ORIGINAL ARTICLE

Suicide and Cardiovascular Death after a Cancer Diagnosis

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ABSTRACT

BACKGROUND

Receiving a diagnosis of cancer is a traumatic experience that may trigger immediate adverse health consequences beyond the effects of the disease or treatment.

METHODS

Using Poisson and negative binomial regression models, we conducted a historical cohort study involving 6,073,240 Swedes to examine the associations between a cancer diagnosis and the immediate risk of suicide or death from cardiovascular causes from 1991 through 2006. To adjust for unmeasured confounders, we also performed a nested, self-matched case-crossover analysis among all patients with cancer who died from suicide or cardiovascular diseases in the cohort.

RESULTS

As compared with cancer-free persons, the relative risk of suicide among patients receiving a cancer diagnosis was 12.6 (95% confidence interval [CI], 8.6 to 17.8) during the first week (29 patients; incidence rate, 2.50 per 1000 person-years) and 3.1 (95% CI, 2.7 to 3.5) during the first year (260 patients; incidence rate, 0.60 per 1000 person-years). The relative risk of cardiovascular death after diagnosis was 5.6 (95% CI, 5.2 to 5.9) during the first week (1318 patients; incidence rate, 116.80 per 1000 person-years) and 3.3 (95% CI, 3.1 to 3.4) during the first 4 weeks (2641 patients; incidence rate, 65.81 per 1000 person-years). The risk elevations decreased rapidly during the first year after diagnosis. Increased risk was particularly prominent for cancers with a poor prognosis. The case-crossover analysis largely confirmed results from the main analysis.

CONCLUSIONS

In this large cohort study, patients who had recently received a cancer diagnosis had increased risks of both suicide and death from cardiovascular causes, as compared with cancer-free persons. (Funded by the Swedish Council for Working Life and Social Research and others.)

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A large body of evidence suggests high levels of distress and psychiatric symptoms among patients who receive a diagnosis of cancer.[1-9] Patients with cancer have been shown to be at increased risk for suicide[10-17] and cardiovascular events.[18-22] However, most results have been interpreted to be consequences of treatment or the burden of living with a progressing cancer. The psychological stress induced by the diagnosis itself may also give rise to such serious consequences. However, only a few studies have explored the period immediately after a cancer diagnosis.[13,14,23]

We recently observed that patients with prostate cancer both in Sweden and the United States have increased risks of suicide and cardiovascular events within weeks after their cancer diagnosis.[24,25] If the observations are proved to be independent from shared causes between cancer and these immediate health outcomes, they may have important implications for both cancer-screening policy and organized supportive care. We therefore used the nationwide registration of cancers and causes of death in Sweden to estimate the risk of death from suicide or cardiovascular diseases among all patients in whom cancer had recently been diagnosed.

Methods

Study Design

We conducted a record-linkage study that was based on the Swedish Population and Housing Census in 1990, including 6,073,240 persons born in Sweden who were 30 years of age or older between January 1, 1991, and December 31, 2006. We used the individually unique national registration numbers to link the census data to the nationwide Cancer, Causes of Death, and Migration Registers. Reporting of cancers by clinicians and pathologists has been required by Swedish law since 1958, and the completeness of the Cancer Register approaches 100%. The study was approved by the regional ethics review board in Stockholm.

Ascertainment of Cancer Diagnosis

All study patients were followed from January 1, 1991, or their 30th birthday, whichever came later, until death, emigration, or December 31, 2006, whichever occurred first. During follow-up, we identified 534,154 patients who had received a first diagnosis of cancer (i.e., that was not detected on autopsy), including 95,786 with prostate cancer, 74,977 with breast cancer (among women), 62,719 with colorectal cancer, 47,169 with melanoma or other skin cancer, 36,648 with lymphatic or hematopoietic cancer, 34,743 with lung cancer, and 13,447 with tumors of the central nervous system (CNS). In addition to the 6 most common forms of cancer, 26,335 highly fatal cancers of the esophagus, liver, and pancreas were pooled together as a group. Another 142,330 patients had other types of cancer.

Ascertainment of Suicide and Cardiovascular Death

Individuals who had not received a cancer diagnosis during follow-up contributed person-time to the cancer-free group. Patients with cancer contributed person-time to the cancer-free group before diagnosis and to the cancer-diagnosis group from the time of diagnosis onward. From the Causes of Death Register, we identified deaths from suicide or cardiovascular events as the underlying cause. We also separately evaluated myocardial infarction, other diseases of the heart, embolism or thrombosis, and stroke. To preclude potential misdiagnosis between stroke look-alikes (e.g., brain tumor) and stroke, we excluded stroke from deaths from cardiovascular causes in the analysis of CNS tumors and excluded CNS tumors from "any cancer" in the analysis of deaths from cardiovascular causes (termed as "any cancer but CNS tumors"; 520,707 patients).

Statistical Analysis

We first calculated the unadjusted incidence rates (number of outcomes divided by accumulated person-years) of suicide and cardiovascular death among patients with a cancer diagnosis and those without a cancer diagnosis. In calculating relative risks and 95% confidence intervals, we compared the rates of suicide and cardiovascular death in the cancer group with those in the cancer-free group. We used Poisson regression for suicide and negative binomial regression for cardiovascular death. Negative binomial regression was chosen when the assumption of equality of the mean and variance in the Poisson model did not hold true. In all statistical models, we adjusted for age at follow-up, sex, calendar period at follow-up, civil status (cohabitation or no cohabitation), socioeconomic status (blue-collar, white-collar, self-employed, or unclassified), and educational level. Narrower categories of age and calendar periods were chosen for cardiovascular death to minimize residual

confounding. Information on civil status and socioeconomic status was obtained from the Census. The highest educational level at cohort entry was retrieved from the Swedish Education Register.

We first calculated the relative risks of suicide and cardiovascular death according to the time since the cancer diagnosis. We selected time windows to focus on the hypothesized most stressful time period[24,25] while ensuring sufficient statistical power to disclose real associations. For cardiovascular death, we studied week 1, weeks 2 to 4, weeks 5 to 26, weeks 27 to 52, and week 53 onward after the cancer diagnosis. Because of the low incidence of suicide, we studied weeks 1 to 12, weeks 13 to 52, and week 53 onward.

To highlight the immediate effect of a diagnosis of any cancer, we separately calculated the relative risk of suicide during the first week after diagnosis. In addition, we studied week 53 onward to compare the risks of both outcomes during the period immediately after diagnosis with the risks during the subsequent periods when the burden of advancing disease or treatment may be expected. We conducted stratified analyses according to age at follow-up, sex, calendar period at follow-up, civil status, socioeconomic status, educational level, and region of residence during the first 4 weeks after a cancer diagnosis for cardiovascular death and during the first 52 weeks after a cancer diagnosis for suicide.

Because preexisting illnesses may modify the effect of a cancer diagnosis on rates of suicide and cardiovascular death, we linked the cohort to the Swedish Inpatient Register, which contains nationwide information on hospital admissions since 1987. We stratified the analyses according to previous hospitalizations for psychiatric or cardiovascular diseases, either as the primary or a secondary diagnosis, since 1987. Patients were classified as having preexisting psychiatric or cardiovascular diseases during the entire follow-up if they were admitted to a hospital before entry in the cohort or from the real admission date if they were admitted after entry.

For the statistical analyses, we used SAS software, version 9.2 (SAS Institute). All codes for discharge diagnoses from the *International Statistical Classification of Diseases and Related Health Problems* are listed in Section 1 in the Supplementary Appendix, available with the full text of this article at NEJM.org.

Cancer, suicide, and cardiovascular diseases may share risk factors, leading to spurious associations among these conditions. To adjust for such confounding, we performed a nested, self-matched, case-crossover analysis[26,27] among all patients with cancer who died from suicide or cardiovascular events. We compared the occurrence of a cancer diagnosis in the prespecified hazard period, which was defined as the 52 weeks preceding suicide and the 4 weeks preceding cardiovascular death, with that in the control periods, which were defined as the 3 52-week periods before the hazard period for suicide and the 17 4-week periods before the hazard period for cardiovascular death. The hazard periods were chosen for comparability with the results of the main analyses; control periods were chosen to account for potentially varying baseline risk over time and to minimize autocorrelation in exposure in the hazard and control periods while limiting carryover effects.

In the case-crossover analysis, patients served as their own controls. We used conditional logistic regression to estimate the odds ratios in the hazard period, as compared with the control periods. Because control information for each patient was based on their own past exposure, self-matching directly eliminated confounding by risk factors that were constant within patients during the sampling period but often differed among subjects. However, since the risks of cancer diagnosis, suicide, and cardiovascular death might vary similarly according to the season, we further adjusted for season in the models.

RESULTS

SUICIDE

During follow-up, 13,284 cases of suicide were observed among cancer-free individuals (incidence rate, 0.18 per 1000 person-years) and 786 among patients in whom any type of cancer had been diagnosed (incidence rate, 0.36 per 1000 person-years), including 29 suicides in the first week after diagnosis (incidence rate, 2.50 per 1000 person-years; relative risk, 12.6; 95% confidence interval [CI], 8.6 to 17.8). We found a relative risk of 4.8 (95% CI, 4.0 to 5.8) during the first 12 weeks after diagnosis (110 patients; incidence rate, 0.95 per 1000 person-years), with the highest relative risk observed for cancers of the esophagus, liver, or pancreas, followed by lung cancer (Table 1). Although the magnitude of elevation in risk decreased rapidly according to the time since the

Table 1. Relative Risks of Suicide or Cardiovascular Death after a Cancer Diagnosis, According to Time Period.

Variable	Any Cancer (N = 534,154)*	Prostate Cancer (N = 95,786)	Breast Cancer (N = 74,977)†	Colorectal Cancer (N = 62,719)	Skin Cancer (N = 47,169)	Lymphatic or Hematopoietic Cancer (N = 36,648)	Lung Cancer (N = 34,743)	CNS Tumors (N = 13,447)‡	Esophageal, Liver, or Pancreatic Cancer (N = 26,335)
	multivariable relative risk (95% confidence interval)§								
Suicide									
Cancer-free	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
After cancer diagnosis									
Weeks 1 to 12	4.8 (4.0–5.8)	3.2 (2.0–4.9)	3.4 (1.3–6.9)	4.7 (2.6–7.8)	1.4 (0.3–3.6)	2.5 (0.8–5.9)	12.3 (7.4–18.9)	7.8 (2.4–18.1)	16.0 (9.2–25.5)
Weeks 13 to 52	2.5 (2.1–2.9)	2.0 (1.5–2.8)	0.7 (0.2–1.7)	2.1 (1.2–3.3)	0.9 (0.2–2.6)	1.7 (0.7–3.2)	6.1 (3.6–9.6)	2.3 (0.6–6.0)	5.2 (2.2–10.1)
Week 53 onward¶	1.8 (1.6–2.0)	1.9 (1.6–2.2)	1.6 (1.2–2.1)	1.6 (1.2–2.0)	1.4 (1.0–1.8)	1.3 (0.6–2.4)	3.3 (1.3–6.8)	2.3 (1.3–3.6)	4.5 (2.2–8.2)
Cardiovascular death									
Cancer-free	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
After cancer diagnosis									
Week 1	5.6 (5.2–5.9)	2.8 (2.3–3.2)	1.8 (1.2–2.4)	5.4 (4.6–6.2)	1.2 (0.8–1.6)	8.7 (7.3–10.2)	12.4 (10.5–14.5)	26.9 (19.9–35.4)	14.9 (12.8–17.3)
Weeks 2 to 4	2.2 (2.1–2.3)	1.4 (1.2–1.6)	1.4 (1.1–1.8)	2.1 (1.8–2.4)	0.8 (0.6–1.0)	3.5 (2.9–4.1)	4.8 (4.0–5.6)	5.3 (3.4–7.8)	5.0 (4.2–6.0)
Weeks 5 to 26	1.5 (1.4–1.5)	0.9 (0.9–1.0)	1.2 (1.0–1.3)	1.2 (1.1–1.3)	0.9 (0.8–1.0)	2.1 (2.0–2.3)	2.6 (2.3–2.9)	4.1 (3.3–5.0)	2.6 (2.3–3.0)
Weeks 27 to 52	1.1 (1.0–1.1)	0.9 (0.8–1.0)	1.0 (0.9–1.1)	0.8 (0.7–0.9)	1.0 (0.9–1.0)	1.3 (1.2–1.5)	2.2 (1.9–2.5)	1.4 (0.9–2.0)	1.8 (1.5–2.2)
Week 53 onward ¶	1.2 (1.1–1.2)	1.0 (1.0–1.1)	1.0 (1.0–1.0)	0.9 (0.9–1.0)	1.0 (1.0–1.1)	1.2 (1.1–1.3)	1.6 (1.4–1.7)	1.1 (1.0–1.2)	1.3 (1.1–1.4)

* To preclude potential misdiagnosis between tumors of the central nervous system (CNS) and stroke, CNS tumors were excluded from "any cancer" in the analysis of cardiovascular death. Other cancers that are not listed were diagnosed in 142,330 patients.

† The analysis for breast cancer was conducted only among women.

‡ To preclude potential misdiagnosis between CNS tumors and stroke, stroke was excluded from "cardiovascular death" in the analysis of CNS tumors.

§ Relative risks were adjusted for age at follow-up (≤49 years, 5-year groups for 50 to 74 years, or ≥75 years for suicide; and ≤44 years, 5-year groups for 45 to 94 years, or ≥95 years for cardiovascular death), sex, calendar period at follow-up (5-year groups for suicide and 1-year groups for cardiovascular death), civil status (cohabitation or noncohabitation), socioeconomic status (blue-collar, white-collar, self-employed, or unclassified), and educational level (≥9 years, <9 years, or missing).

¶ The mean follow-up of patients in whom cancer was diagnosed was 4.07 years (median, 2.65; range, 0 to 15.99).

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cancer diagnosis, the risk remained elevated beyond the first year after diagnosis for all cancers (Table 1).

Focusing on the first 52 weeks after a diagnosis of any cancer, we found a relative risk of 3.1 (95% CI, 2.7 to 3.5) for suicide (260 patients; incidence rate, 0.60 per 1000 person-years). The expected number of suicides, adjusted for all demographic factors, during these 52 weeks was 87, leaving 173 cases associated with cancer diagnosis. The risk elevation was generally stable in terms of age, sex, calendar period, and other demographic factors (Table 2, and Section 2 in the Supplementary Appendix). The incidence rates of

Table 2. Incidence Rates and Relative Risks of Suicide and Cardiovascular Death after a Cancer Diagnosis, According to Age, Sex, Calendar Period, and Previous Hospitalization for Psychiatric or Cardiovascular Diseases.*

Variable	Suicide during First 52 Wk after Diagnosis			Cardiovascular Death during First 4 Wk after Diagnosis		
	No. of Patients	Incidence per 1000 Person-Yr†	Multivariable Relative Risk (95% CI)‡	No. of Patients	Incidence per 1000 Person-Yr†	Multivariable Relative Risk (95% CI)‡
Age at follow-up and cancer status						
≤54 yr						
Cancer-free	7,147	0.18	1.0	13,371	0.34	1.0
Cancer	31	0.44	2.8 (1.9–4.0)	32	5.32	11.9 (8.2–16.6)
55 to 64 yr						
Cancer-free	2,410	0.19	1.0	27,510	2.15	1.0
Cancer	45	0.51	2.8 (2.1–3.8)	160	20.24	8.8 (7.5–10.3)
65 to 74 yr						
Cancer-free	1,754	0.18	1.0	78,107	7.89	1.0
Cancer	86	0.69	3.7 (2.9–4.5)	543	46.72	5.2 (4.8–5.7)
75 to 84 yr						
Cancer-free	1,973	0.20	1.0	199,941	27.80	1.0
Cancer	98	0.65	2.7 (2.2–3.2)	1,237	110.38	3.6 (3.4–3.9)
≥85 yr						
Cancer-free	0	NA	NA	224,215	91.80	1.0
Cancer	0	NA	NA	669	198.15	2.1 (2.0–2.3)
Sex and cancer status						
Men						
Cancer-free	9,471	0.27	1.0	262,217	7.42	1.0
Cancer	205	0.92	3.2 (2.8–3.7)	1,638	78.62	3.3 (3.1–3.5)
Women						
Cancer-free	3,813	0.10	1.0	280,927	7.63	1.0
Cancer	55	0.26	2.5 (1.9–3.2)	1,003	51.98	3.3 (3.1–3.6)
Calendar period at follow-up and cancer status						
1991–1995						
Cancer-free	4,659	0.21	1.0	188,809	8.47	1.0
Cancer	84	0.72	3.2 (2.6–4.0)	1,026	87.64	4.0 (3.7–4.3)
1996–2000						
Cancer-free	4,019	0.18	1.0	173,534	7.68	1.0
Cancer	80	0.59	3.2 (2.5–3.9)	823	67.16	3.3 (3.1–3.6)
2001–2006						
Cancer-free	4,606	0.17	1.0	180,801	6.63	1.0
Cancer	96	0.52	2.9 (2.3–3.5)	792	48.98	2.8 (2.6–3.1)

Table 2. (Continued.)

Variable	Suicide during First 52 Wk after Diagnosis			Cardiovascular Death during First 4 Wk after Diagnosis		
	No. of Patients	Incidence per 1000 Person-Yr†	Multivariable Relative Risk (95% CI)‡	No. of Patients	Incidence per 1000 Person-Yr†	Multivariable Relative Risk (95% CI)‡
Preexisting psychiatric disease and cancer status						
No						
Cancer-free	7,322	0.11	1.0	440,437	6.40	1.0
Cancer	203	0.49	3.8 (3.3–4.4)	2,324	61.32	3.5 (3.4–3.7)
Yes						
Cancer-free	5,962	1.78	1.0	102,707	30.69	1.0
Cancer	57	2.60	1.7 (1.3–2.2)	317	142.25	2.6 (2.3–2.9)
Preexisting cardiovascular disease and cancer status						
No						
Cancer-free	10,822	0.17	1.0	121,655	1.92	1.0
Cancer	185	0.59	3.4 (3.0–4.0)	598	21.20	3.8 (3.5–4.1)
Yes						
Cancer-free	2,462	0.28	1.0	421,489	47.09	1.0
Cancer	75	0.63	2.4 (1.9–3.0)	2,043	171.34	2.8 (2.7–3.0)

* In the analyses of suicide, listed are values for 534,514 patients who received a diagnosis of any type of cancer. To preclude potential misdiagnosis between CNS tumors and stroke, in the analyses of cardiovascular death, we excluded CNS tumors from "any cancer." Accordingly, listed are values for 520,707 patients who received a diagnosis of any cancer with the exception of CNS tumors. NA denotes not applicable.

† Incidence rates were not adjusted for baseline or follow-up variables.

‡ Relative risks were adjusted for age at follow-up (≤49 year, 5-year groups for 50 to 74 years, or ≥75 years for suicide; and ≤44 years, 5-year groups for 45 to 94 years, or ≥95 years for cardiovascular death), sex, calendar period at follow-up (5-year groups for suicide and 1-year groups for cardiovascular death), civil status (cohabitation or noncohabitation), socioeconomic status (blue-collar, white-collar, self-employed, or unclassified), and educational level (≥9 years, <9 years, or missing).

suicide were higher among patients with preexisting psychiatric or cardiovascular diseases, regardless of whether a patient had a recent cancer diagnosis. However, the relative risks of suicide after a cancer diagnosis were stronger among patients without these coexisting illnesses than among patients with those illnesses (Table 2). In the case-crossover analysis, the risk of suicide was 2.6 times as high in the 52 weeks after a cancer diagnosis than at other times (Table 3).

DEATH FROM CARDIOVASCULAR CAUSES

During follow-up, 543,144 deaths from cardiovascular causes were observed among cancer-free individuals (incidence rate, 7.53 per 1000 person-years) and 48,991 among patients who had received the diagnosis of any cancer but CNS tumors (incidence rate, 23.10 per 1000 person-years). The highest relative risk of 5.6 (95% CI, 5.2 to 5.9) was observed during the first week after diagnosis (1318 patients; incidence rate, 116.80 per 1000 person-years). There was a highly elevated risk during the first week after diagnosis of all cancers but skin cancer; the risk elevation was strongest for CNS tumors, followed by cancers of the esophagus, liver, or pancreas and lung cancer (Table 1). The magnitude of risk elevation also decreased rapidly in correlation with the time since the cancer diagnosis, and a significantly elevated risk was not seen beyond the first year for most cancers (Table 1).

Focusing on the first 4 weeks after a diagnosis of any cancer but CNS tumors, we found a relative risk of 3.3 (95% CI, 3.1 to 3.4) for cardiovascular death (2641 patients; incidence rate, 65.81 per 1000 person-years). The adjusted expected number of cardiovascular deaths was 766 during these 4 weeks, leaving 1875 deaths associated with a cancer diagnosis. The incidence rates increased with increasing age, regardless of cancer diagnosis, whereas the relative risk for the comparison

Table 3. Odds Ratios for Suicide or Cardiovascular Death after a Cancer Diagnosis in Case-Crossover Analysis.

Cause of Death	Deceased Patients with Cancer Diagnosis*		Odds Ratio (95% CI)†
	Control Periods	Hazard Period	
	number		
Suicide‡	301	260	2.6 (2.2–3.1)
Cardiovascular death§	11,988	2,641	3.7 (3.6–3.9)
Myocardial infarction	3,662	970	4.5 (4.2–4.8)
Other diseases of the heart	554	134	4.1 (3.4–5.0)
Embolism or thrombosis	477	159	5.7 (4.7–6.8)
Stroke	1,538	220	2.4 (2.1–2.8)
Hemorrhagic	406	65	2.7 (2.1–3.5)
Ischemic	734	116	2.7 (2.2–3.3)

* For suicide, the hazard period was defined as the 52 weeks preceding death and the control periods as the 3 52-week periods preceding the hazard period; for cardiovascular death, the hazard period was defined as the 4 weeks preceding death and the control periods as the 17 4-week periods preceding the hazard period.
† Odds ratios were adjusted for season.
‡ The analysis of suicide included all cancers.
§ The analysis of cardiovascular death included all cancers with the exception of tumors of the central nervous system.

of the cancer group with the cancer-free group, clearly decreased with increasing age (Table 2). Although both incidence rates and relative risks decreased according to the calendar period, patients with newly diagnosed cancer still had an increase in risk by a factor of approximately 3 toward the end of the study period (Table 2). The risk elevation did not vary substantially according to other demographic factors (Section 2 in the Supplementary Appendix).

Similar to suicide, preexisting psychiatric or cardiovascular diseases were associated with an increased incidence of cardiovascular death, but the relative risks of cardiovascular death after a cancer diagnosis were stronger among patients without these preexisting illnesses (Table 2). In the case-crossover analysis, the risk of cardiovascular death was 3.7 times as high in the 4 weeks after a cancer diagnosis as it was at other times (Table 3). A positive association was observed for all subgroups of cardiovascular death, with the strongest association seen for embolism or thrombosis (Table 3).

DISCUSSION

In our nationwide cohort study of more than 6 million persons, those who received a diagnosis of cancer had an increased risk of suicide or death from cardiovascular causes within the first weeks after the diagnosis. This spike in risk was particularly prominent among patients in whom cancers with a poor prognosis were diagnosed and was not explained by preexisting psychiatric or cardiovascular conditions. Although the incidence rate of suicide or cardiovascular death decreased to some extent during the follow-up period, the two outcomes remained a considerable concern for the patients with newly diagnosed cancer throughout the study period. The similar results that were obtained from the case-crossover analysis further allayed the concern that an alternative explanation for the observed associations might be shared causal factors among cancer, suicide, and cardiovascular diseases.

Our study showed that to varying extents there were immediate health hazards after a cancer diagnosis for most cancers and that these hazards were equally shared by men and women. The variation in the risk elevation among different cancers followed a similar pattern for suicide and cardiovascular death, with the strongest findings observed for highly fatal cancers and the smallest, if any, for skin cancer. Further analyses showed a higher relative risk of suicide or cardiovascular death after a diagnosis of melanoma than for other skin cancers (data not shown). This pattern probably reflects varying degrees of psychological stress in patients in whom different cancers were diagnosed. Nevertheless, the first weeks after cancer diagnosis appeared to be a highly stressful time for all patients.

A major strength of our study was the large-scale population-based cohort with essentially complete ascertainment of cancers and fatal outcomes. The absence of data with respect to tumor characteristics, however, limited the possibility of exploring the effect of tumor stage on the associations between cancer diagnosis and either suicide or cardiovascular death. Yet our observation that patients who received a diagnosis of cancer with a poor prognosis were at particularly high risk is informative regarding the additional effect of more advanced disease. The strongest risk elevations were noted immediately after diagnosis and decreased in magnitude over time, which argues against an important effect of cancer progression and treatment on our findings.

Shared causal factors among cancer, suicide, and cardiovascular diseases, as residual confounding, may contribute to our findings. The

case-crossover analysis, comparing different time periods for the same patients, showed largely the same results as the main analyses and allayed such concerns. For example, smoking is known to be associated with both lung cancer and cardiovascular events. In the case-crossover analysis, the relative risk of cardiovascular death during the first 4 weeks after a diagnosis of lung cancer was similar to that in the main analysis (data not shown). Furthermore, although we stratified the analyses according to previous hospitalizations for psychiatric or cardiovascular diseases, we captured only severe conditions for which hospital admission was required. However, if the positive associations were not explained by severe preexisting conditions, it is rather unlikely that they were explained by milder conditions. Our study focused on hard outcomes alone (i.e., completed suicide and cardiovascular death) and thus probably did not capture the full extent of the psychological burden among patients with newly diagnosed cancer. Other potentially relevant outcomes, such as attempted suicide and other severe but nonfatal cardiovascular events, remain to be explored.

Even though we used data from the complete death registration, underreporting of suicide because of misclassification may still be expected in Sweden, as in any other population. Finally, given the outcomes of interest (i.e., cardiovascular death), our study focused only on adults who were 30 years of age or older. Further studies that concentrate on immediate outcomes among children and young adults in whom cancer is diagnosed are warranted. An evaluation of the roles of other factors, such as social support, on the observed associations may shed additional light on targeted prevention strategies.

Our findings suggest that a cancer diagnosis constitutes a major stressor, one that immediately affects the risk of critical, fatal outcomes. We speculate that our findings show only a portion of the range of effects induced by the emotional distress associated with a cancer diagnosis.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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