BMJ Open Suicide after cancer diagnosis in South Korea: a population-based cohort study

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ABSTRACT

Objective The present study aimed to determine whether the suicide risk increased after a cancer diagnosis.

Design Population-based cohort study.

Setting and participants This study incorporated the National Health Insurance Service-National Sample Cohort in South Korea, Of the 975 348 subjects, 39 027 with cancer and 936 321 who were cancer free participated between 2005 and 2013.

Primary outcome measure Suicide.

Results A total of 110 suicides (82 men, 28 women) were identified among these 39027 subjects with cancer during a total of 127 184 person-years; among the 936 321 cancer-free subjects, 2163 suicides were reported during a total of 8222479 person-years. Cox proportional hazards models were used to compare all-cause and suicide mortalities after cancer diagnosis following adjustment for possible confounding covariates. After adjusting for factors related to suicide, we identified an elevated relative risk of suicide among patients with cancer (HR: 1.480, 95% CI: 1.209 to 1.812). Among men, the relative risk was substantially increased among patients with lip, oral cavity/pharyngeal, colon and rectal, pancreatic and lung cancers when compared with cancer-free subjects; whereas among women, the relative risk was substantially increased among patients with colon and rectal cancers. Conclusion Our study observed an increased risk of suicide among patients with cancer that varied according to the anatomical cancer site, even after accounting for clinical comorbidities and psychiatric illness. Our findings indicate a need for social support and suicide prevention strategies for patients with cancer.

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INTRODUCTION

Suicide is considered a major public health challenge and is among the leading global causes of a loss of life years. Notably, South Korea has the highest suicide rate among member nations of the Organization for Economic Co-operation and Development.² Suicide rates have continued to increase in South Korea throughout the past two decades with a peak in 2010, leading to the current designation of suicide as the fourth leading cause of death nationwide.

A cancer diagnosis is a stressful and lifethreatening event that causes considerable physical and psychological suffering. 4 5 The associated distress might not only worsen the quality of life⁶ and accelerate disease

Strengths and limitations of this study

- ► The strengths of this study included the populationbased design and acquisition of data from the National Health Insurance Service-National Sample Cohort, which is representative of the entire Korean population.
- This study featured a robust follow-up resulting from the use of unique personal identification numbers for Korean residents, which were linked to the national mortality database.
- We were unable to examine the risk factors associated with specific cancer types because of the small number of suicides in each specific cancer group.
- We were unable to identify some potential risk factors known to have important influences on suicide among patients with cancer.
- The use of administrative claims data is associated with a reliance on International Classification of Diseases-10 codes to determine comorbidity could lead to misclassification consequent to miscoding behaviours.

progression,7 but may also promote noncancer mortality.^{8 9} Patients with cancer, particularly, have a higher risk of suicide relative to that of the general population, and this risk may increase by up to twofold in many countries. 10-16 A large body of evidence has identified many factors related to suicide among patients with cancer, including particular clinical characteristics, age at diagnosis, prognosis, stage, time since diagnosis, psychiatric health, and sociodemographic factors such as sex, race, and marital status. 17 Previous studies also have found that the incidence of suicide is relatively high among patients with pancreatic, ¹⁰ ¹⁸ ¹⁹ lung, ¹⁰ ¹² ¹³ ¹⁹ ²⁰ colon and rectal, ^{13 21} oral cavity/pharyngeal, ^{12 13 18} laryngeal, ¹³ stomach ¹² 19 and cervical cancer. ²¹

Despite the accumulation of evidence in support of an association between cancer and suicide, several studies have calculated the standardised mortality ratios (SMRs) to compare the suicide rate between patients with cancer and the general population while only evaluating differences in sociodemographic and clinical characteristics. 12 13 16



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Additionally, previous studies have been limited by a failure to adjust for underlying psychiatric conditions, ¹⁰ ¹² ¹³ ¹⁶ even though pre-existing psychiatric conditions might modify the impact of a cancer diagnosis on the risk of suicide, ²² particularly as cancer itself has been identified as a suicide risk factor when coupled with comorbidities such as psychiatric disease. Therefore, we investigated whether the suicide rate is higher among Korean patients with cancer than among the general population after controlling for underlying diseases including psychiatric disorders as well as sociodemographic and clinical characteristics. We further compared the risk of suicide according to the anatomical site of cancer with the risk observed in the general population.

METHODS AND MATERIALS

Data sources

As described in detail previously,²³ data were acquired from the National Health Insurance Service-National Sample Cohort (NHIS-NSC) from 2002 to 2013 and included 1025340 representative subjects (2.2\% of the population) who were randomly stratified and selected based on age, sex, insurance type, income, residential region and individual total medical costs at 2002. As all Korean citizens are obligated to enrol in the single-payer, national health insurance and medical aid programme administered by the National Health Insurance Corporation, this sample cohort is representative of the general Korean population. The NHIS-NSC database includes information regarding patients' unique de-identification numbers, age, sex, insurance type, diagnosis according to the International Classification of Diseases (ICD-10), medical costs and prescribed drugs. In addition, these numbers are linked to mortality information from the Korean National Statistical Office (KNSO). By law, all causes of death must be reported to the KNSO within 1 month of occurrence. Details of the NHIS-NSC database have been provided in a previous report.²⁴

Study participants and follow-up

Of the 1 025 340 subjects, we eliminated 17297 patients who had been diagnosed with cancer between 2002 and 2004, thus ensuring the selection of cancer-free subjects at baseline. We additionally eliminated 32695 subjects for whom information was missing due to a follow-up loss (death, emigration or disqualification from national health insurance) between 2002 and 2004. Overall, this study included 975348 subjects (online supplemental figure 1).

Outcome and follow-up

The outcome variables for this study were all-cause mortality and suicide (ICD-10 code X64–80). All subjects were observed from 1 January 2005 to follow-up loss, death (by suicide or any other cause) or 31 December 2013, whichever occurred first. For subjects who did not develop cancer, follow-up ended on the date of suicide,

other death, emigration or 31 December 2013, whichever occurred first; accumulated person-time was defined as the unexposed person-time. For those who were diagnosed with cancer, the follow-up ended with the occurrence of suicide, other death, emigration out of Korea or 31 December 2013, whichever came first; accumulated person-time was defined as the exposed person-time. Participants diagnosed with cancer during the study period contributed unexposed person-time prior to the date of diagnosis (as recorded in the national health insurance data) and exposed person-time thereafter.

Cancer diagnosis

Cancer diagnoses were organised into 13 diagnostic groups: lip, oral cavity and pharynx (ICD-10 codes C00, C11, C12, C13, C14); stomach (C16); colon and rectum (C17, C18, C19, C20, C21); liver (C22); gallbladder and pancreas (C23, C24, C25); lung (C33, C34); breast (C50); gynaecological (cervix, uterus and ovary: C53, C54, C56); prostate (C61); testis and other male genital organs (C62); bladder (C67); thyroid (C73); and others (oesophagus: C15; larynx: C32; skin: C43, C44; kidney: C64, C65, C66, C68; brain and central nervous system: C70, C71, C72; Hodgkin's lymphoma: C81; non-Hodgkin's lymphoma: C82, C83, C84, C85, C96; leukaemia: C91, C92, C93, C94, C95).

Covariates

Sociodemographic and clinical risk factors for suicide were included in this study. Sociodemographic factors recorded on the date of entry into the study included sex, age (≤ 39 , 40-49, 50-59, 60-69 and ≥ 70 years), region (urban or rural) and household income (income quintiles Q1 (low) to Q5 (high)). We used the average monthly insurance premium as a proxy for household income. In Korea, individuals qualify for medical aid if their household income is less than \$600 per month; otherwise, they qualify for national health insurance. Individuals enrolled in the national health insurance programme were distributed between the 1st and 100th income percentiles, whereas those receiving medical aid were classified at the zero percentile. In this study, the following household income classification was used: Q1, <20%; Q2, 21%-40%; Q3, 41%-60%; Q4, 61%-80% and Q5, >80%. We also included the experience of at least one disability (according to the disabled person welfare law), including intellectual disability, brain lesion, deafness, physical disability, visual impairment, mental disorder, kidney disorder, language disorder, autism, heart disability, respiratory disorder, hepatopathy, facial disorders, having undergone ostomy and epilepsy.

Regarding clinical factors, patients' comorbidities were identified via review of their medical histories 12 months prior to study entry. Using the Charlson Comorbidity Index, we measured 17 comorbidities to control for the case mix.²⁵ Additionally, underlying diagnoses related to psychiatric disorders included substance abuse (F10–F19), schizophrenia disorder (F20–F29), bipolar disorder

Continued

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162128 1 28415	17047	43.68	60965	3503	20.55	42 0.	0.25 78	756167	80.76	6643279	19478	2.58	1624	0.21
28415	13327	34.15	42 582	3963	29.74	37 0.	0.28 14	148801	15.89	1311172	6694	4.50	371	0.25
11501	5283	13.54	15114	1917	36.29	20 0.	0.38	23132	2.47	201010	2604	11.26	111	0.48
81.1 ≥3	3370	8.64	8524	1406	41.72	11 0.	0.33	8221	0.88	67017	1901	23.12	22	69.0
Substance abuse														
No 974052 99.87	38839	99.52	126 696	10701	27.55	105 0.	0.27 93	935213	99.88	8213410	30 463	3.26	2136	0.23
Yes 1296 0.13	188	0.48	488	88	46.81	5 2.	2.66	1108	0.12	6906	214	19.31	27	2.44
Schizophrenia														
No 972723 99.73	38887	99.64	126828	10728	27.59	110 0.	0.28 93	933836	99.73	8201 446	30426	3.26	2104	0.23
Yes 2625 0.27	140	0.36	357	61	43.57	0 0.	0.00	2485	0.27	21033	251	10.10	29	2.37
Bipolar disorders														

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	Total		Cancer						O	Cancer free						
						All-cause	All-cause mortality	Suicide	 				All-cause	All-cause mortality	Suicide	_
Characteristic	u	%	Ľ	%	ΡY	u	*%	u %	u *%		%	ΡY	u	*%	u	*%
No	974537	99.92	38932	99.76	126989	10761	27.64	108 0	0.28 93	935 605	99.92	8216249	30624	3.27	2147	0.23
Yes	811	0.08	92	0.24	195	28	29.47	2	2.11	716	0.08	6230	53	7.40	16	2.23
Major depressive disorder	sorder															
No	964018	98.84	37644	96.46	123 124	10367	27.54	103 0	0.27 92	926374	98.94	8136480	29787	3.22	2028	0.22
Yes	11330	1.16	1383	3.54	4060	422	30.51	7 0	0.51	9947	1.06	85999	890	8.95	135	1.36
Stress-related disorders	ders															
No	943433	96.73	35604	91.23	116429	9719	27.30	102 0	0.29 90	907 829	96.96	7971462	28 968	3.19	1996	0.22
Yes	31915	3.27	3423	8.77	10755	1070	31.26	8	0.23	28492	3.04	251017	1709	00.9	167	0.59
Sleep disorders																
No	965698	99.01	37165	95.23	122 067	10175	27.38	103 0	0.28 92	928533	99.17	8155600	29 788	3.21	2082	0.22
Yes	9650	0.99	1862	4.77	5117	614	32.98	7 0	0.38	7788	0.83	62899	889	11.41	81	1.04
Personality disorders	Š															
No	975030	29.97	39014	99.97	127 158	10 782	27.64	109 0	0.28 90	936016	99.97	8219825	30 660	3.28	2155	0.23
Yes	318	0.03	13	0.03	22	7	53.85	1	7 69	305	0.03	2654	17	5 57	α	2 62

 $^*\%$ of patients with cancer or subjects who were cancer free. PY, person-years.

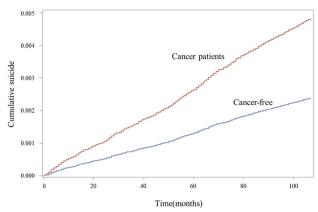


Figure 1 Cumulative suicide rates of patients with cancer versus cancer-free subjects.

(F31), major depressive disorder (F32-F33), anxiety and stress disorders (F40-F48), sleep disorders (F51, G47) and personality disorders (F6).

Statistical analysis

For this study, we determined the distributions of general characteristics by diagnosis of cancer. Additionally, relationships between household income level and suicide were analysed using time-to-event methods. The Kaplan-Meier method was used to generate curves of unadjusted mortality rates, which were compared using the log-rank test. To determine whether the suicide rate was higher among patients with cancer relative to the general population, multivariable analyses involving Cox proportional hazards models were conducted to calculate adjusted HRs plus 95% CIs as estimates of relative suicide rates. The proportionality assumption was tested by examining log curves (-log (survivor function)) versus time. A p value of <0.05 was considered to indicate statistical significance. All statistical analyses were conducted using the SAS software package (V.9.4; SAS Institute).

Patient and public involvement

Patients and the public were not involved in the design or planning of this study.

RESULTS

Table 1 presents the general characteristics of the study participants. Of the 975348 subjects, 39027 (4.0%) received a diagnosis of cancer between 2005 and 2013, and a total of 110 suicides (82 men, 28 women) were identified among these subjects with cancer during a total of 127184 person-years. Of the 936321 cancer-free subjects with a total of 8222479 person-years, 2163 died by suicide during the study period. The suicide rate was 86 per 100.000 person-years in those with cancer compared with 26 in those without cancer. Using Kaplan-Meier survival curves of the unadjusted cumulative suicide rates among patients with cancer and cancer-free subjects (figure 1), a significantly higher risk of suicide was identified among the cancer group (log-rank, p<0.001).

Table 2 presents the results of a Cox proportional hazards analysis of the association between cancer diagnosis and suicide risk. Even after adjusting for factors related to suicide among patients with cancer, we observed an elevated relative risk of suicide (HR: 1.480, 95% CI: 1.209 to 1.812). Notably, the relative suicide risk was significantly more elevated among male subjects (HR: 1.513, 95% CI: 1.191 to 1.922), compared with female subjects (HR: 1.320, 95% CI: 0.895 to 1.947). Higher suicide rates were found to associate with male sex, older age, lower income, presence of a disability, higher Charlson Comorbidity Index and presence of psychiatric illness.

Figures 2–4 present the adjusted risks of suicide according to anatomical cancer site in both male and female subjects. Among men, the relative risk was increased substantially for patients with lip, oral cavity and pharvngeal (HR: 1.987, 95% CI: 1.025 to 3.853), colon and rectal (HR: 1.906; 95% CI: 1.174 to 3.093), pancreatic (HR: 3.777; 95% CI: 1.211 to 11.784) and lung cancers (HR: 2.502; 95% CI: 1.463 to 4.280), compared with the cancer-free group. Among women, the relative risk was substantially increased for patients with colon and rectal cancers (HR: 2.376, 95% CI: 1.120 to 5.041).

DISCUSSION

Summary

In this population-based cohort study, we used data from the NHIS-NSC to investigate whether the risk of suicide was higher among patients with cancer than among the general population. We found that the suicide risk was indeed higher among those diagnosed with cancer during the study period, and that the risk of suicide varied according to the anatomical cancer site, as men diagnosed with lip, oral cavity and pharyngeal, colon and rectal, liver, pancreatic and lung cancers and women diagnosed with colon and rectal cancers had a significantly higher risk of suicide relative to the general population.

Comparison with studies

Our findings were consistent with those of other studies that examined the relationship between cancer diagnosis and suicide, in which the incidence rates of suicide among male and female patients with cancer were, respectively, 1.5 and 1.3 times higher than the rates in the general population after adjusting for factors associated with suicide. Similarly, in the USA, the suicide risk among patients with cancer is approximately twofold of the risk in the general population, ¹³ and European studies have also observed increased suicide rates among patients with cancer. For example, Yousaf et al¹⁴ calculated SMRs of 1.7 and 1.4 for suicide among men and women, respectively, from a Danish cancer registry relative to the general Danish population. A similar study in Norway reported SMRs of 1.55 and 1.35. 12 In Sweden, Björkenstam et al 11 observed SMRs of 2.5 (men and women combined) for the period from 1965 to 1974 and 1.5 for the period from

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Table 2 HRs for suit	HRs for suicide determined through a Cox proportior	igh a Cox proportion	nal hazards model analysis	lel analysis					
	Overalls	Overall suicide (male +female)		Male			Female		
	HR	12 % S6	P value	HR	12 % S6	P value	H	12%56	P value
Cancer									
Yes	1.480	1.209 to 1.812	0.000	1.513	1.191 to 1.922	0.001	1.320	0.895 to 1.947	0.161
No	1.000			1.000			1.000		
Sex									
Male	2.332	2.133 to 2.549	<0.0001						
Female	1.000								
Age									
<39	1.000			1.000			1.000		
40–49	1.906	1.696 to 2.143	<0.0001	2.252	1.952 to 2.598	<0.0001	1.357	1.103 to 1.669	0.004
50–59	2.098	1.837 to 2.396	<0.0001	2.799	2.394 to 3.272	<0.0001	1.067	0.820 to 1.389	0.630
69-09	3.281	2.871 to 3.750	<0.0001	4.360	3.713 to 5.120	<0.0001	1.814	1.420 to 2.316	<0.0001
≥70	6.355	5.561 to 7.263	<0.0001	7.875	6.611 to 9.381	<0.0001	4.436	3.615 to 5.443	<0.0001
Income									
Q1 (low)	1.972	1.742 to 2.233	<0.0001	2.129	1.824 to 2.485	<0.0001	1.727	1.403 to 2.125	<0.0001
02	1.692	1.479 to 1.936	<0.0001	1.815	1.538 to 2.141	<0.0001	1.478	1.173 to 1.863	0.001
Q3	1.352	1.180 to 1.549	<0.0001	1.442	1.221 to 1.703	<0.0001	1.193	0.941 to 1.513	0.145
Q4	1.287	1.130 to 1.465	0.000	1.348	1.149 to 1.581	0.000	1.177	0.941 to 1.471	0.153
Q5 (high)	1.000			1.000			1.000		
City									
Rural	1.087	0.997 to 1.185	0.058	1.098	0.988 to 1.221	0.082	1.081	0.930 to 1.256	0.310
Urban	1.000			1.000			1.000		
Disability									
No	1.000			1.000			1.000		
Yes	1.669	1.457 to 1.912	<0.0001	1.723	1.479 to 2.006	<0.0001	1.304	0.955 to 1.782	0.095
Charlson Comorbidity Index	lex								
0	1.000			1.000			1.000		
	0.935	0.836 to 1.046	0.243	0.901	0.783 to 1.038	0.149	0.989	0.823 to 1.188	0.905
2	1.225	1.018 to 1.475	0.032	1.367	1.093 to 1.710	0.006	0.986	0.706 to 1.377	0.933
≥3	1.328	1.031 to 1.710	0.028	1.381	1.017 to 1.874	0.039	1.254	0.798 to 1.971	0.327
Substance abuse									
No	1.000			1.000			1.000		
Yes	3.196	2.210 to 4.622	<0.0001	3.049	2.010 to 4.625	<0.0001	4.742	2.082 to 10.804	0.000
Schizophrenia									
No	1.000			1.000			1.000		
Yes	4.004	2.974 to 5.390	<0.0001	4.366	3.021 to 6.310	<0.0001	3.507	2.112 to 5.823	<0.0001
									Continued

Table 2 Continued									
	Overall su	Overall suicide (male +female)		Male			Female		
	HR	95% CI	P value	HR	95% CI	P value	HH	95% CI	P value
Bipolar disorders									
OZ	1.000			1.000			1.000		
Yes	1.912	1.153 to 3.168	0.012	2.264	1.252 to 4.094	0.007	1.281	0.461 to 3.559	0.635
Major depressive disorder									
ON	1.000			1.000			1.000		
Yes	2.891	2.366 to 3.533	<0.0001	2.239	1.678 to 2.989	<0.0001	4.030	3.042 to 5.340	<0.0001
Stress-related disorders									
° N	1.000			1.000			1.000		
Yes	1.349	1.138 to 1.600	0.001	1.449	1.156 to 1.816	0.001	1.284	0.990 to 1.667	0.060
Sleep disorders									
No	1.000			1.000			1.000		
Yes	1.717	1.362 to 2.164	<0.0001	1.377	0.990 to 1.915	0.057	2.261	1.630 to 3.137	<0.0001
Personality disorders									
° N	1.000			1.000			1.000		
Yes	2.949	1.495 to 5.816	0.002	3.428	1.504 to 7.812	0.003	1.822	0.521 to 6.368	0.347

Type of cancer	Total	Sui	cide	
Type of cancer	n	n	Row%	HR(95% CI)
Cancer-free	936,321	2,163	0.23	. 1441
Lip, oral cavity and pharynx	2,054	11	0.54	
Stomach	5,203	15	0.29	1.225
Colon and rectum	4,976	24	0.48	2.065
Liver	3,076	9	0.29	3.617
Pancreas	972	4	0.41	2.250
Lung	3,647	15	0.41	
Breast	2,673	3	0.11	1.146
Cervix, uterus, and ovary	1,775	4	0.23	0.343
Testis	1,498	2	0.13	-
Blader	807	4	0.50	1.644
Thyroid	5,531	4	0.07	0.828
Others	6,815	15	0.22	1.208
				0 1 2 3 4 5

Figure 2 Adjusted risks of suicide by cancer type (all participants).

1985 to 1994. In Asia, a Korean study used cancer registry data to calculate SMRs of 2.05 among male patients and 1.87 among female patients for the period from 1993 to $2005.^{10}$

Several studies have found associations of cancers at certain anatomical sites with particularly elevated suicide rates. However, reports differ with regard to the anatomical sites associated with the greatest suicide risks. 11-1416 In our study of patients in Korea, we found that the suicide risks were especially high among male patients with lip, oral cavity and pharyngeal, colon and rectal, liver, pancreatic, and lung cancers and among female patients with colon and rectal cancer, findings that were concordant with reports from Western countries. 11-13 26 Although the reasons underlying the associations of particular cancer types with increased suicide rates are unknown, patients with those cancers might struggle with grave prognoses. 8 14 16 This is corroborated by a finding that the suicide risk was higher among patients with cancers that conferred a poor prognosis (ie, 5-year relative survival of <10%), especially within the first year of diagnosis. Additionally, certain types of cancers, especially head and neck cancers, might have more profound effects on the quality of life and induce stronger degrees of anxiety or fear because of symbolic values, changes in appearance, or difficulties with speech, swallowing, and breathing.² One study identified a 25% prevalence of depression among patients with lung cancer,²⁸ and another study suggested that the lower quality of life among patients with lung cancer is related to emotional distress.²⁹ Similarly, a high prevalence of depression has been observed among patients with head and neck cancer.³⁰

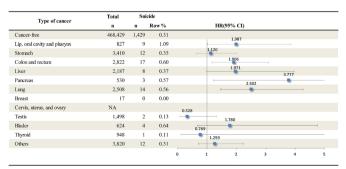


Figure 3 Adjusted risks of suicide by cancer type (men).

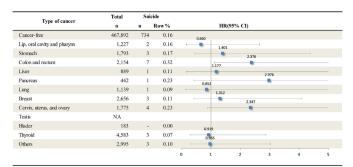


Figure 4 Adjusted risks of suicide by cancer type (women).

Strengths and limitations

The strengths of this study included the population-based design and acquisition of data from the NHIS-NSC, which is representative of the entire Korean population. In addition, this study featured a robust follow-up resulting from the use of unique personal identification numbers for Korean residents, which were linked to the national mortality database. Despite these strengths, our findings should be interpreted in light of the study's limitations. First, we were unable to examine the risk factors associated with specific cancer types because of the small number of suicides in each specific cancer group. Further study needs to examine the relationship between cancer and suicide according to cancer stage and cancer type by linking cancer registration data and claims data (not sample data) of all citizens. Second, as with other studies that employ administrative claims data, ²³ we were unable to identify some potential risk factors known to have important influences on suicide among patients with cancer, such as the family history of suicide attempts, history of suicide attempts and patients' histories of selfharm, which were unknown. Third, the use of administrative claims data is associated with particular issues. For example, a reliance on ICD-10 codes to determine comorbidity could lead to misclassification consequent to miscoding behaviours. Fourth, an inaccuracy on the ICD-10 codes for the diagnoses might have yielded some misclassifications due to the unavoidable characteristics of claims data, including miscoding of data by the original coder. Fifth, given the retrospective nature of this chart review study, we could not evaluate psychiatric symptoms after a cancer diagnosis, which are known to have an important influence on suicidal behaviours among patients with cancer, despite the availability of information regarding the history of psychiatric care. Sixth, our limited data set did not permit consideration of the influence of disease stage at diagnosis in our suicide risk analysis.

CONCLUSION

In our study of a cohort representative of the Korean population, patients with cancer were found to exhibit an increased risk of suicide, which varied according to the anatomical cancer site even after accounting for clinical comorbidities and psychiatric illness. These results

provide further evidence of a relationship between cancer diagnosis and suicide. Further research into the suicide risks of patients with cancer should extend the range of concerns to include disease stage and clinical treatment.

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Patient consent for publication Not required.

Ethics approval This study adhered to the tenets of the Declaration of Helsinki. The study design was reviewed and approved by the ethical review board at the Graduate School of Public Health in Yonsei University (2-1040939-AB-N-01-2014-239). Since our study used administrative cohort data, the requirement for informed consent was waived as the National Health Insurance Service-National Sample Cohort was constructed after anonymisation according to strict confidentiality guidelines.

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