

Case series

Temporal trends and characteristics of suicide among women with gynecologic malignancy in the United States

Caroline J. Violette^{a,b,1}, Rachel S. Mandelbaum^a, David J. Nusbaum^a, Christina J. Duval^a, Shinya Matsuzaki^a, Hiroko Machida^c, Lynda D. Roman^{a,d}, Koji Matsuo^{a,d,1,*}

^a Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Southern California, Los Angeles, CA, United States

^b Emory University School of Medicine, Atlanta, GA, United States

^c Department of Obstetrics and Gynecology, Tokai University School of Medicine, Kanagawa, Japan

^d Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA, United States

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ABSTRACT

Objective: To examine the trends, characteristics, and outcomes of women with gynecologic malignancies who died of suicide in the United States.

Methods: This is a retrospective, observational study using the Surveillance, Epidemiology and End Results program from 1973 to 2013. Women with uterine, ovarian, and cervical cancers who had cause of death recorded as suicide or self-inflicted injury were included, and temporal trends, patient and tumor characteristics, and outcomes were assessed.

Results: Of 467,368 women with gynecologic cancers, there were 309 (0.07%) suicides during the study period. Across the three malignancies, suicide rates significantly decreased during the study period, with uterine cancer exhibiting the highest interval decrease (relative reduction: uterine cancer 88.2%, cervical cancer 78.1%, and ovarian cancer 73.6%; all, $P < 0.05$). Women with cervical cancer were younger at age of suicide (median age, 50 versus 60–68 years), and women with ovarian cancer had a shorter time to suicide from diagnosis (median time, 27 versus 66–67 months) (both, $P < 0.05$). On multivariable analysis, white race (hazard ratio [HR] 3.619), Western U.S. residence (HR 2.012), ovarian cancer (HR 1.991), cervical cancer (HR 1.765), stage IV disease (HR 1.735), and divorced status (HR 1.491) remained independent clinico-pathological characteristics associated with increased risk of suicide (all, $P < 0.05$).

Conclusion: This study found that suicide rates in women with gynecologic malignancies have decreased in the United States. Characteristics of suicide vary across cancer types, and certain risk factors of suicide identified in this study may be useful to triage patients at risk for suicidal behavior and inform prevention strategies.

1. Introduction

Suicide rates in the United States have increased more than 30% over the past decade and a half, and suicide is now the tenth leading cause of death in all age groups (Hedegaard et al., 2018; Ruch et al., 2019). Furthermore, unlike other developed countries life expectancy in the United States is decreasing, considerably in part to the increase in suicide rates (Murphy et al., 2017). Suicide rates in cancer patients are 1.9 times those of the general population and women with gynecologic malignancies in particular are 30% more likely to commit suicide compared to those with other types of malignancy (Ward et al., 2013; Misono et al., 2008).

With advancements in cancer treatments over the past several decades, 5-year survival rates have increased for gynecologic malignancies (Benedet, 2000). Literature on incidence, trends, and risk factors of suicide in women with gynecologic malignancies remains limited. These are critical to define for clinicians to better serve women with gynecologic cancers and develop suicide risk-identification and prevention strategies. The objective of this study was to evaluate population trends of suicide rates and factors associated with suicide in women with uterine, ovarian, or cervical cancer in the United States between 1973 and 2013.

* Corresponding author at: Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Southern California, Norris Comprehensive Cancer Center, 2020 Zonal Avenue, IRD 520, Los Angeles, CA 90033, United States.

E-mail address: koji.matsuo@med.usc.edu (K. Matsuo).

¹ Contributed equally to the work.

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2. Materials and methods

2.1. Data source

This is a retrospective study examining the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program. The SEER program is the largest population-based tumor registry in the United States, covering approximately 35% of the population in the latest version (<https://seer.cancer.gov/>). The Institutional Review Board at the University of Southern California exempted this study due to the use of publicly available de-identified data.

2.2. Eligibility and clinical information

Women who had a diagnosis of uterine cancer, ovarian cancer, or cervical cancer between 1973 and 2013 were eligible for the analysis. SEER*Stat 8.3.2 (IMS Inc., Calverton, MD, USA) was used to generate the datasets for the three cancers and then merged to compile the master dataset. Clinical information for analysis included patient age at cancer diagnosis, year, race/ethnicity, registry area, marital status, cancer type, cancer stage, and survival outcome. Vaginal and vulvar cancers were not examined due to rarity.

2.3. Study definition

Recorded cancer stages were based on the AJCC surgical-pathological staging classification schema or extent of disease codes assigned in each database (Edge and Compton, 2010). Suicide was ascertained by cause of death recorded as "suicide or self-inflicted injury" in the database, and time to suicide was defined as the time interval between the cancer diagnosis and suicide. Cases without suicide were censored at the last follow-up visit. In addition, age at suicide was estimated by adding age at cancer diagnosis and time to suicide.

2.4. Statistical consideration

For continuous variables, normality was assessed with the Kolmogorov-Smirnov test to report mean (\pm standard deviation) or median (interquartile range), and differences were assessed by the one-way ANOVA or Kruskal-Wallis *H* test as appropriate. For ordinal or categorical variables, descriptive statistics with number and percentage per group were reported, and statistical difference was assessed by the chi-squared test. The Kaplan-Meier method was used to construct the cumulative incidence curves of suicide, and difference between the curves was assessed with log-rank test.

To assess the temporal trends of suicide, the National Cancer Institute's Joinpoint Trend Software (version 4.4.0.0, National Cancer Institute, Bethesda, MD, USA) was utilized for analysis (<http://surveillance.cancer.gov/joinpoint>). Calendar years were used as time increments for percent suicide rate with 95% confidence interval (CI) in each year. Linear segmented regression was used for temporal trends, and log-transformation was performed to determine the annual percentage change (APC) of the slope with a 95% CI (Kim et al., 2000).

To identify the independent risk factors for suicide, a Cox proportional hazard regression model was fitted for analysis, as suicide after cancer diagnosis is a time-dependent event. Age, year of diagnosis, race/ethnicity, registry area, marital status, cancer type, and cancer stage were entered in the final model, and adjusted-hazard ratio (HR) with 95% CI was estimated for each variable. All analyses were based upon two-sided hypotheses, and a $P < 0.05$ was interpreted as statistical significance. SPSS 24.0 (IBM, Armonk, NY) was utilized for all analyses.

3. Results

There were 246,736 women with uterine cancer, 133,481 women with ovarian cancer, and 87,151 women with cervical cancer included in this analysis (total, $n = 467,368$). Cancer-specific patient characteristics are shown in Table 1. Of the women included, the majority were white (56.2%), lived in the Western U.S. (51.6%), and were married (49.6%). The majority of women with uterine and cervical cancers had stage I disease (62.6% and 41.1%, respectively), whereas a majority of women with ovarian cancer had stage III-IV disease (61.4%). There were 309 (0.07%) suicides during the study period.

Across the three cancer types, the incidences of suicide were fairly rare as $< 0.1\%$: cervical cancer 80 (0.09%) out of 87,151, ovarian cancer 97 (0.07%), out of 133,481, and uterine cancer 132 (0.05%) out of 246,736. Trends of suicide were examined per cancer type (Fig. 1 and Table 2). Across the three malignancies, suicide rates significantly decreased during the study period, with uterine cancer exhibiting the highest interval decrease (0.18% to 0.02%, relative reduction 88.2%),

Table 1
Patient demographics by cancer type ($N = 467,369$).

Characteristic	Uterine cancer	Ovarian cancer	Cervical cancer
Number	$n = 246,736$	$n = 133,481$	$n = 87,151$
Age			
< 30	63 (55–72)	63 (52–74)	49 (38–62)
30–39	1,260 (0.5%)	4,619 (3.5%)	5,926 (6.8%)
40–49	7,429 (3.0%)	6,229 (4.7%)	18,400 (21.1%)
50–59	24,523 (9.9%)	17,049 (12.8%)	21,062 (24.2%)
60–69	64,335 (26.1%)	28,503 (21.4%)	16,384 (18.8%)
70–79	73,857 (29.9%)	30,782 (23.1%)	12,484 (14.3%)
80–89	49,786 (20.2%)	27,087 (20.3%)	7,973 (9.1%)
≥ 90	22,225 (9.0%)	16,243 (12.2%)	4,120 (4.7%)
≥ 90	3,321 (1.3%)	2,969 (2.2%)	7,092 (1.5%)
Year			
< 1980	21,588 (8.7%)	10,356 (7.8%)	8,916 (10.2%)
1980–1989	28,563 (11.6%)	17,241 (12.9%)	11,648 (13.4%)
1990–1999	41,512 (16.8%)	24,793 (18.6%)	17,629 (20.2%)
2000–2009	103,269 (41.9%)	57,940 (43.4%)	35,601 (40.8%)
≥ 2010	51,804 (21.0%)	23,151 (17.3%)	13,357 (15.3%)
Race/ethnicity			
White	190,461 (77.2%)	102,755 (77.0%)	50,528 (58.0%)
Black	19,177 (7.8%)	9,763 (7.3%)	12,590 (14.4%)
Hispanic	19,372 (7.9%)	11,459 (8.6%)	15,194 (17.4%)
Asian	12,978 (5.3%)	7,538 (5.6%)	6,357 (7.3%)
Others	3,593 (1.5%)	1,689 (1.3%)	1,687 (1.9%)
Unknown	1,155 (0.5%)	277 (0.2%)	795 (0.9%)
Registry area			
West	126,824 (51.4%)	69,115 (51.8%)	45,636 (52.4%)
Central	57,954 (23.5%)	31,171 (23.4%)	20,904 (24.0%)
East	61,958 (25.1%)	33,195 (24.9%)	20,611 (23.6%)
Marital status			
Married	127,653 (51.7%)	65,207 (48.9%)	39,015 (44.8%)
Single	35,956 (14.6%)	21,149 (15.8%)	18,478 (21.2%)
Divorced	21,311 (8.6%)	11,663 (8.7%)	10,516 (12.1%)
Separated	3,183 (1.3%)	1,906 (1.4%)	2,199 (2.5%)
Widowed	47,864 (19.4%)	28,894 (21.6%)	11,922 (13.7%)
Unknown*	10,769 (4.4%)	4,662 (3.5%)	5,021 (5.8%)
Cancer stage			
I	154,564 (62.6%)	28,098 (21.1%)	38,448 (44.1%)
II	10,379 (4.2%)	9,559 (7.2%)	10,862 (12.5%)
III	21,012 (8.5%)	40,433 (30.3%)	12,749 (14.6%)
IV	18,552 (7.5%)	41,507 (31.1%)	8,738 (10.0%)
Unknown	42,229 (17.1%)	13,884 (10.4%)	16,354 (18.8%)

Median (interquartile range) or number (percentage per column) is shown. All the listed covariates showed statistical significance of $P < 0.05$. *Including domestic partner.

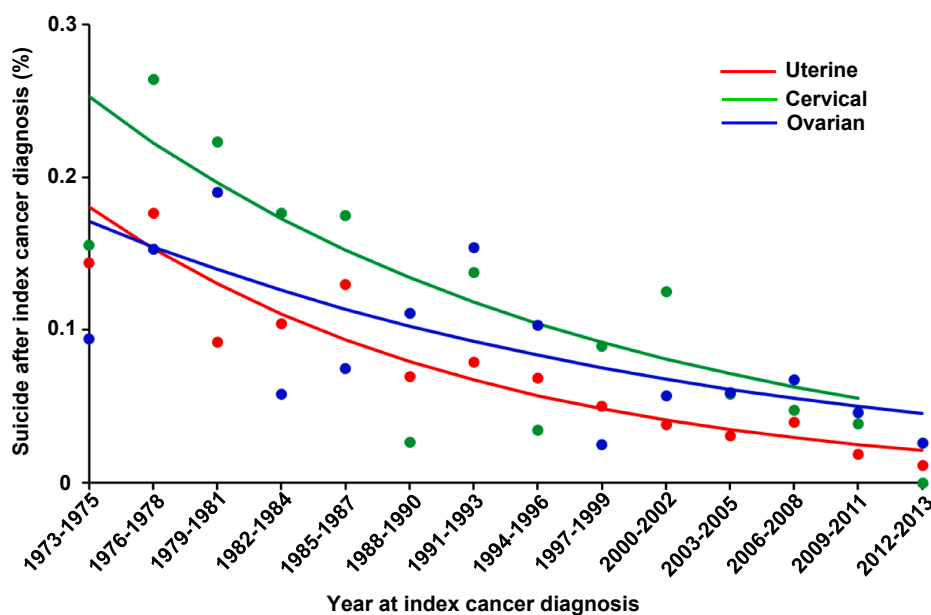


Fig. 1. Trends of suicide among women with gynecologic malignancies between 1973 and 2013. Dots represent observed values and lines represent modeled values. Y-axis is truncated to 0–0.3%.

Table 2
Characteristics of suicide by cancer type ($n = 309$).

Characteristic	Uterine cancer	Cervical cancer	Ovarian cancer
Crude suicide rate	0.05%	0.09%	0.07%
Suicide rate (1973–1975) [†]	0.18%	0.25%	0.17%
Suicide rate (2012–2013) [†]	0.02%	0.06%*	0.05%
Relative decrease	88.2%	78.1%*	73.6%
Age at cancer diagnosis	61 (53–67)	42 (34–51.5)	57 (49.5–64)
Age at suicide	68 (57–79)	50 (41–60)	60 (54–68)
Time from diagnosis to suicide	66 (18–137)	67 (18–137)	27 (12–71)

Number, percentage per column, or median with interquartile range is shown. [†]Based on modeled values. *Results for 2009–2011.

followed by cervical cancer (0.25% to 0.06%, relative reduction 78.1%) and ovarian cancer (0.17% to 0.05%, relative reduction 73.6%) (all, $P < 0.05$).

Women with cervical cancer were younger at suicide compared to those with ovarian and uterine cancers (median age, 50, 60, and 68 years, respectively, $P < 0.05$; Table 2). Similarly, women with cervical cancer were younger at cancer diagnosis compared to those with ovarian and uterine cancers (median age, 42, 57, and 61 years, respectively, $P < 0.05$). The median time between cancer diagnosis and suicide was 52 months (IQR 15–115), and women with ovarian cancer had a shorter time to suicide from cancer diagnosis (median, 27 months) compared to other cancers (66–67 months, $P < 0.05$; Table 2).

Patient demographics associated with suicide were examined. On univariable analysis, age, year, race/ethnicity, registry area, marital status, cancer stage, and cancer type were significantly associated with suicide (all, $P < 0.05$; Table 3). Specifically on a time-dependent analysis (Table 4), younger age, cancer diagnosis in an earlier year, white / Asian races, Western U.S. residence, divorced marital status, stage IV cancer, and ovarian / cervical cancers were significantly

associated with increased risk of suicide on univariable analysis (all, $P < 0.05$),

On a time-dependent multivariable analysis (Table 4), White race (adjusted-HR 3.619, 95%CI 1.696–7.722), Western U.S. residence (HR 2.012, 95%CI 1.469–2.756), ovarian cancer (HR 1.991, 95%CI 1.461–2.712), cervical cancer (HR 1.765, 95%CI 1.290–2.413), stage IV disease (HR 1.735, 95%CI 1.147–2.424), and divorced status (HR 1.491, 95%CI 1.053–2.112) remained independent clinico-pathological characteristics associated with increased risk of suicide (all, $P < 0.05$).

Cancer type-specific characteristics of suicide were examined (Fig. 2 and Table 2). In a cohort-level analysis, women with cervical cancer (0.09%) had the highest rate of suicide for the entirety of the study period followed by those with ovarian (0.07%) and uterine cancer (0.05%, $P < 0.001$). However, when suicide risk was examined over time (Fig. 2), in the first 10 years after cancer diagnosis, women with ovarian cancer had the highest rate of suicide compared to those with other cancer types: 5-year rates, 0.08% for ovarian, 0.06% for cervical, and 0.03% for uterine; and 10-year rates, 0.14% for ovarian, 0.11% for cervical, and 0.06% for uterine ($P < 0.001$).

4. Discussion

Key findings of this study are that suicide rates in women with gynecologic malignancies have significantly decreased in the past decades in the United States. Moreover, this study identified certain risk factors for suicide that may be useful to triage patients at risk for suicidal behavior and inform prevention strategies.

A previous study using the SEER database reported that the incidence of suicide in women with gynecologic malignancies is higher compared to women with other malignancies, however temporal trends of suicide have not been evaluated in this patient population (Ward et al., 2013). Thus, our study adds new insights in the literature by providing the recent trends of suicide.

The downward trending suicide rates in patients with gynecologic malignancy could be explained by two main hypotheses: improvements in prognosis for patients, and an increased awareness in the medical

Table 3
Patient demographics by suicide status (N = 467,369).

Characteristic	No suicide	Suicide	P-value
Number	n = 467,059 (99.93%)	n = 309 (0.07%)	
Age			< 0.001
< 30	61 (51–71)	56 (44–64)	
30–39	11,789 (99.86%)	16 (0.14%)	
40–49	32,019 (99.88%)	39 (0.12%)	
50–59	62,582 (99.92%)	52 (0.08%)	
60–69	109,222 (99.93%)	73 (0.07%)	
70–79	117,123 (99.93%)	82 (0.07%)	
80–89	84,814 (99.96%)	32 (0.04%)	
≥ 90	42,574 (99.97%)	14 (0.03%)	
Year			< 0.001
< 1980	7,091 (99.99%)	1 (0.01%)	
1980–1989	40,795 (99.84%)	65 (0.16%)	
1990–1999	57,387 (99.89%)	65 (0.11%)	
2000–2009	83,870 (99.92%)	64 (0.08%)	
≥ 2010	196,708 (99.95%)	102 (0.05%)	
Race/ethnicity			< 0.001
White	343,478 (99.92%)	266 (0.08%)	
Black	41,523 (99.98%)	7 (0.02%)	
Hispanic	46,009 (99.97%)	16 (0.03%)	
Asian	26,856 (99.94%)	17 (0.06%)	
Others	6,966 (99.96%)	3 (0.04%)	
Unknown	2,227 (100%)	0	
Registry area			< 0.001
West	241,381 (99.92%)	194 (0.08%)	
Central	109,977 (99.96%)	52 (0.05%)	
East	115,701 (99.95%)	63 (0.05%)	
Marital status			0.007
Married	231,708 (99.93%)	167 (0.07%)	
Single	75,542 (99.95%)	41 (0.05%)	
Divorced	43,449 (99.91%)	41 (0.09%)	
Separated	7,280 (99.89%)	8 (0.11%)	
Widowed	88,639 (99.95%)	41 (0.05%)	
Unknown*	20,441 (99.95%)	11 (0.05%)	
Cancer stage			< 0.001
I	220,968 (99.94%)	142 (0.06%)	
II	30,780 (99.94%)	20 (0.06%)	
III	74,158 (99.95%)	36 (0.05%)	
IV	68,762 (99.95%)	35 (0.05%)	
Unknown	72,391 (99.90%)	76 (0.10%)	
Cancer type			< 0.001
Uterus	246,604 (99.95%)	132 (0.05%)	
Ovary	133,384 (99.93%)	97 (0.07%)	
Cervix	87,071 (99.91%)	80 (0.09%)	

Median (interquartile range) or number (percentage per row) is shown. Mann-Whitney *U* test or Chi-squared test for *P*-values. Significant *P*-values are emboldened. *Including domestic partner.

community regarding the association between mental health and chronic disease. The improvement in treatment options and prognosis likely contribute to a decrease in the sense of hopelessness, a known risk factor for suicide, that often accompanies a cancer diagnosis (Benedet, 2000; Westin et al., 2016; Uslu-Sahan et al., 2019).

Our findings support previous literature in that white race and advanced stage disease are risk factors for suicide in women with gynecologic malignancies. In addition, this study provides new information regarding risk stratification by marital status. Our results demonstrate that the highest risk of suicide was seen in women who were divorced. It is well demonstrated in the literature that the presence of social support is protective against suicide and suicide rates are higher in men and women of divorced status in the general population (Bell et al., 2018; Kposowa, 2003).

To our knowledge, our study is the first to examine region as a risk factor for suicide in this population. Regional disparities in suicide risk are well documented, and recent data demonstrates that suicide rates have increased disproportionately in rural counties, of which a large percentage are found in the Western US. Contributing factors could include economic instability, lack of access to care and social stigma that deters people from seeking help within these communities (Hedegaard et al., 2018; Jagodic et al., 2012). Collectively, our results support previously identified risk factors for suicide in this population, while also offering a novel analysis of risk based on marital status and region.

Our study shows that suicide risk is highest for women with ovarian cancer in the first decade after cancer diagnosis, followed by a plateau 10 years from diagnosis. This can be partially explained by data showing the poor prognosis of advanced disease with the 5-year recurrence rate being ~75% (Huang et al., 2008). Thus, for women with ovarian cancer, our results demonstrate that there is ample opportunity to provide these women with support and access to a multidisciplinary team to mitigate this risk.

In contrast to the initially high suicide rate in ovarian cancer in the first several years from diagnosis, suicide rates in women with cervical cancer continued to increase throughout the follow-up time and peaked later in the study period. This delayed increase in the risk of suicide in patients with cervical cancer may be attributed to the stigma of this disease, in that women with cervical cancer can confront serious life-long adverse effects on quality-of-life even after cure of disease. Collectively, our results and this supporting evidence clearly suggest a need for prolonged mental health care and life-long support for women with cervical cancer.

Our study identified that the highest risk characteristics were white or Asian race, Western U.S. residence, divorced marital status, advanced disease, and a diagnosis of cervical / ovarian cancers. This is of importance as clinicians cannot effectively intervene if they are unaware of the risk factors and/or tools and resources to utilize.

Strengths of the study include the large sample size and time span during which data was collected and analyzed. The inclusion of temporal trends and time-dependent analysis of suicide risk enriched the analytic quality. Despite these strengths, a number of limitations exist. First, the SEER database does not have information for previous or comorbid psychiatric diagnoses, such as depression. Studies have shown that a history of psychiatric or mood disorders is the most powerful predictor of suicidal behavior (Hawton and Van Heeringen, 2009). Second, there may be unmeasured bias for analysis. These include cancer recurrence status, tumor burden and site, family support, and performance status; all of which may possibly contribute to the suicide risk. Information for physician-assisted suicide was not available in the database. Lastly, financial distress and debt are common in cancer patients and this has been shown to correlate with increased risk of suicide, yet we were unable to assess the socioeconomic status of these patients (Meltzer et al., 2011; Banegas et al., 2016).

In conclusion, this study showed that suicide rates are decreasing across all three gynecologic malignancies with variable differences in characteristics of suicide in each cancer type, most likely reflecting a distinct reason for suicide in each cancer. It is critically important that physicians be aware of this information, and are prepared to provide patients with adequate counseling and resources at the time of diagnosis to work towards eliminating suicide in this population. While the findings of decreasing suicide are reassuring, there is still opportunity and a clear need for the implementation of systematic depression and suicide screening in this high-risk population.

Author contributions

Conceptualization: C.J.V., K.M.; Data curation: H.M.; Formal

Table 4
Multivariable analysis for risk factors of suicide.

Characteristic	Univariable		Multivariable	
	HR (95%CI)	P-value	Adjusted-HR (95%CI)	P-value
Age	0.991 (0.983–0.998)	0.018	0.993 (0.984–1.003)	0.153
Year	0.982 (0.971–0.993)	0.001	0.989 (0.977–1.001)	0.077
Race/ethnicity		0.004*		< 0.001*
White	3.386 (1.598–7.176)	0.001	3.619 (1.696–7.722)	0.001
Black	1		1	
Hispanic	1.643 (0.663–4.071)	0.284	1.335 (0.534–3.340)	0.537
Asian	2.774 (1.141–6.743)	0.024	2.387 (0.968–5.885)	0.059
Others	2.043 (0.528–7.901)	0.301	1.585 (0.406–6.182)	0.507
Unknown	n/a	0.918	n/a	0.917
Registry area		0.001*		< 0.001*
West	1.724 (1.267–2.344)	0.001	2.012 (1.469–2.756)	< 0.001
Central	1		1	
East	1.324 (0.916–1.912)	0.135	1.413 (0.975–2.048)	0.068
Marital status		0.075*		0.149*
Married	1		1	
Single	0.908 (0.642–1.283)	0.584	0.941 (0.659–1.343)	0.737
Divorced	1.517 (1.074–2.143)	0.018	1.491 (1.053–2.112)	0.024
Separated	1.829 (0.900–3.718)	0.095	1.841 (0.899–3.771)	0.095
Widowed	0.901 (0.630–1.288)	0.566	1.025 (0.700–1.502)	0.898
Unknown [†]	0.994 (0.540–1.830)	0.984	1.091 (0.590–2.017)	0.782
Cancer stage		< 0.001*		0.019*
I	1		1	
II	1.296 (0.803–2.094)	0.288	1.141 (0.700–1.860)	0.596
III	1.389 (0.956–2.017)	0.085	1.110 (0.747–1.649)	0.605
IV	2.326 (1.588–3.406)	< 0.001	1.735 (1.147–2.624)	0.009
Unknown	1.627 (1.221–2.169)	0.001	1.532 (1.121–2.095)	0.007
Cancer type		< 0.001*		< 0.001*
Uterus	1		1	
Ovary	2.120 (1.621–2.771)	< 0.001	1.991 (1.461–2.712)	< 0.001
Cervix	1.750 (1.324–2.314)	< 0.001	1.765 (1.290–2.413)	< 0.001

Cox proportional hazard regression models for analysis. Significant P-values are emboldened. All listed covariates were entered in the final model. *P-value for interaction. [†]Including domestic partner. Abbreviations: HR, hazard ratio; and CI, confidence interval.

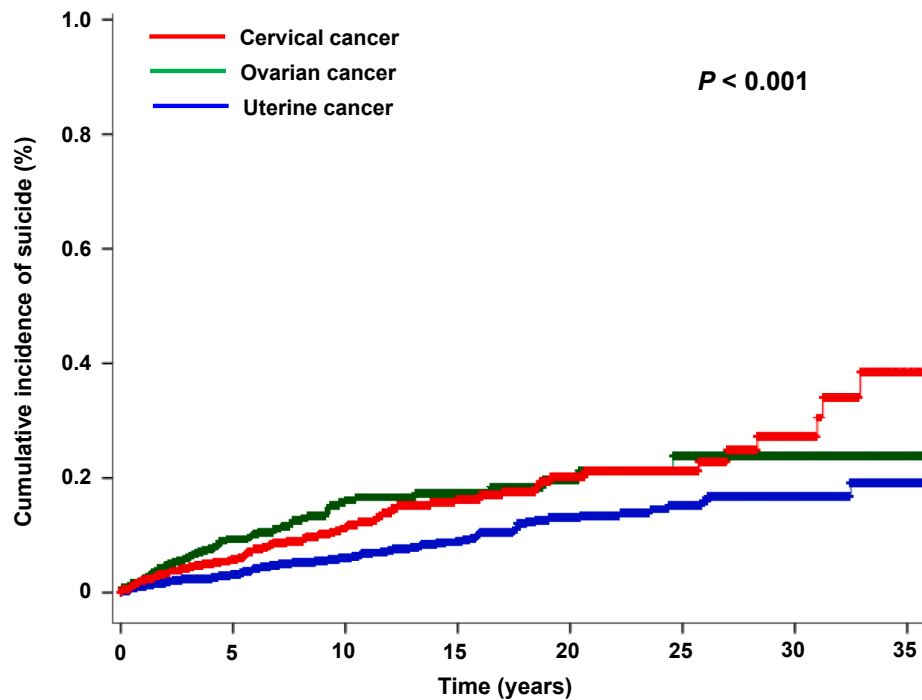


Fig. 2. Cumulative incidence of suicide per cancer type. Log-rank test for P-value. The Y-axis is truncated to 0–1%.

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Declaration of Competing Interest

Consultant, Quantgene (L.D.R.); Honorarium, Chugai, textbook editorial expense, Springer, and meeting attendance expense, VBL therapeutics (K.M.); none for others.

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