suicide in patients with bone and soft tissue cancer? Suicide and Sarcoma. Clin Orthop Relat Res 2017;475:1439–45.
29 Zhou H, Xian W, Zhang Y, et al. Trends in incidence and associated risk factors of suicide mortality in patients with non-small cell lung cancer. Cancer Med 2018;7:1416–55.
30 Kam D, Salib A, Gorgy G, et al. Incidence of suicide in patients with head and neck cancer. JAMA Otolaryngol Head Neck Surg 2015;141:1075–81.
31 Yang J, He G, Chen S, et al. Incidence and risk factors for suicide death in male patients with genital-system cancer in the United States. Eur J Surg Oncol 2019;45:1069–76.
32 Saad AM, Gad MM, Al-Husseini MJ, et al. Suicidal death within a year of a cancer diagnosis: a population-based study. Cancer 2019;125:972–9.
33 Anderson C, Park EM, Rosenstein DL, et al. Suicide rates among patients with cancers of the digestive system. Psychooncology 2018;27:2277–86.
34 Simpson WG, Klaassen Z, Jen RP, et al. Analysis of suicide risk in patients with penile cancer and review of the literature. Clin Genitourin Cancer 2018;16:e257–61.
35 Pham TT, Talukder AM, Walsh NJ, et al. Clinical and epidemiological factors associated with suicide in colorectal cancer. Support Care Cancer 2019;27:617–21.
36 Samawi HH, Shaheen AA, Tang PA, et al. Risk and predictors of suicide in colorectal cancer patients: a surveillance, epidemiology, and end results analysis. Curr Oncol 2017;24:513–7.
37 Mann JJ, Metts AV. The economy and suicide. Crises 2017;38:141–6.
38 Rizzo RF. Physician-assisted suicide in the United States: the underlying factors in technology, health care and palliative medicine—Part one. Theor Med Bioeth 2000;21:277–89.
39 Klaassen Z, Goldberg H, Chandrasekar T, et al. Changing trends for suicidal death in patients with bladder cancer: a 40+ year population-level analysis. Clin Genitourin Cancer 2018;16:206–12.
40 Banyasz A, Wells-Di Gregorio SM, Gregorio SMW-D. Cancer-related suicide: a biopsychosocial-existential approach to risk management. Psychooncology 2018;27:2661–4.