

# Subsequent risk of suicide among 9,300,812 cancer survivors in US: A population-based cohort study covering 40 years of data

Qiang Liu (刘强),<sup>1</sup> Xiangyu Wang (王翔宇),<sup>1</sup> Xiangyi Kong (孔祥溢),<sup>1</sup> Zhongzhao Wang (王仲照),<sup>1</sup> Mengliu Zhu (朱梦柳), Yinpeng Ren (任胤朋), Hao Dong (董浩), Yi Fang (方仪),\* and Jing Wang (王靖)\*

Department of Breast Surgical Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China

## Summary

**Background** Large cohort studies that estimate the variation in suicide risk among cancer patients, depending on disease type and patient characteristics, are lacking. We aimed to investigate suicide risk among patients with different cancers types in the United States (US) and to identify subsets of patients at particularly high risk.

**Methods** A total of 9,300,812 cases of cancer in the Surveillance, Epidemiology, and End Results (SEER) database that were diagnosed between 1975 and 2016 were included in the study. Standardized mortality ratio (SMR) and absolute excess risk (AER) of suicide were estimated.

**Findings** From the included cases, 14,423 cancer patients were identified as having died by suicide, representing 0.26% of all deaths. We found that cancer patients had a higher risk of suicide compared with the general population, which equated to 0.8 excess deaths per 10,000 person-years. Greater suicide risk was correlated with the following: specific cancer sites, male sex, American Indian/Alaskan Native ancestry, being divorced, being uninsured, distance of metastasis, aged between 60 and 69 at diagnosis, and having a more recent diagnosis. The greatest SMR and AER were found in patients with cancers of the respiratory system, followed by those of the oral cavity and pharynx, myeloma, bones and joints, digestive system, and brain and other nervous system cancers.

**Interpretation** Suicide risk among cancer patients varies greatly and depends on both disease type and patient characteristics. A tailored clinical management should be considered for patients at a higher risk of suicide.

**Funding** Natural Science Foundation of China.

**Copyright** © 2022 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

**Keywords:** Suicide risk; Cancer patients; Epidemiology; SEER; United States

## Introduction

Approximately 19.3 million new cancer cases, as well as an estimated 10.0 million cancer deaths, occurred worldwide in 2020. Cancer incidence and mortality are increasing rapidly all over the world: cancer is the major cause of death before the age of 70 years in 112 of 183 countries.<sup>1,2,3</sup> Similarly, suicide is a leading cause of death in the majority of Western countries.<sup>4</sup> The Global Burden of Disease Study and the World Health Organization (WHO) estimate that about 800,000 people die

from suicide every year, or one person every 40 s.<sup>5,6</sup> In the United States (US), suicide is the 10th leading cause of death, and cancer patients have an even higher suicide rate than the general US population.<sup>7</sup> Previous studies have shown that, similar to the general population, sex and age are risk factors for suicide among cancer patients.<sup>7-10</sup> As cancer treatment has led to better survival rates, it is crucial to consider issues facing cancer patients, particularly their higher risk of suicide.

Thanks to initiatives by the National Cancer Institute, awareness of the psychosocial needs of patients diagnosed with cancer is increasing.<sup>11</sup> To that end, it may be helpful to determine which subgroups of cancer patients have a higher suicide risk. In 2008, Misono et al. investigated suicide risk among cancer patients using the Surveillance, Epidemiology, and End Results (SEER) database.<sup>7</sup> Data from 1973 to 2002, which

\*Corresponding authors.

E-mail addresses: [liuqiang@email.ncu.edu.cn](mailto:liuqiang@email.ncu.edu.cn) (Q. Liu), [fangyi@cicams.ac.cn](mailto:fangyi@cicams.ac.cn) (Y. Fang), [wangjing@cicams.ac.cn](mailto:wangjing@cicams.ac.cn) (J. Wang).

<sup>1</sup> These authors contributed equally to this work.

eClinicalMedicine

2022;44: 101295

Published online xxx

<https://doi.org/10.1016/j.eclinm.2022.101295>

eclinm.2022.101295

### Research in context

#### *Evidence before this study*

We searched PubMed for epidemiological studies, reviews, and guidelines published in English between January 1, 2000 and January 12, 2022, using the search terms “suicide” and “cancer.” We found several studies that investigated the association of cancer and suicide risk, but these were limited to either specific cancer sites or those that combined all cancers, not considering potential heterogeneity in the associations between various cancers and suicide. The existing evidence regarding suicide risk among cancer patients and how it changes over time remains to be understood.

#### *Added value of this study*

Overall, cancer patients in the US had a higher risk of suicide compared with the general population. We found these suicide risks varied greatly by cancer sites, as well as by patient characteristics, and that these risks have increased in more recent years. The greatest suicide risks were found in patients with cancers of the respiratory system, followed by those of the oral cavity and pharynx, myeloma, bones and joints, digestive system, and brain and nervous system cancers.

#### *Implications of all the available evidence*

To our knowledge, our study is the most comprehensive comparing the suicide risk of patients with a wide range of cancer sites with the suicide risk of the US general population. Our findings suggest that more tailored clinical management, prevention, and health policies should be considered for subsets of cancer patients at high risk of suicide.

included about 3.6 million cancer cases, showed that cancers of certain sites were associated with a higher risk of suicide. In 2015, Kam et al. analyzed suicide risk in patients diagnosed with head and neck cancer. Using data from 1973 to 2011, they found that patients with head and neck cancer experienced more than three times the rate of suicide compared with the US general population.<sup>12</sup> Recently, Zaorsky et al. reported that risk of suicide for cancer patients has increased in recent years, and that cancer patients diagnosed from 2011 to 2014 experienced more than 36 times the risk of the general US population.<sup>10</sup> Previous study may have ignored the situation when patients with multiple primary tumors, which could confuse the results. Past studies evaluating suicide risk among cancer patients have shown large discrepancies, which may be due to recent progress in cancer screening, diagnosis and treatment strategies, as well as population differences between countries. Hence, suicide risk among cancer patients, and how it changes over time, remain to be fully understood.

In our study, we performed in-depth analyses of the suicide risk of patients with cancer of cancer sites/organ systems, incorporating updated data from the SEER database. We estimated the suicide risk of patients with cancer, as compared with that of the general US population, depending on various sociodemographic factors and cancer types.

### Methods

#### Data source

In this population-based cohort study, we used SEER\*-Stat software, version 8.3.9 to access the SEER 18 registries, which includes data for approximately 27.8% of the US population from 1975 to 2016.<sup>13</sup> SEER is a cancer registry database that collects data on cancer cases from various locations and sources throughout the US.<sup>13</sup> Comparisons with the general US population were based on the 2000 US census as well as incidence per million from the US population, as this is widely accepted and statistically sound.<sup>14</sup> This study was approved by the institutional review board of the National Cancer Center of China, and written informed consent was waived given retrospective nature of the study.

#### Study population

For analyses of all cancers combined, we included all patients diagnosed with a malignant cancer. Patients were classified according to the “Site Recode the International Classification of Diseases for Oncology, third edition (ICD-O-3) /WHO 2008” guidelines, which identify cancers of all sites/organ systems including cancers of the oral cavity and pharynx, digestive system, respiratory system, bones and joints, brain and other nervous system, breast, urinary tract, female reproductive system, male reproductive system, soft tissues including the heart, skin (excluding basal cell carcinoma and squamous cell carcinoma, endocrine system, eye and orbit, as well as mesothelioma, leukemia, lymphoma, Kaposi sarcoma, and miscellaneous. For site-specific analyses, only patients with a single primary cancer were included, as suicides in patients with multiple primary cancers would confound any association of a particular cancer site and suicide.

We obtained cancer sites, sex, age, race, insurance status, marital status, time of diagnosis, tumor stage, cause of death, vital status and survival time for each patient. Those identified by death certificate or autopsy were excluded. We considered patients to have died by suicide only if the “COD to site record” class in the SEER program was coded as “suicide and self-inflicted injury.” Patient age was defined as age at cancer diagnosis. Patient race was classified into four major categories: American Indian/Alaskan Native, Asian or Pacific

Islander, white and Black according to the “Race Recode (W, B, AI, API)” class. Patient marital status was classified as divorced, married, separated, unmarried or domestic partner, single (never married), widowed, or unknown.

### Statistical analysis

To compare the rate of suicide among cancer patients with that of the US general population (as collected by the National Center for Health Statistics), we obtained absolute excess risk estimates (AER) through a standardized method implemented by the SEER\*Stat software.<sup>15</sup> Standardized mortality ratio (SMR) was calculated in SEER\*Stat software using MP-SIR section, which provides the relative risk of death for patients with cancer as compared to US general population; here, the SMR was defined as the actual count of deaths caused by suicide / the number of events expected to be experienced, and confidence intervals were calculated by exact method implemented in the SEER \*stat software. The AER was defined as ((Observed count - Expected count) x 10,000) / Person years at risk. Analysis for suicide risk over time after cancer diagnosis was adjusted for the sex, age, and race of cancer patients in the SEER database. Changing trend of SMR and AER over year of diagnosis was tested by using Mann Kendall Trend Test.<sup>16</sup> All statistical analyses were performed by the Surveillance Research Program, National Cancer Institute SEER\*Stat software (seer.cancer.gov/seerstat) version 8.3.9 and R Statistical Software version 4.0.3 (R Foundation for Statistical Computing), without multiple comparison corrections as the analyses were exploratory.

### Role of the funding source

The funding source did not have any involvement in study design; data collection, data analysis or interpretation, writing, or submission of this article.

## Results

### Overall findings and baseline characteristics

Overall, 9,300,812 patients (48.8% female) aged from 0 to 80+ years were diagnosed with cancer between 1975 and 2016. Of these patients, 6,417,560 (69.0%) were over age 60 when diagnosed. We identified 14,423 patients with cancer who died by suicide, which represents 0.26% of all deaths. Characteristics of the study population, which had a mean survival time of 5.66 years (with a range of 0 to 41.92 years) are summarized in Table 1. We found that the overall SMR for the entire population was 1.45 (95% CI, 1.42–1.49) and the overall AER per 10,000 person-years with risk was 0.8. We observed variations in suicide risk depending on cancer sites/organ systems, the time since diagnosis,

and patient characteristics (age, race, sex, insurance and marital status, and tumor stage) (Table 1). For the whole population, there was an increasing trend in the SMR ( $Z = 3.80$ ,  $P < 0.001$ ) and AER ( $Z = 3.92$ ,  $P < 0.001$ ) of suicides among cancer patients in recent years.

### Differences in suicide risk by primary cancer sites/ human organ systems

We found variations in SMRs and AERs for cancer sites/organ systems Table 2; The suicide risk among patients with cancers in most sites/organ systems was greater than that of the US general population, with the exception of cancers of the following types: skin excluding basal and squamous, endocrine system, and eye and orbit (Table S2). Among all primary cancer sites, patients with cancer of the hypopharynx had the largest SMR and AER, with a 7.59-fold risk compared with the general population (equating to 15.2 additional deaths per 10,000 person-years). This suicide risk was followed by mesothelioma, cancer of the oropharynx, and cancers of the nasopharynx, esophagus, pancreas, floor of mouth, lung and bronchus, and tongue. The largest SMR and AER were found among patients with cancers of the respiratory system, who had a 3.16-fold risk of suicide compared with the general population (equating to 4.29 additional deaths per 10,000 person-years). This suicide risk was followed by cancers of the oral cavity and pharynx, myeloma, bones and joints, digestive system, brain and nervous system. (Tables S1, S2).

### Differences in suicide risk over time following diagnosis

We found variations in suicide risk depending on cancer sites/ organ systems, and these risks changed over time post-diagnosis (Figure 1, Table S3). For all cancers combined, the SMR was highest in the first 2 months after diagnosis (SMR, 3.74; 95% CI, 3.23–4.3) (Figure 1); this phenomenon was observed for most of the organ systems. Interestingly, patients with cancers of soft tissue including heart, brain and other nervous system, urinary system, and lymphoma experienced the highest SMRs and AERs in the first 3 to 5 months, while the SMRs and AERs of patients with cancers of bones and joints fluctuated over time (Figure 1). Patients with cancers of the respiratory system, oral cavity, and pharynx experienced consistently higher suicide risk over time compared with the general population (Figure 1). We found that the greatest suicide risk occurred in patients with cancer of the hypopharynx in the first 2 months following diagnosis; in this time period these patients had a 15.8-fold risk compared with the general population (equating to 33.54 additional deaths per 10,000 person-years with risk). (Table S3)

Characteristic	Patients with cancer	Death of suicide No. (%)	% Suicide of total	Suicides per 100,000 Person-years	Person-years	SMR <sup>b</sup> (95%CI)	AERs per 10,000 Person-Years (95%CI)
Total	9,300,812	14,423	0.26	27.38	52,667,544	1.45*(1.42–1.49)	0.8(0.799–0.8)
Sex							
Female	4,538,448 (48.8)	2463 (17.1)	0.10	8.91	27,644,787	1.39*(1.31–1.47)	0.237(0.237–0.238)
Male	4,762,364 (51.2)	11,960 (82.9)	0.41	47.80	25,022,757	1.47*(1.43–1.51)	1.45(1.449–1.451)
Race							
American Indian/ Alaska Native	46,277 (0.5)	57 (0.4)	0.22	24.01	237,448	1.94*(1.19–3)	0.782(0.78–0.79)
Asian or Pacific Islander	544,116 (5.9)	523 (3.6)	0.18	17.36	3,012,373	1.77*(1.55–2)	0.688(0.687–0.689)
Black	923,739 (9.9)	463 (3.2)	0.08	10.46	4,427,413	1.73*(1.51–1.97)	0.469(0.468–0.47)
White	7,706,141 (82.9)	13,351 (92.6)	0.29	29.96	44,555,847	1.43*(1.4–1.47)	0.837(0.837–0.838)
Unknown	80,539 (0.9)	29 (0.2)	0.37	6.67	434,463	NA	NA
Age group							
<=19	101,043 (1.1)	92 (0.6)	0.38	9.04	1,017,148	1.13(0.89–1.43)	0.132(0.131–0.133)
20–29	1,464,934 (15.8)	1683 (11.7)	0.14	43.75	3,847,289	1.28*(1.1–1.47)	0.418(0.417–0.419)
30–39	141,028 (1.5)	269 (1.9)	0.82	18.30	1,469,566	1.36*(1.23–1.51)	0.505(0.504–0.506)
40–49	338,899 (3.6)	616 (4.3)	0.61	18.98	3,244,928	1.37*(1.26–1.47)	0.485(0.485–0.486)
50–59	811,452 (8.7)	1238 (8.6)	0.42	18.45	6,709,434	1.43*(1.36–1.52)	0.646(0.645–0.646)
60–69	1,684,983 (18.1)	2476 (17.2)	0.33	21.50	11,517,362	1.53*(1.46–1.6)	0.967(0.967–0.968)
70–79	2,437,266 (26.2)	4061 (28.2)	0.30	28.52	14,240,118	1.49*(1.42–1.56)	1.168(1.167–1.169)
>=80	2,321,207 (25.0)	3988 (27.7)	0.24	37.55	10,621,699	1.45*(1.33–1.57)	1.142(1.401–1.144)
Tumor stage							
Distant	1,339,655 (14.4)	1324 (9.2)	0.12	55.00	21,897,102	2.57*(2.29–2.87)	2.591(2.588–2.595)
In situ	149,999 (1.6)	266 (1.8)	0.46	29.08	2,407,481	0.94(0.73–1.19)	-0.155(-0.153- -0.156)
Localized	3,139,493 (33.8)	4060 (28.1)	0.41	20.49	914,642	1.03(0.97–1.09)	0.053(0.053–0.053)
Regional	1,387,118 (14.9)	1582 (11.0)	0.23	23.72	19,810,554	1.42*(1.29–1.55)	0.628(0.627–0.629)
Unknown/unstaged	314,828 (3.4)	385 (2.7)	0.18	39.78	6,669,902	1.61*(1.23–2.07)	1.1(1.093–1.102)
Missing	2,969,719 (31.9)	6806 (47.2)	0.28	31.08	967,863	1.59*(1.55–1.64)	1.052(1.052–1.053)
Marital status							
Divorced	761,080 (8.2)	1580 (11.0)	0.35	40.70	3,881,817	2.72*(2.52–2.94)	2.314(2.312–2.316)
Married	5,131,685 (55.2)	7987 (55.4)	0.28	24.71	32,320,089	1.21*(1.17–1.25)	0.412(0.411–0.412)
Separated	101,983 (1.1)	124 (0.9)	0.18	24.94	497,168	1.77*(1.35–2.28)	0.982(0.978–0.986)
Single (never married)	1,259,066 (13.5)	2165 (15.0)	0.33	30.56	7,084,356	1.96*(1.84–2.08)	1.41(1.409–1.411)
Unmarried or Domestic Partner	8116 (0.1)	3 (0.0)	0.14	18.94	15,839	1.01(0.03–5.64)	0.019(0.015–0.023)
Widowed	1,407,949 (15.1)	1455 (10.1)	0.13	26.97	5,395,041	2.06*(1.9–2.22)	1.266(1.265–1.268)
Unknown	630,933 (6.8)	1109 (7.7)	0.39	31.93	3,473,235	1.50*(1.37–1.64)	1.01(1.01–1.01)
Insurance							
Any Medicaid	451,971 (4.9)	322 (2.2)	0.15	29.08	1,107,325	2.54*(2.04–3.12)	2.033(2.028–2.039)
Insured	2,647,117 (28.5)	2429 (16.8)	0.26	27.82	8,729,899	1.28*(1.17–1.39)	0.492(0.491–0.493)
Insured/No specifics	627,104 (6.7)	619 (4.3)	0.22	32.64	1,896,591	1.42*(1.2–1.68)	0.771(0.769–0.773)
Uninsured	99,292 (1.1)	111 (0.8)	0.26	40.18	276,234	2.72*(1.82–3.9)	2.896(2.883–2.91)
Unknown	268,285 (2.9)	262 (1.8)	0.28	32.50	806,064	1.40*(1.1–1.75)	0.872(0.868–0.876)
Missing	5,207,043 (56.0)	10,680 (74.0)	0.28	26.80	39,851,431	1.46*(1.42–1.5)	0.813(0.813–0.814)
Year of diagnosis							
1975–1979	345,410 (3.7)	875 (6.1)	0.27	29.75	2,941,003	1.68*(1.56–1.8)	1.15(1.147–1.15)
1980–1989	864,538 (9.3)	2423 (16.8)	0.31	33.54	7,223,604	1.75*(1.67–1.82)	1.323(1.322–1.324)
1990–1999	1,465,678 (15.8)	3272 (22.7)	0.28	26.54	12,326,902	1.35*(1.3–1.41)	0.634(0.633–0.634)
2000–2009	3,723,168 (40.0)	5665 (39.3)	0.26	24.18	23,423,714	1.19*(1.13–1.26)	0.339(0.338–0.339)
2009–2016	2,902,018 (31.2)	2188 (15.2)	0.22	32.40	6,752,321	1.54*(1.41–1.68)	0.963(0.962–0.965)

**Table 1: Suicide SMRs and AERs per 10,000 person-years at risk according to key patient characteristics for all cancer combined.**

Abbreviations: SMR, standardized mortality ratio; AER, absolute excess risk.

a \* means that 95% confidence interval does not cross 1.0 and also the SMR is significant.

b Reference population: general US population based on the 2000 US standard population, Patients with multiple primary tumors were excluded automatically.

### Differences in suicide risk by sex

In our population, the patients who died by suicide were predominately male (11,960, 82.9%), accounting for more than four times the number of female patients. For all cancers combined, men had higher SMRs and

AERs than women (Table 1). However, the association between risk of suicide and sex also varied by cancer sites/organ system. For most cancer sites/organ systems, men demonstrated higher SMRs and AERs than women (Table 3). Interestingly, we found that female

Single primary cancer <sup>b</sup>	Observed	Expected	SMR <sup>c</sup> (95%CI)	AERs per 10,000 Person-Years (95%CI)
All Sites	6806	4683.5	1.45*(1.42–1.49)	0.8(0.799–0.8)
Oral Cavity and Pharynx	421	141.05	2.98*(2.71–3.28)	4.3(4.293–4.304)
Lip	64	35.01	1.83*(1.41–2.33)	2.564(2.555–2.573)
Tongue	95	29.23	3.25*(2.63–3.97)	4.795(4.783–4.806)
Digestive System	1065	649.97	1.64*(1.54–1.74)	1.201(1.2–1.203)
Stomach	104	35.7	2.91*(2.38–3.53)	3.611(3.602–3.619)
Colon and Rectum	721	537.65	1.34*(1.24–1.44)	0.65(0.649–0.651)
Colon excluding Rectum	478	366.37	1.30*(1.19–1.43)	0.569(0.568–0.57)
Cecum	99	72.21	1.37*(1.11–1.67)	0.669(0.667–0.672)
Ascending Colon	59	50.05	1.18(0.9–1.52)	0.317(0.315–0.319)
Transverse Colon	37	29.18	1.27(0.89–1.75)	0.476(0.473–0.479)
Descending Colon	51	26.52	1.92*(1.43–2.53)	1.725(1.718–1.732)
Sigmoid Colon	183	144.45	1.27*(1.09–1.46)	0.525(0.523–0.526)
Rectum and Rectosigmoid Junction	243	171.29	1.42*(1.25–1.61)	0.833(0.832–0.835)
Rectosigmoid Junction	71	53.9	1.32*(1.03–1.66)	0.627(0.624–0.63)
Rectum	172	117.38	1.47*(1.25–1.7)	0.929(0.927–0.932)
Respiratory System	796	252.13	3.16*(2.94–3.38)	4.289(4.286–4.293)
Larynx	151	67.8	2.23*(1.89–2.61)	3.187(3.18–3.193)
Lung and Bronchus	625	174.74	3.58*(3.3–3.87)	4.722(4.718–4.727)
Soft Tissue including Heart	47	34.16	1.38*(1.01–1.83)	0.622(0.618–0.625)
Skin excluding Basal and Squamous	329	322.51	1.02(0.91–1.14)	0.038(0.038–0.038)
Melanoma of the Skin	307	298.85	1.03(0.92–1.15)	0.052(0.052–0.052)
Breast	497	366.14	1.36*(1.24–1.48)	0.223(0.223–0.223)
Female Genital System	191	150.52	1.27*(1.1–1.46)	0.167(0.167–0.168)
Cervix Uteri	55	33.37	1.65*(1.24–2.15)	0.433(0.431–0.435)
Ovary	49	25.98	1.89*(1.4–2.49)	0.572(0.57–0.474)
Male Genital System	1913	1684.36	1.14*(1.09–1.19)	0.434(0.433–0.434)
Prostate	1777	1563.58	1.14*(1.08–1.19)	0.443(0.442–0.443)
Testis	124	110.94	1.12(0.93–1.33)	0.313(0.311–0.315)
Urinary System	640	485.57	1.32*(1.22–1.42)	0.786(0.785–0.801)
Urinary Bladder	461	352.53	1.31*(1.19–1.43)	0.839(0.837–0.84)
Kidney and Renal Pelvis	168	124.81	1.35*(1.15–1.57)	0.678(0.676–0.68)
Brain and Other Nervous System	57	39.74	1.43*(1.09–1.86)	0.631(0.628–0.634)
Brain	48	34.46	1.39*(1.03–1.85)	0.574(0.571–0.577)
Endocrine System	104	114.17	0.91(0.74–1.1)	–0.105(–0.104–0.105)
Thyroid	96	108.02	0.89(0.72–1.09)	–0.13(–0.129–0.13)
Lymphoma	338	238.46	1.42*(1.27–1.58)	0.736(0.735–0.738)
Hodgkin Lymphoma	85	61.48	1.38*(1.1–1.71)	0.641(0.639–0.644)
Hodgkin - Nodal	85	60.53	1.40*(1.12–1.74)	0.678(0.675–0.68)
Non-Hodgkin Lymphoma	253	176.98	1.43*(1.26–1.62)	0.772(0.77–0.774)
NHL - Nodal	183	119.4	1.53*(1.32–1.77)	0.96(0.958–0.963)
NHL - Extranodal	70	57.57	1.22(0.95–1.54)	0.385(0.383–0.388)
Myeloma	65	30.62	2.12*(1.64–2.71)	1.986(1.98–1.993)
Leukemia	134	106.37	1.26*(1.06–1.49)	0.458(0.456–0.46)
Lymphocytic Leukemia	81	80.01	1.01(0.8–1.26)	0.022(0.022–0.023)
Chronic Lymphocytic Leukemia	66	58.89	1.12(0.87–1.43)	0.26(0.258–0.262)
Myeloid and Monocytic Leukemia	47	23.71	1.98*(1.46–2.64)	1.625(1.619–1.632)
Miscellaneous	81	24.92	3.25*(2.58–4.04)	4.21(4.199–4.222)

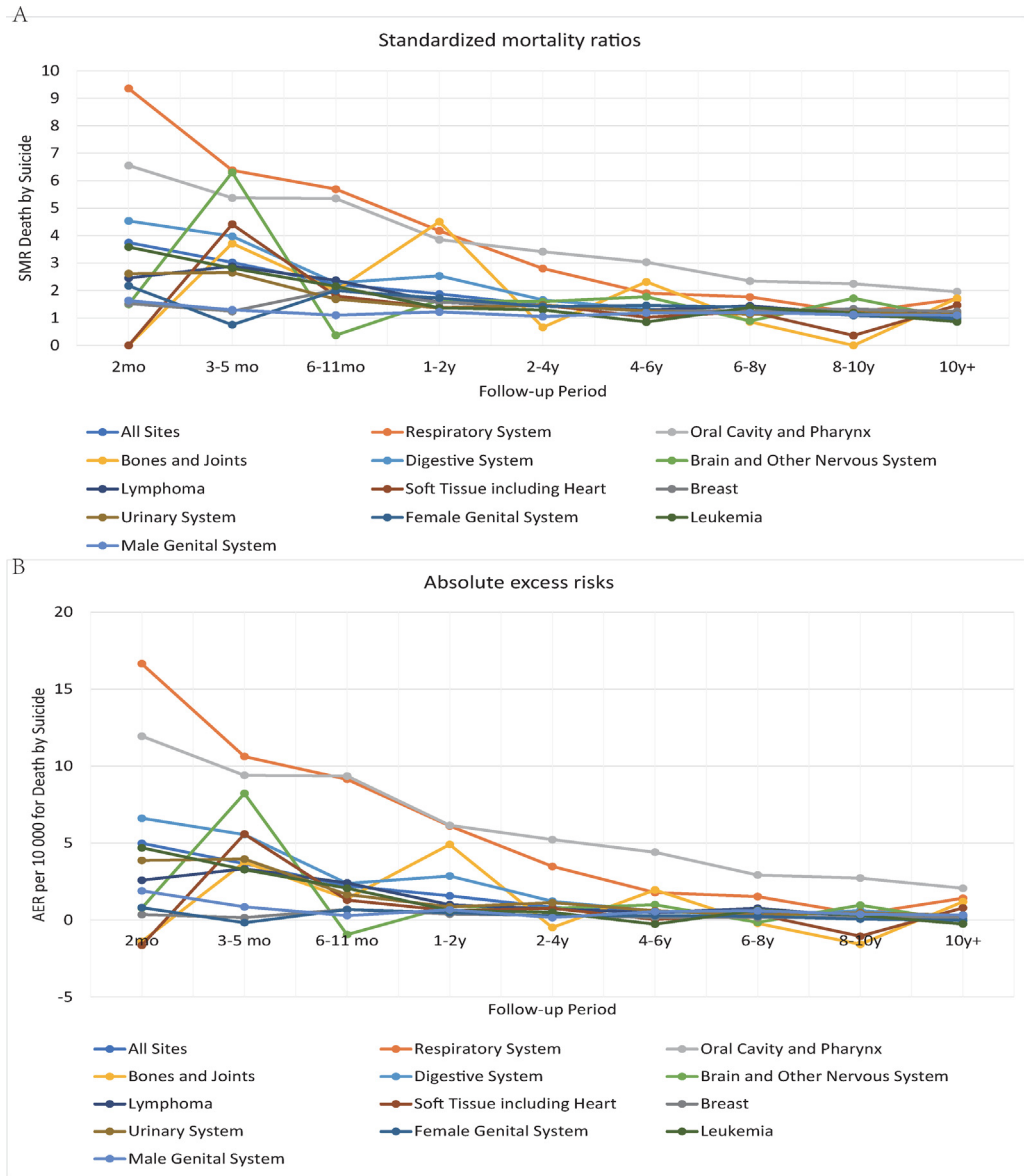
**Table 2: Suicide SMRs and AERs per 10,000 person-years at risk according to cancer sites/organ systems.**

Abbreviations: SMR, standardized mortality ratio; AER, absolute excess risk;

a \* means that 95% confidence interval does not cross 1.0 and also the SMR is significant.

b Patients with single primary cancer only recorded in the SEER registry.

c Reference population: general US population based on the 2000 US standard population; Patients with multiple primary tumors were excluded automatically; adjusted for age, sex, and race distributions of cancer patients.



**Figure 1.** Suicide Standardized Mortality Ratios (SMRs) and Absolute Excess Risks (AERs) per 10,000 person-years at risk according to cancer sites/organ systems by follow-up period. (All confidence intervals of SMRs can be found at corresponding supplementary table; Estimates of SMRs (A) and AERs (B) are presented in Table S3 in the Supplement). X axis denotes the time after cancer diagnosis. Y axis denotes SMR (A) and AER (B) of suicide by different latency periods. Color code denotes different cancer sites/organ systems by follow-up period.

patients with lymphoma, leukemia, or cancer of the urinary system showed higher SMRs than men with the same cancer; this phenomenon was also observed in cancer sites such as the oropharynx, esophagus, tongue, stomach, larynx, and lip. (Table S4).

**Differences in suicide risk by race and marital status**

Predominantly, patients who died by suicide were white (13,351, 92.6%). For all cancers combined, patients who

identified as American Indian/Alaskan Native had the highest SMR (1.94, 95% CI, 1.19–3.00), followed by Asian or Pacific Islander, Black and white. Patients who indicated they were divorced had the highest SMR and AER (SMR, 2.72, 95% CI, 2.52–2.94; AER, 2.314, 95%CI, 2.312–2.316), followed by widowed, single (never married), separated, married, and unmarried or domestic partner (Table 1). These associations of suicide with race and marital status varied by cancer sites/organ systems (Figure 2). Patients who identified as Asian or

Primary Cancer	Male			Female		
	Observed	Expected	SMR <sup>c</sup> (95%CI)	Observed	Expected	SMR <sup>c</sup> (95%CI)
Mesothelioma	15	2.1	7.16*(4.01–11.81)	1	0.28	3.58(0.09–19.97)
Respiratory System	709	221.78	3.20*(2.97–3.44)	87	30.36	2.87*(2.3–3.54)
Oral Cavity and Pharynx	384	127.56	3.01*(2.72–3.33)	37	13.49	2.74*(1.93–3.78)
Digestive System	918	554.96	1.65*(1.55–1.76)	147	95.01	1.55*(1.31–1.82)
Brain and Other Nervous System	45	32.33	1.39*(1.02–1.86)	12	7.4	1.62(0.84–2.83)
Lymphoma	280	198.44	1.41*(1.25–1.59)	58	40.02	1.45*(1.1–1.87)
Soft Tissue including Heart	41	28.65	1.43*(1.03–1.94)	6	5.51	1.09(0.4–2.37)
Breast	18	9.86	1.82*(1.08–2.88)	479	356.27	1.34*(1.23–1.47)
Urinary System	590	452.26	1.30*(1.2–1.41)	50	33.31	1.50*(1.11–1.98)
Female Genital System	0	0	0(0–0)	191	150.52	1.27*(1.1–1.46)
Leukemia	112	92.64	1.21(1–1.45)	22	13.73	1.60*(1–2.43)
Male Genital System	1913	1684.36	1.14*(1.09–1.19)	0	0	0(0–0)

**Table 3: Variation in sex of suicide SMRs and AERs per 10,000 person-years at risk according to cancer sites/organ systems.**

Abbreviations: SMR, standardized mortality ratio; AER, absolute excess risk.

a \* means that 95% confidence interval does not cross 1.0 and also the SMR is significant.

b Patients with cancer of single primary cancer classified by organ systems recorded in the SEER registry.

c Reference population: general US population based on the 2000 U.S. standard population; adjusted for age, sex, and race distributions of cancer patients.

Pacific Islander had the highest SMR in cancers of the respiratory system, while patients who identified as Black demonstrated the highest SMR in cancers of both the breast and oral cavity and pharynx (Table S5). While patients who indicated they were divorced had the highest SMR among most sites/organ systems, those who were widowed had the highest SMR and AER in cancer of bones and joints; they often had the second-highest SMR and AER (after those of divorced status) in other sites/organ systems as well (Figure 2, Table S6).

#### Differences in risk of suicide by age at diagnosis

For all patients combined, the rate of suicide increased with age, peaking with patients who were diagnosed between the ages of 60 and 69 (SMR, 1.53, 95% CI, 1.46–1.6; AER, 0.967, 95% CI, 0.967–0.968) and then decreasing. Additionally, no significant difference of suicide risk was observed in patients diagnosed before age 19 (Table 1). These associations between risk of suicide and age varied by sites/organ systems (Fig. S1; Table S7). For example, patients with cancers of the digestive system, breast, and leukemia had the highest suicide rate when diagnosed between the ages of 20 to 29. With cancers of the respiratory system, risk of suicide increased with age, reaching its peak with those aged between 70 and 79 at diagnosis. Similarly, patients with bone and joint cancers demonstrated the highest SMR and AER when diagnosed between 70 and 79 years of age (Fig. S1).

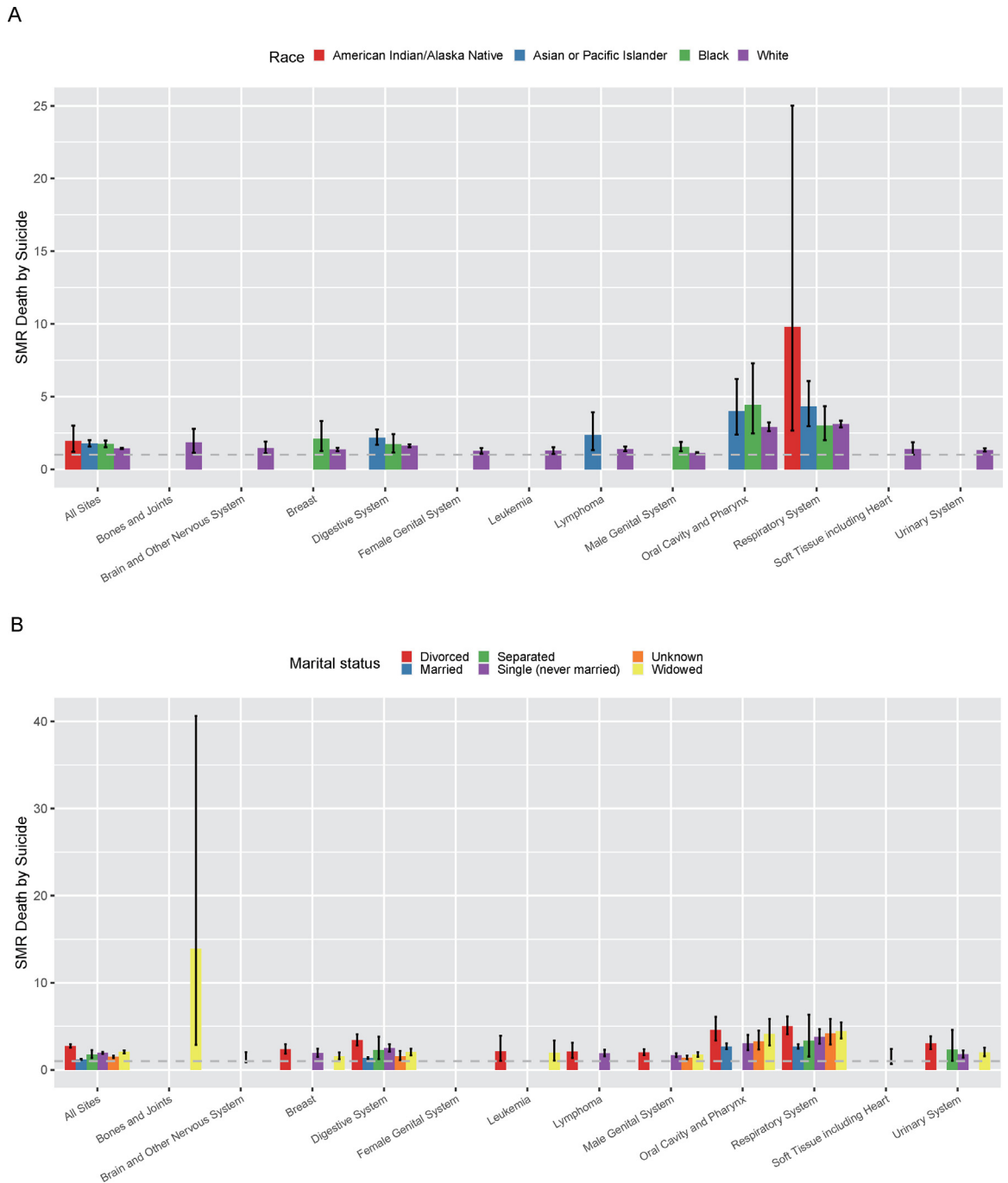
#### Differences in risk of suicide by year of diagnosis

For the population as a whole, patients diagnosed between 1980 and 1989 had the highest risk of suicide:

a 1.75-fold risk compared with the general population (equating to 1.32 additional deaths per 10,000 person-years with risk.) We also observed that the SMR ( $Z = 3.80$ ,  $P < 0.001$ ) and AER ( $Z = 3.92$ ,  $P < 0.001$ ) showed increased trend between 2010 and 2016 (Table 1, Fig. S2). The suicide risk during different periods varied by cancer sites/organ system (Fig. S2; Table S8). Most cancers were associated with an elevated SMR and AER in patients diagnosed between 1980 and 1989, which then decreased until 1999, and increased again in more recent years. Notably, the risk of suicide in patients with breast cancer, when compared with that of the general US population, decreased over the entire study period (Fig. S2).

#### Discussion

This study identified both patient characteristics and disease types associated with higher suicide risk, which will assist oncologists and psychiatrists in identifying patients who need psychological support. In our population-based study of more than 9 million individuals, data revealed that cancer patients in the US experienced a 45% increase in suicide risk when compared with the general population. Using SEER registry data through 2002, Misono et al. reported an SMR of 1.88 among cancer patients in the US, and suggested SMRs were greatest in the first 5 years after diagnosis.<sup>7</sup> Our results build on these and move forwards, as we found that SMR was highest in the first 2 months after diagnosis in most cancer types, and that another peak can occur 3–5 months after diagnosis. Similar to our results, Henson's study using population-based data from England reported a SMR of 1.2.<sup>17</sup> However, Zaorsky et al. reported an extremely high SMR of 4.44, which means



**Figure 2.** Suicide rates among cancer patients by race and marital status according to cancer sites/organ systems. (All confidence intervals of SMRs can be found at corresponding supplementary table; Reference population is the general US population, SMR indicates standardized mortality ratio). X axis denotes different cancer sites/organ systems. Y axis denotes SMR. Color code denotes race (A) and marital status (B). Error bars denote the 95% CI of SMRs.

suicide risk among cancer patients was more than four-fold than the general US population and one that in recent years even reached 36.91,<sup>10</sup> which is inconsistent with our results. We believe that two potential

explanations may account for this discrepancy. First, it may be due to a calculation error, which could have occurred if only using linked county attribute data that only impacted the SMR tables. Second, this study may



have included patients with multiple primary tumors, which could confound the results. Han et al. reported a decreasing trend of cancer-related suicide in the Multiple Cause of Death database, which included 6487 cases with cancer.<sup>18</sup> However, this result was limited to cancer patients among suicides rather than the reverse, so it should be interpreted with caution. In contrast, our study found an increasing trend in suicide risk among cancer patients diagnosed between 2000 and 2016.

Our study revealed that suicide risk peaked within the first 2 months after cancer diagnosis and then decreased, which suggests that the mental and psychological stress associated with a cancer diagnosis lessens over time. Differences in the high-risk periods might be due to the heterogeneity of prognosis and treatment strategies in different cancer groups, therefore leading to different psychological status in patients. Clinically, our results suggest psychological assessment should be administered soon after diagnosis in different critical period, especially for cancer types with a high risk of suicide. As for general population in US, risk of suicide was highest among people with 50 to 69 years old, followed by 70+ years old and 15 to 49 years old according to data from global burden of disease [Ref: Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2017 (GBD 2017) Results. Seattle, United States: Institute for Health Metrics and Evaluation (IHME), 2018]. We found the risk of suicide increased with age, peaking with patients who were diagnosed between the ages of 60 and 69 and then decreasing in most cancer groups, which showed a similar pattern with the general population. Clinically, our findings suggest more psychological attention should be considered for these high-risk subsets.

Our current work adds to the existing literature examining suicide among cancer patients.<sup>9,19–23</sup> Most previous studies limited to certain cancer types or certain time period, thereby ignoring the heterogeneity of different cancer sites and changing trend of the risk along time after cancer diagnosis. We are the first to report the SMR was greatest in the first 2 months after cancer diagnosis in most cancer types, which suggest more attention should be paid to cancer patients within this period. We found the profile of suicide risk has changed over time in the past 40 years, which might be due to the progress of screening, diagnosis and treatment strategies in cancer. As we all know, with the rapid development of medical technology, more cancer patients are diagnosed and better survival rates have been achieved in the past few decades,<sup>24</sup> and most cancer patients are diagnosed with low-risk disease which is unlikely the direct cause of death that could be one explanation for the changing of suicide risk profile. In addition, there are no indication that specific cancers where these treatment changes have been made that leading to changes in suicide risk. Furthermore, despite the promotion of hospice care for patients with

incurable cancer,<sup>25</sup> the suicide risk remains elevated in recent years, which suggest it is insufficient to only focus on patients with incurable patients, future efforts regarding psychosocial, pain management and symptom control for patients with early-stage cancer should also be considered. Although male patients showed higher suicide risk in most of cancer types, we found female patients even showed higher suicide risk in several cancer groups. As these exceptions of cancer types might be associated with severe symptoms and worse prognosis, we hypothesize that this might be due to gender differences regarding psychological distress for these cancer types. Future study focusing on psychological reactions of different gender to different cancer types, treatment plans and symptoms might be helpful for answering this phenomenon.

Our study may be limited by bias and the possible misclassification of suicide in the SEER database. Additionally, we were unable to investigate comorbid medical and psychiatric conditions, including factors that could influence the incidence of cancer, such as alcohol and tobacco use, which may be associated with their own risk of suicide (relative risk ranging from 1.4 to 4.3).<sup>26–28</sup> Since alcohol and tobacco use could be common in patients with lung, head, and neck cancer, this may account for some of the increased suicide risk in these subgroups.<sup>29,30</sup>

Despite these limitations, our study has several strengths. First, to our knowledge, we used the largest patient cohort among all such studies. Second, we performed more in-depth analyses, providing an overview of the suicide risks associated with all cancers, and also how these risks varied depending on patient characteristics, which was unavailable in previous studies. Third, several personal characteristics have been examined in more detail, including marital status, insurance status and age group.

#### Declaration interests

The authors declare no competing interests.

#### Funding

Dr. Jing Wang reports grants from Natural Science Foundation of China (No. 82,173,328, No. 81,872,160), grants from Beijing Municipal Natural Science Foundation (No. 7,191,009), grants from The Beijing Hope Run Special Fund of Cancer Foundation of China (No. LC2020L01), during the conduct of the study; Dr. Xiangyi Kong reports grants from Natural Science Foundation of China (No. 82,103,047), grants from Beijing Municipal Natural Science Foundation (No. 7,204,293), grants from The Special Research Fund for Central Universities, Peking Union Medical College (No. 3,332,019,053), grants from The Beijing Hope Run Special Fund of Cancer Foundation of China (No. LC2019B03), grants from The Golden Bridge Project Seed Fund of Beijing Association for Science and

Technology (No. ZZ20004), grants from The 2021 Chaoyang District Social Development Science and Technology Plan Project (Medical and Health Field) (No. CYSF2115), grants from The Chinese Young Breast Experts Research project (No. CYBER-2021-005), grants from The XianSheng Clinical Research Special Fund of China International Medical Foundation (No. Z-2014-06-2103), during the conduct of the study; Dr. Yi Fang reports grants from Natural Science Foundation of China (No. 82,072,940), grants from The Beijing Hope Run Special Fund of Cancer Foundation of China (No. LC2019L07), grants from The China National Key R&D (or Research and Development) Program (No. 2020AAA0105000 and 2020AAA0105004), during the conduct of the study; Dr. Xiangyu Wang reports grants from The Natural Science Foundation of China (No. 82,102,887), during the conduct of the study. All the other authors have nothing to disclose.

### Contributors

Q.L designed the study. Q.L, XY.W, ML.Z, YP.R, and H. D contributed to collection and assembly of data. Q.L, XY.W, XY.K, and ZZ.W contributed to data analysis and interpretation. Q.L, XY.W, XY.K, Y.F, and J.W contributed to manuscript writing, discussion and revision. All authors read and approved the final manuscript. Q.L, Y. F and J.W had final responsibility for the decision to submit for publication. We acknowledge the valuable statistical suggestions from Dr. Haihua Liu during revision process of this paper. We thank Miss Ping He for suggestions and sincere support during the process of article submission and revisions.

### Data sharing statement

All supporting data are included in the manuscript and supplemental files. Additional data are available upon reasonable request to corresponding author.

### Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2022.101295.

### References

- 1 Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin*. 2019;69(1):7–34.
- 2 Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209–249.
- 3 Bray F, Laversanne M, Weiderpass E, Soerjomataram I. The ever-increasing importance of cancer as a leading cause of premature death worldwide. *Cancer*. 2021;127(16):3029–3030. <https://doi.org/10.1002/cncr.33587>.
- 4 Law K.C. Suicide acts in 8 states: incidence and case fatality rates by demogra. 2011.

- 5 Organization WH. *Preventing Suicide: A Global Imperative*. World Health Organization; 2014.
- 6 Roth GA, Abate D, Abate KH, et al. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392(10159):1736–1788.
- 7 Misono S, Weiss NS, Fann JR, Redman M, Yueh B. Incidence of suicide in persons with cancer. *J Clin Oncol*. 2008;26(29):4731.
- 8 Spicer RS, Miller TR. Suicide acts in 8 states: incidence and case fatality rates by demographics and method. *Am J Public Health*. 2000;90(12):1885.
- 9 Anguiano L, Mayer DK, Piven ML, Rosenstein D. A literature review of suicide in cancer patients. *Cancer Nurs*. 2012;35(4):E14–E26.
- 10 Zaorsky NG, Zhang Y, Tuanquin L, Bluethmann SM, Park HS, Chinchilli VM. Suicide among cancer patients. *Nat Commun*. 2019;10(1):1–7.
- 11 Faul LA, Luta G, Sheppard V, et al. Associations among survivorship care plans, experiences of survivorship care, and functioning in older breast cancer survivors: CALGB/Alliance 369901. *J Cancer Surviv*. 2014;8(4):627–637.
- 12 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(12):1075–1081.
- 13 Scosyrev E, Messing J, Noyes K, Veazie P, Messing E. Surveillance epidemiology and end results (SEER) program and population-based research in urologic oncology: an overview. *Urologic Oncology: Seminars and Original Investigations*; 2012. Elsevier; 2012:126–132.
- 14 Klein R.J. Age adjustment using the 2000 projected US population: department of health & human services, Centers for Disease Control and . . . ; 2001.
- 15 Fox AJ. Statistical methods in cancer research. Volume II—The design and analysis of cohort studies. *IARC Sci Publ*. 1987;82(82):1.
- 16 Khambhammettu P. Appendix Mann-Kendall analysis for the fort ord site. *Annual Groundwater Monitoring Report* 2005.
- 17 Henson KE, Brock R, Charnock J, Wickramasinghe B, Pitman A. Risk of suicide after cancer diagnosis in England. *JAMA Psychiatry*. 2018;76(1).
- 18 Han X, Hu X, Zhao J, Ma J, Ahmedin J, Robin YK. Trends of cancer-related suicide in the United States: 1999–2018. *JNCI J Natl Cancer Inst*. 2021;113(9):1258–1262.
- 19 Hem E, Loge JH, Haldorsen T, Ekeberg Å. Suicide risk in cancer patients from 1960 to 1999. *J Clin Oncol*. 2004;22(20):4209–4216.
- 20 Tanaka H, Tsukuma H, Masaoka T, et al. Suicide risk among cancer patients: experience at one medical center in Japan, 1978–1994. *Jpn J Cancer Res*. 1999;90(8):812–817.
- 21 Abdel-Rahman O. Socioeconomic predictors of suicide risk among cancer patients in the United States: a population-based study. *Cancer Epidemiol*. 2019;63: 101601.
- 22 Osazuwa-Peters N, Simpson MC, Zhao L, et al. Suicide risk among cancer survivors: head and neck versus other cancers. *Cancer*. 2018;124(20):4072–4079.
- 23 Du L, Shi HY, Yu HR, et al. Incidence of suicide death in patients with cancer: a systematic review and meta-analysis. *J Affect Disord*. 2020;276:711–719.
- 24 Bluethmann SM, Mariotto AB, Rowland JH. Anticipating the “silver tsunami”: prevalence trajectories and comorbidity burden among older cancer survivors in the United States. *Cancer Epidemiol Biomarkers Prev*. 2016;25:1029–1036. <https://doi.org/10.1158/1055-9965.EPI-16-0133>. PMID: 27371756; PMCID: PMC4933329.
- 25 Kumar P, Wright AA, Hatfield LA, Temel JS, Keating NL. Family perspectives on hospice care experiences of patients with cancer. *J Clin Oncol*. 2017;35(4):432.
- 26 Miller M, Hemenway D, Bell NS, Yore MM, Amoroso PJ. Cigarette smoking and suicide: a prospective study of 300,000 male active-duty army soldiers. *Am J Epidemiol*. 2000;151(11):1060–1063.
- 27 Pirkola SP, Suominen K, Isometsä ET. Suicide in alcohol-dependent individuals. *CNS Drugs*. 2004;18(7):423–436.
- 28 Wilcox HC, Conner KR, Caine ED. Association of alcohol and drug use disorders and completed suicide: an empirical review of cohort studies. *Drug Alcohol Depend*. 2004;76:S11–S59.
- 29 Sturgis EM, Wei Q, Spitz MR. Descriptive epidemiology and risk factors for head and neck cancer. *Semin Oncol*. 2004;3:726–733. <https://doi.org/10.1053/j.seminoncol.2004.09.013>. PMID: 15599850.
- 30 Wingo PA, Ries LA, Giovino GA, et al. Annual report to the nation on the status of cancer, 1973–1996, with a special section on lung cancer and tobacco smoking. *J Natl Cancer Inst*. 1999;91(8):675–690.