Longitudinal Analysis of Mental Disorder Burden Among Elderly Patients With Gastrointestinal Malignancies

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ABSTRACT

Background: Patients with cancer are at high risk for having mental disorders, resulting in widespread psychosocial screening efforts. However, there is a need for population-based and longitudinal studies of mental disorders among patients who have gastrointestinal cancer and particular among elderly patients. **Patients and Methods:** We used the SEER-Medicare database to identify patients aged ≥ 65 years with colorectal, pancreatic, gastric, hepatic/biliary, esophageal, or anal cancer. Earlier (12 months before or up to 6 months after cancer diagnosis) and subsequent mental disorder diagnoses were identified. **Results:** Of 112,283 patients, prevalence of an earlier mental disorder was 21%, 23%, 20%, 20%, 19%, and 26% for colorectal, pancreatic, gastric, hepatic/biliary, esophageal, and anal cancer, respectively. An increased odds of an earlier mental disorder was associated with pancreatic cancer (odds ratio [OR], 1.17; 95% CI, 1.11–1.23), esophageal cancer (OR, 1.10; 95% CI, 1.02–1.18), and anal cancer (OR, 1.17; 95% CI, 1.05–1.30) compared with colorectal cancer and with having regional versus local disease (OR, 1.09; 95% CI, 1.06–1.13). The cumulative incidence of a subsequent mental disorder at 5 years was 19%, 16%, 14%, 13%, 12%, and 10% for patients with anal, colorectal, esophageal, gastric, hepatic/biliary, and pancreatic cancer, respectively. There was an association with having regional disease (hazard ratio [HR], 1.08; 95% CI, 1.04–1.12) or distant disease (HR, 1.36; 95% CI, 1.28–1.45) compared with local disease and the development of a mental disorder. Although the development of a subsequent mental disorder was more common among patients with advanced cancers, there continued to be a significant number of patients with earlier-stage disease at risk. **Conclusions:** This study suggests a larger role for incorporating psychiatric symptom screening and management throughout oncologic care.

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Background

Patients with cancer who have a mental disorder at cancer diagnosis or who develop new mental disorders later in the oncologic course represent a particularly vulnerable subgroup at risk for worse cancer outcomes.^{1–3} A comorbid mental disorder is a known risk factor for inferior oncologic outcomes.⁴ Thus, efforts to integrate symptom management, palliative care, and psycho-oncologic care have been introduced into consensus guidelines.^{5,6} Similarly, the American College of Surgeons Commission on Cancer standards require accredited cancer centers to provide psychosocial distress screening to identify patients at high risk for a mental disorder and to monitor the referral for psychosocial care.⁷ These efforts are more often aimed at patients earlier in their cancer diagnosis and treatment. However, it has been shown that there is a sharp increase in mental disorder diagnoses not only leading up to a cancer diagnosis but also in the following months and years of the oncologic course.⁸ For patients with a gastrointestinal cancer, population-based estimates and longitudinal studies of mental disorders remain lacking.⁹

In addition, despite the fact that most patients with cancer are aged ≥ 65 years, there remains a need for behavioral and psychological studies in this population.¹⁰ Unfortunately, elderly patients have many mental disorder risk factors, including having less-aggressive oncologic management, baseline cognitive deficits, poor functional status, and a greater number of medical comorbidities.¹⁰ Thus, we set out to perform a longitudinal study of mental disorders among elderly patients with gastrointestinal cancers.

Patients and Methods

Data Source

We used the SEER-Medicare linked database and identified patients whose first cancer was a primary colorectal, pancreatic, gastric, hepatic/biliary, esophageal, or anal

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cancer during 2004 through 2013. SEER-Medicare is a large dataset maintained by the NCI that details inpatient and outpatient medical claims from Medicare beneficiaries who are included in the SEER registry.^{11,12}

Patient Selection

The cohort included patients aged ≥ 65 years with Medicare Parts A and B enrollment without HMO coverage starting 12 months before cancer diagnosis to ensure completeness of claims data. Only patients with complete staging information were included. Censoring occurred at the end of December 2014 or when Medicare coverage was lost.

Mental Disorder Identification

Medicare billing claims were used to identify mental disorders and professional management for a mental disorder (see supplemental eAppendix 1, available with this article at JNCCN.org). Mental disorders included depressive, anxiety, psychotic, and bipolar disorders. An early mental disorder was limited to 12 months before and up to 6 months after cancer diagnosis, and a subsequent mental disorder was at any point after 6 months from cancer diagnosis. Given the limitations of the data, the exact timeline between mental disorder development and cancer diagnosis was impossible to entirely tease apart. Earlier mental disorders were intended to include diagnoses made throughout the diagnostic workup, the information-sharing period regarding diagnosis and prognosis, and treatment initiation. This is the period during which mental disorders may be diagnosed as a result of psychosocial distress screening occurring as part of the comprehensive oncologic care model.⁷ Subsequent mental disorders included those overlapping with cancer progression and additional treatments.

Demographic and Clinical Characteristics

Using data from the SEER registry, we determined age, sex, race, Hispanic ethnicity, marital status, area income, cancer stage, and disease subsite.¹³ Dual Medicaid insurance and Charlson comorbidity score modified for patients with cancer were determined through claims data.^{14,15}

Statistical Analysis

Clinical and demographic characteristics were compared between groups using chi-square tests. A multivariate logistic regression model was used to determine associations with early mental disorders. We calculated the cumulative incidence of subsequent mental disorders among those without an early mental disorder. Multivariate subdistribution hazard models (Fine-Gray regressions) were used to determine risk factors for the development of a subsequent mental disorder. We also performed sensitivity testing limited to persons who had received an influenza vaccination (supplemental eAppendix 1).

Figure 1. Cohort selection from the SEER-Medicare database.

Influenza vaccination has previously been used to determine use of routine preventive services, because it is recommended for all adults.^{16,17}

Table 1. Patient Characteristics According to Early Mental Disorder Status

Variable	No Mental Disorder n (%)	Diagnosed Mental Disorder n (%)	P Value
Disease subsite			<.0001
Colorectal	60,283 (68%)	16,138 (68%)	
Pancreatic	7,977 (9%)	2,401 (10%)	
Gastric	7,204 (8%)	1,792 (8%)	
Hepatic/Biliary	7,513 (8%)	1,891 (8%)	
Esophageal	4,158 (5%)	1,001 (4%)	
Anal	1,422 (2%)	503 (2%)	
Age group			<.0001
65–74 y	39,687 (45%)	10,105 (43%)	
75–84 y	36,474 (41%)	9,686 (41%)	
≥85 y	12,396 (14%)	3,935 (17%)	
Sex			<.0001
Male	46,484 (52%)	8,767 (37%)	
Female	42,073 (48%)	14,959 (63%)	
Race			<.0001
White	72,890 (82%)	20,873 (88%)	
Black	8,096 (9%)	1,778 (7%)	
Asian/Pacific Islander	6,882 (8%)	926 (4%)	
North American Native	374 (0%)	82 (0%)	
Unknown	315 (0%)	67 (0%)	
Ethnicity			.95
Non-Hispanic	82,625 (93%)	22,140 (93%)	
Hispanic	5,932 (7%)	1,586 (7%)	
Marital status			<.0001
Married/Domestic partner	48,436 (55%)	10,264 (43%)	
Widowed	22,854 (26%)	7,731 (33%)	
Single	7,184 (8%)	2,280 (10%)	
Separated/Divorced	6,427 (7%)	2,357 (10%)	
Unknown	3,656 (4%)	1,094 (5%)	

(continued)

Statistical significance was set at 0.05, and all tests were 2-tailed. Data analysis and statistical testing was performed using R version 3.5 (R Foundation for Statistical Computing).

Results

We identified 112,283 patients who met inclusion criteria (Figure 1), including 76,421 with colorectal, 10,378 with pancreatic, 8,996 with gastric, 9,404 with hepatic/biliary, 5,159 with esophageal, and 1,925 with anal cancer. A total of 23,726 patients (21%) had an early mental disorder, comprising 16,138 (21%) of the colorectal cohort, 2,401

Table 1. Patient Characteristics According to Early Mental Disorder Status (cont.)

Variable	No Mental Disorder n (%)	Diagnosed Mental Disorder n (%)	P Value
Area income			<.0001
Highest	21,408 (24%)	5,265 (22%)	
Third	20,451 (23%)	5,408 (23%)	
Second	19,730 (22%)	5,612 (24%)	
Lowest	18,752 (21%)	5,755 (24%)	
Unknown	8,216 (9%)	1,686 (7%)	
Dual Medicaid insurance			<.0001
No	70,008 (79%)	16,274 (69%)	
Yes	18,549 (21%)	7,452 (31%)	
Charlson comorbidity score			<.0001
0	41,169 (46%)	8,229 (35%)	
1	22,492 (25%)	6,037 (25%)	
2	11,973 (14%)	3,891 (16%)	
≥3	12,923 (15%)	5,569 (23%)	
Cancer stage			<.0001
Local	38,832 (44%)	10,326 (44%)	
Regional	35,476 (40%)	9,970 (42%)	
Distant	14,249 (16%)	3,430 (14%)	

(23%) of the pancreatic cohort, 1,792 (20%) of the gastric cohort, 1,891 (20%) of the hepatic/biliary cohort, 1,001 (19%) of the esophageal cohort, and 503 (26%) of the anal cancer cohort (Table 1). A comparison of patients included and excluded from the study is presented in supplemental eAppendix 2. The included cohort had more patients who were married (52% vs 43%) and fewer with dual Medicaid insurance (23% vs 29%).

Early mental disorders were more likely in patients who were older (24% of those aged ≥85 years), female (26%), White (22%), unmarried, and from a lower income area, and those with dual Medicaid insurance (29%), more comorbidities (Charlson comorbidity index score ≥1), and regional disease (22%), and were less likely in those with distant disease at diagnosis (19%).

Multivariate logistic regression analysis showed that increased odds of an early mental disorder were associated with pancreatic cancer (odds ratio [OR], 1.17; 95% CI, 1.11–1.23), esophageal cancer (OR, 1.10; 95% CI, 1.02–1.18), and anal cancer (OR, 1.17; 95% CI, 1.05–1.30) compared with colorectal cancer (Table 2). We also found an association between an early mental disorder and younger age (OR, 0.94; 95% CI, 0.90–0.97 for age 75–84 vs 65–74 years), female sex (OR, 1.81; 95% CI, 1.76–1.87), White race and non-Hispanic ethnicity, being unmarried, being from a lower income area,

Table 2. Multivariate Logistic Regression Analysis of Characteristics Associated With an Early Mental Disorder

Variable	Odds Ratio (95% CI)	P Value
Disease subsite		
Colorectal	Ref	
Pancreatic	1.17 (1.11–1.23)	<.0001
Gastric	1.05 (0.99–1.11)	.09
Hepatic/Biliary	0.95 (0.90–1.00)	.06
Esophageal	1.10 (1.02–1.18)	.01
Anal	1.17 (1.05–1.30)	.005
Age group		
65–74 y	Ref	
75–84 y	0.94 (0.90–0.97)	<.0001
≥85 y	0.97 (0.93–1.02)	.26
Sex		
Male	Ref	
Female	1.81 (1.76–1.87)	<.0001
Race		
White	Ref	
Black	0.53 (0.50–0.56)	<.0001
Asian/Pacific Islander	0.37 (0.34–0.40)	<.0001
North American Native	0.61 (0.48–0.78)	<.0001
Unknown	0.76 (0.58–1.00)	.05
Ethnicity		
Non-Hispanic	Ref	
Hispanic	0.73 (0.68–0.77)	<.0001
Marital status		
Married/Domestic partner	Ref	
Widowed	1.14 (1.10–1.19)	<.0001
Single	1.24 (1.18–1.31)	<.0001
Separated/Divorced	1.34 (1.27–1.42)	<.0001
Unknown	1.18 (1.10–1.27)	<.0001

(continued)

Table 2. Multivariate Logistic Regression Analysis of Characteristics Associated With an Early Mental Disorder (cont.)

Variable	Odds Ratio (95% CI)	P Value
Area income		
Highest	Ref	
Third	1.01 (0.97–1.06)	.66
Second	1.05 (1.01–1.10)	.02
Lowest	1.10 (1.05–1.15)	<.0001
Unknown	0.79 (0.75–0.84)	<.0001
Dual Medicaid insurance		
No	Ref	
Yes	1.73 (1.67–1.80)	<.0001
Charlson comorbidity score		
0	Ref	
1	1.33 (1.28–1.38)	<.0001
2	1.59 (1.52–1.67)	<.0001
≥3	2.14 (2.05–2.23)	<.0001
Cancer stage		
Local	Ref	
Regional	1.09 (1.06–1.13)	<.0001
Distant	0.97 (0.92–1.01)	.16

addition, there was an association with having regional or distant disease at the time of diagnosis.

We investigated the number of patients with an early or subsequent mental disorder receiving outpatient treatment from a mental health professional. There were 6,497 patients (27%) who received treatment from a mental health professional (Table 4). No significant differences by disease subtype or stage were seen, but older patients, men, those with dual Medicaid insurance, and those with more comorbidities were more likely to have received treatment from a mental health professional.

We performed secondary analyses limited to patients who had routine interaction with the healthcare system, defined as receiving the influenza vaccination (supplemental eAppendix 3). Cancer subsite and demographic findings were consistent with the primary analysis. The incidence of developing a subsequent mental disorder at 5 years was 11% to 23% depending on cancer subsite. Another secondary analysis was performed classifying an early mental disorder as a condition identified in any billing claim 12 months before the date of cancer diagnosis (supplemental eAppendix 4). We found that fewer patients met criteria for an early mental disorder diagnosis (11%), whereas the 5-year incidence of a subsequent mental disorder was higher (21%–30% depending on cancer subsite).

having dual Medicaid insurance (OR, 1.73; 95% CI, 1.67–1.80), having more comorbidities, and having regional disease.

The cumulative incidence of developing a subsequent mental disorder at 5 years was 19%, 16%, 14%, 13%, 12%, and 10% for patients with anal, colorectal, esophageal, gastric, hepatic/biliary, and pancreatic cancer, respectively (Figure 2). On multivariate analysis, there was an association between a subsequent mental disorder and esophageal cancer (hazard ratio [HR], 1.61; 95% CI, 1.48–1.75), gastric cancer (HR, 1.15; 95% CI, 1.08–1.23), hepatic/biliary (HR, 1.29; 95% CI, 1.20–1.38), and pancreatic cancer (HR, 1.39; 95% CI, 1.29–1.50) compared with colon cancer (Table 3). In

Figure 2. Development of a subsequent mental disorder following a gastrointestinal cancer diagnosis among patients without an early mental disorder. The reference time point is the cancer diagnosis, with a subsequent mental disorder defined as occurring at least 6 months after the cancer diagnosis.

Lastly, we performed additional analyses of mental disorder subcategories (supplemental eAppendix 5). The most common early and subsequent diagnoses were depressive disorders, followed by anxiety, psychotic, and bipolar disorders. Having any subsequent mental disorder was also more likely for those with a different, earlier mental disorder. The pattern of clinical and demographic associations in the primary analysis were generally consistent across this secondary analysis (supplemental eAppendix 5).

Discussion

We conducted a population-based study to determine the burden of mental disorders among elderly patients with gastrointestinal cancers in the United States. Depending on the cancer subsite, 19% to 26% of patients had a diagnosed early mental disorder, and an additional 10% to 19% of patients developed a subsequent mental disorder. These diagnoses were more likely among patients with more advanced disease, but rates were substantial among all subgroups.

Our estimates for the rates of early and subsequent mental disorders are similar to prior literature.^{8,18–22} However, one limitation of registry studies is the reliance on accurate diagnostic coding by health practitioners, which can result in an underrepresentation of the true prevalence of comorbidities because there is no

guarantee that patients interact with the healthcare system and receive accurate diagnostic codes.^{23,24} We used strategies to address this known issue, including defining an early mental disorder as one diagnosed 12 months before or up to 6 months after the cancer diagnosis to account for patients who have more limited interactions with the healthcare system.⁸ Second, we performed an analysis limited to patients receiving routine influenza vaccinations. Because influenza vaccination is recommended universally for adults, all patients should be interacting with the healthcare system on at least an annual basis, and hence this surrogate has been used previously.^{16,17} Third, we investigated the number of patients receiving care from a mental health professional, which more accurately identifies patients with more severe psychiatric burden.²⁵

The explanation for the high rates of early mental disorders among patients with gastrointestinal cancer in the current study is likely multifactorial. Several studies have shown that rates of mental disorders begin to increase before the cancer diagnosis, with the thought that the initial symptoms and diagnostic workup induce a stress response that can trigger a mood disorder.^{8,26–28} For other patients with a longstanding mental disorder, there has been great heterogeneity among studies to determine whether there is an increased risk for cancer or if other modifying factors and behaviors are responsible.²⁹ Patients with mental disorders are more likely to have certain cancer risk factors, such as metabolic syndrome, a smoking history, and worse healthcare access.^{30–33} Detangling the causality in the precancer diagnosis period remains challenging.

There are also many explanations for the high rates of subsequent mental disorder diagnoses found in the current study. Cancer diagnosis, treatment, and progression are all major stressors. These stressors can result in an inflammatory response and immune system activation, which is well-known to be associated with mental disorders.³⁴ Elevations in inflammatory markers such as C-reactive protein and cytokines, including IL-6, IL-8, and tumor necrosis factor- α , have been associated with many mental disorders.^{35–37} For some patients, the cancer-related inflammatory response can cause certain mental disorders, but mental disorders themselves can also increase systemic inflammation.³⁸

With regard to determining the patients at highest risk for mental disorders, a multitude of clinical factors play a role. We found that having more advanced disease was associated with an early mental disorder. One reason is that among patients with mental disorders, routine medical care and screening are much lower than the general population.^{2,3} We also found that patients with more advanced disease were more likely to develop

Table 3. Characteristics Associated With Development of a Subsequent Mental Disorder^a

Variable	Hazard Ratio (95% CI)	P Value
Disease subsite		
Colorectal	Ref	
Pancreatic	1.39 (1.29–1.50)	<.0001
Gastric	1.15 (1.08–1.23)	<.0001
Hepatic/Biliary	1.29 (1.20–1.38)	<.0001
Esophageal	1.61 (1.48–1.75)	<.0001
Anal	1.12 (1.00–1.26)	.06
Age group		
65–74 y	Ref	
75–84 y	1.15 (1.11–1.19)	<.0001
≥85 y	1.32 (1.25–1.39)	<.0001
Sex		
Male	Ref	
Female	1.23 (1.19–1.28)	<.0001
Race		
White	Ref	
Black	0.77 (0.72–0.82)	<.0001
Asian/Pacific Islander	0.56 (0.52–0.61)	<.0001
North American Native	0.90 (0.69–1.18)	.46
Unknown	0.68 (0.50–0.94)	.02
Ethnicity		
Non-Hispanic	Ref	
Hispanic	0.89 (0.83–0.95)	.001
Marital status		
Married/Domestic partner	Ref	
Widowed	0.98 (0.94–1.02)	.36
Single	1.02 (0.96–1.08)	.60
Separated/Divorced	0.99 (0.93–1.05)	.72
Unknown	0.97 (0.89–1.06)	.50

(continued)

Table 3. Characteristics Associated With Development of a Subsequent Mental Disorder^a (cont.)

Variable	Hazard Ratio (95% CI)	P Value
Area income		
Highest	Ref	
Third	1.03 (0.98–1.08)	.20
Second	1.05 (1.00–1.10)	.05
Lowest	1.07 (1.02–1.13)	.008
Unknown	0.98 (0.92–1.04)	.55
Dual Medicaid insurance		
No	Ref	
Yes	1.29 (1.23–1.34)	<.0001
Charlson comorbidity score		
0	Ref	
1	1.20 (1.15–1.25)	<.0001
2	1.32 (1.25–1.38)	<.0001
≥3	1.47 (1.40–1.54)	<.0001
Cancer stage		
Local	Ref	
Regional	1.08 (1.04–1.12)	<.0001
Distant	1.36 (1.28–1.45)	<.0001

^aThese patients did not have an early mental disorder, and hazard ratio estimates were determined from a subdistribution hazard model.

consistent with our finding of advanced disease as a risk factor for developing a mental disorder. As for the risk of having an early mental disorder, it is thought that those with pancreatic cancer may develop symptoms of anxiety or depression prodromal to the diagnosis.⁴⁴ In some cases the psychological symptoms, including appetite loss, weight loss, or fatigue, may be early cancer symptoms, but other theories have suggested immunologic, paraneoplastic, biochemical, and hormonal explanations connecting the cancer to depression.⁴⁴ For patients with anal cancer, the workup and diagnostic procedures put patients at particular risk for significant psychological stress.^{45,46}

With regard to other clinical and demographic characteristics, we found that mental disorders were more common among patients with a greater number of medical comorbidities. Similar to the relationship between poorer oncologic outcome and subsequent mental disorder development, the association between mental disorders, physical comorbidities, and negative health behaviors may be responsible.^{30–33}

Another finding was that lower income, as measured by dual Medicaid insurance and living in a lower income area, was a risk factor for having a mental disorder. Potential explanations include that lower socioeconomic

subsequent mental disorders. The explanation may be that a poorer prognosis and disease recurrence trigger significantly more psychological stress.^{39,40}

On one hand, we found that the highest risk factor for a subsequent mental disorder was having esophageal or pancreatic cancer. On the other hand, the associations with having an early mental disorder were much less pronounced, albeit highest for patients with pancreatic or anal cancer. To make a generalization, patients with esophageal or pancreatic cancer tend to have a worse overall prognosis and more devastating treatment effects, resulting in worse health-related quality of life compared with those with colorectal cancer.^{41–43} This is

Table 4. Patient Characteristics According to Receipt of Psychiatric/Psychological Treatment^a

Variable	No Professional Psychiatric/Psychological Management n (%)	Received Professional Psychiatric/Psychological Management n (%)	P Value
Disease subsite			.06
Colorectal	11,798 (68%)	4,340 (67%)	
Pancreatic	1,754 (10%)	647 (10%)	
Gastric	1,281 (7%)	511 (8%)	
Hepatic/Biliary	1,336 (8%)	555 (9%)	
Esophageal	705 (4%)	296 (5%)	
Anal	355 (2%)	148 (2%)	
Age group			.0001
65–74 y	7,423 (43%)	2,682 (41%)	
75–84 y	7,053 (41%)	2,633 (41%)	
≥85 y	2,753 (16%)	1,182 (18%)	
Sex			<.0001
Male	6,188 (36%)	2,579 (40%)	
Female	11,041 (64%)	3,918 (60%)	
Race			<.0001
White	15,291 (89%)	5,582 (86%)	
Black	1,138 (7%)	640 (10%)	
Asian/Pacific Islander	690 (4%)	236 (4%)	
North American Native	65 (0%)	17 (0%)	
Unknown	45 (0%)	22 (0%)	
Ethnicity			.90
Non-Hispanic	16,080 (93%)	6,060 (93%)	
Hispanic	1,149 (7%)	437 (7%)	
Marital status			<.0001
Married/Domestic partner	7,923 (46%)	2,341 (36%)	
Widowed	5,639 (33%)	2,092 (32%)	
Single	1,394 (8%)	886 (14%)	
Separated/Divorced	1,528 (9%)	829 (13%)	
Unknown	745 (4%)	349 (5%)	
Area income			<.0001
Highest	3,632 (21%)	1,633 (25%)	
Third	3,897 (23%)	1,511 (23%)	
Second	4,246 (25%)	1,366 (21%)	
Lowest	4,299 (25%)	1,456 (22%)	
Unknown	1,155 (7%)	531 (8%)	

(continued)

position is associated with access to fewer healthcare resources and with unhealthy behaviors, such as smoking and obesity, which are associated with developing a mental disorder.^{29–33,47}

Table 4. Patient Characteristics According to Receipt of Psychiatric/Psychological Treatment^a (cont.)

Variable	No Professional Psychiatric/Psychological Management n (%)	Received Professional Psychiatric/Psychological Management n (%)	P Value
Dual Medicaid insurance			<.0001
No	12,352 (72%)	3,922 (60%)	
Yes	4,877 (28%)	2,575 (40%)	
Charlson comorbidity score			<.0001
0	6,434 (37%)	1,795 (28%)	
1	4,540 (26%)	1,497 (23%)	
2	2,745 (16%)	1,146 (18%)	
≥3	3,510 (20%)	2,059 (32%)	
Cancer stage			.16
Local	7,564 (44%)	2,762 (43%)	
Regional	7,193 (42%)	2,777 (43%)	
Distant	2,472 (14%)	958 (15%)	

^aThis cohort included patients with early or subsequent mental disorder diagnoses.

Our study found that women were at higher risk for having a mental disorder, which is consistent with prior reports.⁴⁸ One thought is that rather than having biologic or hormonal underpinnings, the explanation has more to do with social disadvantages, such as intimate-partner violence putting women at risk for mental disorders, women being more likely to have mental disorders at a young age, women having a different set of cultural norms with associated role limitations and economic discrimination, and women being more likely to report psychological symptoms and receive a mental disorder diagnosis from a practitioner.⁴⁹

In addition, our study found that White and non-Hispanic patients were more likely to have an early or subsequent mental disorder, which is a well-recognized finding.^{50,51} However, we caution against overinterpretation of these results, because disparities may exist despite our findings. For example, one well-known exception is that Black Americans tend to have higher rates of schizophrenia.⁵² In addition, despite lower rates overall, it is thought that non-White Americans have higher psychological symptom burden, have less access to mental care, and are less likely to receive a mental disorder diagnosis because of practitioner bias and discrimination.⁵³

Our study found that patients aged >75 years were less likely to have an early mental disorder, but more likely to go on to develop a subsequent mental disorder. In general, most literature supports the finding that older age is protective against having a mental disorder, although debate exists.⁵⁴ Older patients tend

to have more comorbidities and are less likely to receive aggressive cancer treatment.¹⁰ However, whether our finding that older age was associated with a subsequent mental disorder among patients with gastrointestinal cancer is related to the interplay between cancer prognosis, treatment, and age needs to be further explored.

Interestingly, the analysis of patients receiving management from a mental healthcare professional showed a somewhat different pattern of demographic risk factors. This finding may have been partly because patients with more severe mental disorders received professional psychiatric/psychological care, given that we found it to be associated with many demographic characteristics that were also associated with having an early or subsequent mental disorder (single marital status, dual Medicaid insurance, more medical comorbidities). However, there are many confounders; for example, the association with living in an affluent area or being older and receiving professional mental healthcare may be a marker for access. Thus, the findings are likely multifactorial and need to be better elucidated in future studies.

Limitations of this study include that it uses administrative billing claims to define the endpoint of mental disorder. Medicare claims were created and used for physician and institutional payment rather than research purposes. Ideally, diagnoses would be in accordance with the *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition; DSM-5).⁵⁵ However, diagnostic codes in billing claims rely on practitioner familiarity with the diagnosis of these disorders. As we have shown in our study, most patients with cancer who have a mental disorder are not receiving care from a mental health professional, and therefore the mental disorder diagnosis often falls to a general practitioner or oncologist who is likely less familiar with the specific DSM-5 criteria for a diagnosis of depressive, anxiety, psychotic, or bipolar disorder. As discussed previously, reliance on diagnostic and procedure codes can result in an underrepresentation of mental disorders. Despite our use of contemporary methods for analyzing healthcare claims, there will continue to be discrepancies with determining the number of mental disorders.⁵⁶

Furthermore, there is some amount of uncertainty regarding the timing of mental disorder development and cancer diagnosis. For some patients, the cancer, its psychological burden, and resultant treatment toxicities

may contribute to a new mental disorder, whereas for other patients there is an association between long-standing mental disorder and having risk factors for the development and asymptomatic progression of cancer. In the current study we used a generous window to define an early mental disorder (12 months before and up to 6 months after cancer diagnosis), although conclusions were similar when a shorter window was used (12 months before or up to the date of cancer diagnosis). In addition, we were not able to control for cancer treatments, laboratory or imaging tests, clinical performance status, or behavioral practices such as smoking or substance use, which can result in residual confounding.

Similar to other retrospective studies, there can be selection bias, and prospective cohort studies would be needed to confirm the results of this study. Excluded patients were more likely to be unmarried and have dual Medicaid insurance, and hence may be more likely to have mental disorders. In addition, the patients in our cohort were from an elderly Medicare population, which may not accurately represent younger patients or those with different or inadequate insurance. Similarly, racial minorities were underrepresented, a common issue among similar studies that makes generalization to those populations challenging.⁹

Conclusions

This population-based study of patients with gastrointestinal malignancies described the current burden of mental disorders in the Medicare population. Although we found that comorbid mental disorders were more common among patients with more advanced cancers, there continues to be a significant number of patients with early-stage disease who are at risk.

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Supplemental online content for:

Longitudinal Analysis of Mental Disorder Burden Among Elderly Patients With Gastrointestinal Malignancies

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eAppendix 1. Supplemental Methods

Mental Disorder Identification

Medicare billing claims were used to identify patients with a mental disorder and professional management for a mental disorder. We included patients with depressive disorders (ICD-9 diagnosis codes 296.2–296.36, 300.4, 311), anxiety disorders (ICD-9 diagnosis codes 293.84, 300–300.09, 300.10, 300.2–300.3, 300.5, 308–308.9, 309.81, 313.0), psychotic disorders (ICD-9 diagnosis codes 293.81–293.82, 295–295.95, 297–298.9), and bipolar disorders (ICD-9 diagnosis codes 296.0–296.16, 296.4–296.99). Ideally, diagnoses would be in accordance with the *Diagnostic and Statistical Manual of Mental Disorders* (5th Edition; DSM-5, 2013). However, the current study relies on ICD-9 diagnostic codes, which in turn rely on practitioner familiarity with the diagnosis of these disorders. As we have shown in our study, most patients with cancer who have a mental disorder are not receiving care from a mental health professional, and therefore the mental disorder diagnosis often falls to a general practitioner or oncologist who is likely less familiar with the specific DSM-5 criteria for a diagnosis of depressive, anxiety, psychotic, or bipolar disorder.

An early mental disorder was defined as a condition identified in any billing claim 12 months before to 6 months after the gastrointestinal cancer diagnosis. To reduce immortal time bias, only patients living at least 6 months after cancer diagnosis were included in this study. A subsequent mental disorder was defined as a condition identified 6 months after the cancer diagnosis until death or censorship.

Professional management of persons with a mental disorder was determined through outpatient claims billed by a mental health professional (Health Care Financing Administration [HCFA] specialty codes 26, 27, 62, 68, 86 from a noninstitutional provider claim; revenue center codes 0114, 0124, 0134, 0144, 0154, 0204, 0513, 0900–0919, 0961, 1000, 1001 from an institutional provider claim), or any claim for a psychologic procedure (HCFA Common Procedure Coding System [HCPCS] 90785–90899, 96101–96103, 0359T–0374T). We limited this classification to patients with professional mental health management within 12 months from their earliest claim recognizing a mental disorder and excluded patients who had died or became censored for the 12-month period.

Influenza Vaccination Identification

We performed sensitivity testing by limiting the analysis to persons who had received an influenza vaccination. The following HCPCS codes were included to identify receipt of the vaccine: G0008, G8482, G9141, G9142, Q2034–Q2039, 90470, 90630, 90653–90664, 90666, 90672–90674, 90682, 90685–90688, 90724, 90756.

eAppendix 2. Exclusion Analysis

eTable 1. Differences Between Excluded and Included Cohorts			
	Excluded Cohort n (%)	Included Cohort n (%)	Difference, %
Total, N	139,370	112,283	
Disease subsite			
Colon	35,478 (25%)	57,902 (52%)	26%
Rectal	11,298 (8%)	18,519 (16%)	8%
Pancreatic	26,665 (19%)	10,378 (9%)	−10%
Gastric	11,430 (8%)	8,996 (8%)	0%
Hepatic	11,149 (8%)	5,108 (5%)	−3%
Esophageal	7,252 (5%)	5,159 (5%)	−1%
Anal	2,892 (2%)	1,925 (2%)	0%
Small bowel	4,903 (4%)	0 (0%)	−4%
Appendix	1,139 (1%)	0 (0%)	−1%
Biliary	7,332 (5%)	4,296 (4%)	−1%
Peritoneal	1,740 (1%)	0 (0%)	−1%
Other	18,092 (13%)	0 (0%)	−13%
Age group			
<65 y	20,422 (15%)	0 (0%)	−15%
65–74 y	39,675 (28%)	49,792 (44%)	16%
75–84 y	49,892 (36%)	46,160 (41%)	5%
≥85 y	29,381 (21%)	16,331 (15%)	−7%
Sex			
Male	72,408 (52%)	55,251 (49%)	−3%
Female	66,962 (48%)	57,032 (51%)	3%
Race			
White	114,510 (82%)	93,763 (84%)	1%
Black	16,617 (12%)	9,874 (9%)	−3%
Asian/Pacific Islander	6,988 (5%)	7,808 (7%)	2%
North American Native	740 (1%)	456 (0%)	0%
Unknown	515 (0%)	382 (0%)	0%
Ethnicity			
Non-Hispanic	128,945 (93%)	104,765 (93%)	1%
Hispanic	10,425 (7%)	7,518 (7%)	−1%
Marital status			
Married/Domestic partner	60,534 (43%)	58,700 (52%)	9%
Widowed	4,0224 (29%)	30,585 (27%)	−2%
Single	17,568 (13%)	9,464 (8%)	−4%
Separated/Divorced	13,048 (9%)	8,784 (8%)	−2%
Unknown	7,996 (6%)	4,750 (4%)	−2%

(continued on next page)

eAppendix 2. Exclusion Analysis (cont.)

eTable 1. Differences Between Excluded and Included Cohorts (cont.)			
	Excluded Cohort n (%)	Included Cohort n (%)	Difference, %
Area income			
Highest	27,539 (20%)	25,595 (23%)	3%
Third	30,353 (22%)	25,595 (23%)	1%
Second	31,787 (23%)	25,595 (23%)	0%
Lowest	36,743 (26%)	25,596 (23%)	−4%
Unknown	12,948 (9%)	9,902 (9%)	0%
Dual Medicaid insurance			
No	98,678 (71%)	86,282 (77%)	6%
Yes	40,692 (29%)	26,001 (23%)	−6%
SEER region			
Greater California	26,419 (19%)	19,359 (17%)	−2%
New Jersey	23,054 (17%)	16,788 (15%)	−2%
Greater Georgia	11,637 (8%)	8,780 (8%)	−1%
Kentucky	11,935 (9%)	8,461 (8%)	−1%
Los Angeles	10,245 (7%)	8,359 (7%)	0%
Louisiana	9,705 (7%)	7,107 (6%)	−1%
Detroit	8,119 (6%)	6,954 (6%)	0%
Iowa	6,705 (5%)	7,392 (7%)	2%
Connecticut	7,379 (5%)	7,175 (6%)	1%
Seattle	6,219 (4%)	5,774 (5%)	1%
San Francisco	4,796 (3%)	4,369 (4%)	0%
Atlanta	3,309 (2%)	2,807 (2%)	0%
San Jose	2,716 (2%)	2,734 (2%)	0%
New Mexico	2,912 (2%)	2,413 (2%)	0%
Utah	2,338 (2%)	2,014 (2%)	0%
Hawaii	1,606 (1%)	1,554 (1%)	0%
Rural Georgia	276 (0%)	243 (0%)	0%
Cancer stage			
Local	33,398 (24%)	49,158 (44%)	20%
Regional	29,661 (21%)	45,446 (40%)	19%
Distant	45,401 (33%)	17,679 (16%)	−17%
Unknown	30,910 (22%)	0 (0%)	−22%

The excluded cohort consists of patients with a gastrointestinal malignancy diagnosed in 2004–2013, enrolled in Medicare Parts A and B, and with survival data. Duplicate entries were also removed from the excluded cohort.

eAppendix 3. Subgroup: Routine Influenza Vaccination

eTable 2. Patient Characteristics According to Baseline Mental Disorder Status Among Those Who Received a Routine Influenza Vaccination

	No Mental Disorder n (%)	Diagnosed Mental Disorder n (%)	P Value
Disease subsite			<.0001
Colorectal	27,100 (66%)	7,733 (66%)	
Pancreatic	4,188 (10%)	1,334 (11%)	
Gastric	3,409 (8%)	891 (8%)	
Hepatic/Biliary	3,728 (9%)	1,007 (9%)	
Esophageal	1,980 (5%)	522 (4%)	
Anal	660 (2%)	254 (2%)	
Age group			<.0001
65–74 y	15,640 (38%)	4,479 (38%)	
75–84 y	18,681 (45%)	5,128 (44%)	
≥85 y	6,744 (16%)	2,134 (18%)	
Sex			<.0001
Male	20,506 (50%)	4,158 (35%)	
Female	20,559 (50%)	7,583 (65%)	
Race			<.0001
White	34,903 (85%)	10,582 (90%)	
Black	2,312 (6%)	554 (5%)	
Asian/Pacific Islander	3,593 (9%)	531 (5%)	
North American Native	115 (0%)	36 (0%)	
Unknown	142 (0%)	38 (0%)	
Ethnicity			.13
Non-Hispanic	39,076 (95%)	11,131 (95%)	
Hispanic	1,989 (5%)	610 (5%)	
Marital status			<.0001
Married/Domestic partner	23,402 (57%)	5,382 (46%)	
Widowed	11,002 (27%)	3,925 (33%)	
Single	2,720 (7%)	940 (8%)	
Separated/Divorced	2,194 (5%)	946 (8%)	
Unknown	1,747 (4%)	548 (5%)	
Area income			<.0001
Highest	11,100 (27%)	2,884 (25%)	
Third	10,011 (24%)	2,828 (24%)	
Second	9,199 (22%)	2,876 (24%)	
Lowest	7,693 (19%)	2,487 (21%)	
Unknown	3,062 (7%)	666 (6%)	

(continued)

eTable 2. Patient Characteristics According to Baseline Mental Disorder Status Among Those Who Received a Routine Influenza Vaccination (cont.)

	No Mental Disorder n (%)	Diagnosed Mental Disorder n (%)	P Value
Dual Medicaid insurance			<.0001
No	33,916 (83%)	8,666 (74%)	
Yes	7,149 (17%)	3,075 (26%)	
Charlson comorbidity score			<.0001
0	16,230 (40%)	3,686 (31%)	
1	11,325 (28%)	3,138 (27%)	
2	6,416 (16%)	2,083 (18%)	
≥3	7,094 (17%)	2,834 (24%)	
Cancer stage			.007
Local	18,657 (45%)	5,268 (45%)	
Regional	16,336 (40%)	4,838 (41%)	
Distant	6,072 (15%)	1,635 (14%)	

eAppendix 3. Subgroup: Routine Influenza Vaccination (cont.)

eTable 3. Multivariate Logistic Regression Analysis of Characteristics Associated With Early Mental Disorder Among Patients Who Received a Routine Influenza Vaccination

	Odds Ratio (95% CI)	P Value
Disease subsite		
Colorectal	Ref	
Pancreatic	1.17 (1.09–1.26)	<.0001
Gastric	1.06 (0.98–1.15)	.17
Hepatic/Biliary	0.99 (0.91–1.07)	.73
Esophageal	1.12 (1.01–1.24)	.03
Anal	1.20 (1.03–1.39)	.02
Age group		
65–74 y	Ref	
75–84 y	0.90 (0.86–0.94)	<.0001
≥85 y	0.92 (0.86–0.98)	.009
Sex		
Male	Ref	
Female	1.76 (1.68–1.84)	<.0001
Race		
White	Ref	
Black	0.53 (0.48–0.58)	<.0001
Asian/Pacific Islander	0.38 (0.34–0.42)	<.0001
North American Native	0.82 (0.56–1.21)	.31
Unknown	0.87 (0.61–1.26)	.47
Ethnicity		
Non-Hispanic	Ref	
Hispanic	0.78 (0.70–0.86)	<.0001
Marital status		
Married/Domestic partner	Ref	
Widowed	1.16 (1.10–1.23)	<.0001
Single	1.24 (1.14–1.34)	<.0001
Separated/Divorced	1.39 (1.28–1.51)	<.0001
Unknown	1.17 (1.05–1.30)	.003
Area income		
Highest	Ref	
Third	1.02 (0.96–1.09)	.47
Second	1.09 (1.03–1.16)	.003
Lowest	1.08 (1.01–1.15)	.02
Unknown	0.80 (0.72–0.88)	<.0001
Dual Medicaid insurance		
No	Ref	
Yes	1.74 (1.64–1.84)	<.0001

(continued)

eTable 3. Multivariate Logistic Regression Analysis of Characteristics Associated With Early Mental Disorder Among Patients Who Received a Routine Influenza Vaccination (cont.)

	Odds Ratio (95% CI)	P Value
Charlson comorbidity score		
0	Ref	
1	1.23 (1.17–1.30)	<.0001
2	1.42 (1.34–1.52)	<.0001
≥3	1.78 (1.68–1.89)	<.0001
Cancer stage		
Local	Ref	
Regional	1.07 (1.02–1.12)	.007
Distant	0.99 (0.92–1.05)	.68

eAppendix 3. Subgroup: Routine Influenza Vaccination (cont.)

eFigure 1. Development of a subsequent mental disorder following a gastrointestinal cancer diagnosis among patients without an early mental disorder who had received a routine influenza vaccination.

eAppendix 3. Subgroup: Routine Influenza Vaccination (cont.)

eTable 4. Characteristics Associated With Development of a Subsequent Mental Disorder Among Patients Who Received a Routine Influenza Vaccination^a

	Hazard Ratio (95% CI)	P Value
Disease subsite		
Colorectal	Ref	
Pancreatic	1.38 (1.25–1.53)	<.0001
Gastric	1.17 (1.07–1.28)	.0009
Hepatic/Biliary	1.27 (1.15–1.39)	<.0001
Esophageal	1.43 (1.27–1.62)	<.0001
Anal	1.17 (0.99–1.38)	.06
Age group		
65–74 y	Ref	
75–84 y	1.10 (1.05–1.16)	.0002
≥85 y	1.26 (1.18–1.36)	<.0001
Sex		
Male	Ref	
Female	1.22 (1.16–1.28)	<.0001
Race		
White	Ref	
Black	0.82 (0.74–0.92)	.0004
Asian/Pacific Islander	0.56 (0.50–0.62)	<.0001
North American Native	0.75 (0.43–1.29)	.30
Unknown	0.64 (0.40–1.02)	.06
Ethnicity		
Non-Hispanic	Ref	
Hispanic	0.87 (0.78–0.98)	.02
Marital status		
Married/Domestic partner	Ref	
Widowed	1.00 (0.94–1.06)	.97
Single	1.00 (0.91–1.10)	.98
Separated/Divorced	0.98 (0.88–1.09)	.70
Unknown	1.00 (0.90–1.12)	.95
Area income		
Highest	Ref	
Third	1.02 (0.95–1.09)	.57
Second	1.08 (1.01–1.15)	.03
Lowest	1.07 (1.00–1.15)	.07
Unknown	0.99 (0.90–1.08)	.78
Dual Medicaid insurance		
No	Ref	
Yes	1.30 (1.22–1.38)	<.0001

(continued)

eTable 4. Characteristics Associated With Development of a Subsequent Mental Disorder Among Patients Who Received a Routine Influenza Vaccination^a (cont.)

	Hazard Ratio (95% CI)	P Value
Charlson comorbidity score		
0	Ref	
1	1.13 (1.07–1.20)	<.0001
2	1.21 (1.13–1.30)	<.0001
≥3	1.48 (1.38–1.58)	<.0001
Cancer stage		
Local	Ref	
Regional	1.09 (1.04–1.14)	.0007
Distant	1.37 (1.26–1.50)	<.0001

^aThese patients did not have an early mental disorder, and hazard ratio estimates were determined from a subdistribution hazard model.

eAppendix 4. Secondary Analysis: Alternate Classification of Early Mental Disorder

eTable 5. Patient Characteristics According to Baseline Mental Disorder Status Among Patients With an Early Mental Disorder^a

	No Mental Disorder n (%)	Diagnosed Mental Disorder n (%)	P Value
Disease subsite			<.0001
Colorectal	67,599 (68%)	8,822 (69%)	
Pancreatic	9,146 (9%)	1,232 (10%)	
Gastric	8,052 (8%)	944 (7%)	
Hepatic/Biliary	8,334 (8%)	1,070 (8%)	
Esophageal	4,701 (5%)	458 (4%)	
Anal	1,642 (2%)	283 (2%)	
Age group			<.0001
65–74 y	44,384 (45%)	5,408 (42%)	
75–84 y	40,969 (41%)	5,191 (41%)	
≥85 y	14,121 (14%)	2,210 (17%)	
Sex			<.0001
Male	51,012 (51%)	4,239 (33%)	
Female	48,462 (49%)	8,570 (67%)	
Race			<.0001
White	82,561 (83%)	11,202 (87%)	
Black	8,847 (9%)	1,027 (8%)	
Asian/Pacific Islander	7,320 (7%)	488 (4%)	
North American Native	406 (0%)	50 (0%)	
Unknown	340 (0%)	42 (0%)	
Ethnicity			.48
Non-Hispanic	92,833 (93%)	11,932 (93%)	
Hispanic	6,641 (7%)	877 (7%)	
Marital status			<.0001
Married/Domestic partner	53,584 (54%)	5,116 (40%)	
Widowed	26,182 (26%)	4,403 (34%)	
Single	8,146 (8%)	1,318 (10%)	
Separated/Divorced	7,422 (7%)	1,362 (11%)	
Unknown	4,140 (4%)	610 (5%)	
Area income			<.0001
Highest	24,001 (24%)	2,672 (21%)	
Third	22,928 (23%)	2,931 (23%)	
Second	22,231 (22%)	3,111 (24%)	
Lowest	21,336 (21%)	3,171 (25%)	
Unknown	8,978 (9%)	924 (7%)	

(continued)

eTable 5. Patient Characteristics According to Baseline Mental Disorder Status Among Patients With an Early Mental Disorder^a (cont.)

	No Mental Disorder n (%)	Diagnosed Mental Disorder n (%)	P Value
Dual Medicaid insurance			<.0001
No	78,074 (78%)	8,208 (64%)	
Yes	21,400 (22%)	4,601 (36%)	
Charlson comorbidity score			<.0001
0	45,842 (46%)	3,556 (28%)	
1	25,329 (25%)	3,200 (25%)	
2	13,594 (14%)	2,270 (18%)	
≥3	14,709 (15%)	3,783 (30%)	
Cancer stage			<.0001
Local	43,093 (43%)	6,065 (47%)	
Regional	40,407 (41%)	5,039 (39%)	
Distant	15,974 (16%)	1,705 (13%)	

^aDefined as 12 months prior up to the date of cancer diagnosis.

eAppendix 4. Secondary Analysis: Alternate Classification of Early Mental Disorder (cont.)

eTable 6. Multivariate Logistic Regression Analysis of Characteristics Associated With an Early Mental Disorder^a

	Odds Ratio (95% CI)	P Value
Disease subsite		
Colorectal	Ref	
Pancreatic	1.12 (1.05–1.20)	.0009
Gastric	0.99 (0.92–1.07)	.82
Hepatic/Biliary	0.94 (0.87–1.01)	.08
Esophageal	0.96 (0.87–1.06)	.45
Anal	1.14 (1.00–1.30)	.053
Age group		
65–74 y	Ref	
75–84 y	0.90 (0.86–0.94)	<.0001
≥85 y	0.93 (0.88–0.99)	.02
Sex		
Male	Ref	
Female	2.04 (1.96–2.13)	<.0001
Race		
White	Ref	
Black	0.55 (0.51–0.59)	<.0001
Asian/Pacific Islander	0.37 (0.33–0.41)	<.0001
North American Native	0.68 (0.50–0.93)	.01
Unknown	0.92 (0.66–1.27)	.60
Ethnicity		
Non-Hispanic	Ref	
Hispanic	0.71 (0.65–0.76)	<.0001
Marital status		
Married/Domestic partner	Ref	
Widowed	1.17 (1.11–1.23)	<.0001
Single	1.32 (1.24–1.42)	<.0001
Separated/Divorced	1.38 (1.29–1.48)	<.0001
Unknown	1.20 (1.09–1.32)	.0001
Area income		
Highest	Ref	
Third	1.06 (1.00–1.12)	.06
Second	1.11 (1.05–1.17)	.0003
Lowest	1.09 (1.03–1.16)	.004
Unknown	0.87 (0.80–0.94)	.0006
Dual Medicaid insurance		
No	Ref	
Yes	1.87 (1.79–1.96)	<.0001

(continued)

eTable 6. Multivariate Logistic Regression Analysis of Characteristics Associated With an Early Mental Disorder^a (cont.)

	Odds Ratio (95% CI)	P Value
Charlson comorbidity score		
0	Ref	
1	1.60 (1.52–1.68)	<.0001
2	2.08 (1.97–2.21)	<.0001
≥3	3.23 (3.06–3.40)	<.0001
Cancer stage		
Local	Ref	
Regional	0.93 (0.89–0.97)	.0009
Distant	0.85 (0.80–0.90)	<.0001

^aDefined as 12 months prior up to the date of cancer diagnosis.

eAppendix 4. Secondary Analysis: Alternate Classification of Early Mental Disorder (cont.)

eFigure 2. Development of a subsequent mental disorder following a gastrointestinal cancer diagnosis among patients without an early mental disorder (defined as 12 months prior to the date of cancer diagnosis). The cumulative incidence of developing a subsequent mental disorder 5 years from a cancer diagnosis was 30%, 25%, 24%, 22%, 21%, and 22% for patients with anal, colorectal, esophageal, gastric, hepatic/biliary, and pancreatic cancers, respectively.

eAppendix 4. Secondary Analysis: Alternate Classification of Early Mental Disorder (cont.)

eTable 7. Multivariate Analysis of Characteristics Associated With the Development of a Subsequent Mental Disorder^a

	Hazard Ratio (95% CI)	P Value
Disease subsite		
Colorectal	Ref	
Pancreatic	1.26 (1.20–1.32)	<.0001
Gastric	1.12 (1.07–1.18)	<.0001
Hepatic/Biliary	1.12 (1.07–1.18)	<.0001
Esophageal	1.38 (1.30–1.47)	<.0001
Anal	1.13 (1.03–1.23)	.009
Age group		
65–74 y	Ref	
75–84 y	1.08 (1.05–1.11)	<.0001
≥85 y	1.17 (1.13–1.22)	<.0001
Sex		
Male	Ref	
Female	1.28 (1.25–1.32)	<.0001
Race		
White	Ref	
Black	0.70 (0.67–0.74)	<.0001
Asian/Pacific Islander	0.53 (0.50–0.57)	<.0001
North American Native	0.77 (0.62–0.95)	.02
Unknown	0.68 (0.53–0.86)	.0016
Ethnicity		
Non-Hispanic	Ref	
Hispanic	0.86 (0.82–0.91)	<.0001
Marital status		
Married/Domestic partner	Ref	
Widowed	1.02 (0.99–1.05)	.25
Single	1.05 (1.00–1.10)	.052
Separated/Divorced	1.07 (1.02–1.12)	.007
Unknown	1.03 (0.97–1.09)	.40
Area income		
Highest	Ref	
Third	1.00 (0.97–1.04)	.92
Second	1.02 (0.98–1.06)	.26
Lowest	1.07 (1.03–1.11)	.0003
Unknown	0.90 (0.86–0.94)	<.0001
Dual Medicaid insurance		
No	Ref	
Yes	1.28 (1.24–1.32)	<.0001

(continued)

eTable 7. Multivariate Analysis of Characteristics Associated With the Development of a Subsequent Mental Disorder^a (cont.)

	Hazard Ratio (95% CI)	P Value
Charlson comorbidity score		
0	Ref	
1	1.13 (1.10–1.17)	<.0001
2	1.21 (1.16–1.25)	<.0001
≥3	1.25 (1.20–1.29)	<.0001
Cancer stage		
Local	Ref	
Regional	1.15 (1.12–1.18)	<.0001
Distant	1.20 (1.15–1.25)	<.0001

^aThese patients did not have an early mental disorder, and hazard ratio estimates were determined from a subdistribution hazard model. Early mental disorder is defined as 12 months prior up to the date of cancer diagnosis.

eAppendix 5. Secondary Analysis: Investigating Depressive, Anxiety, Psychotic, and Bipolar Disorder Diagnoses

Results

We performed additional analyses separating mental disorder diagnoses into specific depressive, anxiety, psychotic, and bipolar disorders (eTables 8–10, eFigure 3). Most findings in the primary analysis were consistent across the secondary analyses and those of individual mental disorders. However, we found that bipolar and anxiety disorders were not more likely in older patients (in contrast to depressive and psychotic disorders). On multivariate analysis, there was no association between age and the development of a subsequent bipolar or anxiety disorder (in contrast to depressive and psychotic disorders).

In addition, analysis of subsequently diagnosed depressive, anxiety, psychotic, and bipolar disorders among patients who previously had a different mental disorder diagnosis is shown in eFigure 3. We found that for each mental disorder subgroup, a subsequent mental disorder diagnosis was always more common among patients who already had a different mental disorder diagnosis.

eAppendix 5. Secondary Analysis: Investigating Depressive, Anxiety, Psychotic, and Bipolar Disorder Diagnoses (cont.)

Table 8. Patient Characteristics According to Early Depressive, Anxiety, Psychotic, and Bipolar Disorder Status

	Depressive Disorder ^a		Anxiety Disorder ^a		Psychotic Disorder ^a		Bipolar Disorder ^a	
	None n (%)	Diagnosed n (%)	None n (%)	Diagnosed n (%)	None n (%)	Diagnosed n (%)	None n (%)	Diagnosed n (%)
Disease subsite								
Colorectal	66,275 (68%)	10,146 (67%)	68,799 (68%)	7,622 (68%)	73,795 (68%)	2,626 (73%)	75,694 (68%)	727 (69%)
Pancreatic	8,797 (9%)	1,581 (10%)	9,211 (9%)	1,167 (10%)	10,134 (9%)	244 (7%)	10,281 (9%)	97 (9%)
Gastric	7,839 (8%)	1,157 (8%)	8,152 (8%)	844 (8%)	8,769 (8%)	227 (6%)	8,921 (8%)	75 (7%)
Hepatic/Biliary	8,162 (8%)	1,242 (8%)	8,591 (8%)	813 (7%)	9,098 (8%)	306 (9%)	9,327 (8%)	77 (7%)
Esophageal	4,524 (5%)	635 (4%)	4,666 (5%)	493 (4%)	5,036 (5%)	123 (3%)	5,111 (5%)	48 (5%)
Anal	1,595 (2%)	330 (2%)	1,684 (2%)	241 (2%)	1,857 (2%)	68 (2%)	1,897 (2%)	28 (3%)
Age group								
65–74 y	43,338 (45%)	6,454 (43%)	44,734 (44%)	5,058 (45%)	48,556 (45%)	1,236 (34%)	49,225 (44%)	567 (54%)
75–84 y	40,050 (41%)	6,110 (40%)	41,676 (41%)	4,484 (40%)	44,582 (41%)	1,578 (44%)	45,776 (41%)	384 (37%)
≥85 y	13,804 (14%)	2,527 (17%)	14,693 (15%)	1,638 (15%)	15,551 (14%)	780 (22%)	16,230 (15%)	101 (10%)
Sex								
Male	49,812 (51%)	5,439 (36%)	51,625 (51%)	3,626 (32%)	53,653 (49%)	1,598 (44%)	54,822 (49%)	429 (41%)
Female	47,380 (49%)	9,652 (64%)	49,478 (49%)	7,554 (68%)	55,036 (51%)	1,996 (56%)	56,409 (51%)	623 (59%)
Race								
White	80,388 (83%)	13,375 (89%)	83,764 (83%)	9,999 (89%)	90,787 (84%)	2,976 (83%)	92,832 (83%)	931 (88%)
Black	8,824 (9%)	1,050 (7%)	9,139 (9%)	735 (7%)	9,430 (9%)	444 (12%)	9,786 (9%)	88 (8%)
Asian/Pacific Islander	7,243 (7%)	565 (4%)	7,422 (7%)	386 (3%)	7,664 (7%)	144 (4%)		
North American Native	401 (0%)	55 (0%)	423 (0%)	33 (0%)				
Unknown	336 (0%)	46 (0%)	355 (0%)	27 (0%)				
Ethnicity								
Non-Hispanic	90,711 (93%)	14,054 (93%)	94,318 (93%)	10,447 (93%)	101,395 (93%)	3,370 (94%)	103,773 (93%)	992 (94%)
Hispanic	6,481 (7%)	1,037 (7%)	6,785 (7%)	733 (7%)	7,294 (7%)	224 (6%)	7,458 (7%)	60 (6%)
Marital status								
Married/Domestic partner	52,329 (54%)	6,371 (42%)	53,744 (53%)	4,956 (44%)	57,436 (53%)	1,264 (35%)	58,311 (52%)	389 (37%)
Widowed	25,489 (26%)	5,096 (34%)	26,973 (27%)	3,612 (32%)	29,385 (27%)	1,200 (33%)	30,313 (27%)	272 (26%)
Single	8,053 (8%)	1,411 (9%)	8,490 (8%)	974 (9%)	8,951 (8%)	513 (14%)	9,289 (8%)	175 (17%)
Separated/Divorced	7,280 (7%)	1,504 (10%)	7,665 (8%)	1,119 (10%)	8,363 (8%)	421 (12%)	8,621 (8%)	163 (15%)
Unknown	4,041 (4%)	709 (5%)	4,231 (4%)	519 (5%)	4,554 (4%)	196 (5%)	4,697 (4%)	53 (5%)
Area income								
Highest	23,289 (24%)	3,384 (22%)	24,181 (24%)	2,492 (22%)	26,033 (24%)	640 (18%)	26,433 (24%)	240 (23%)
Third	22,380 (23%)	3,479 (23%)	23,306 (23%)	2,553 (23%)	25,089 (23%)	770 (21%)	25,619 (23%)	240 (23%)
Second	21,743 (22%)	3,599 (24%)	22,698 (22%)	2,644 (24%)	24,450 (22%)	892 (25%)	25,091 (23%)	251 (24%)
Lowest	20,985 (22%)	3,522 (23%)	21,676 (21%)	2,831 (25%)	23,500 (22%)	1,007 (28%)	24,257 (22%)	250 (24%)
Unknown	8,795 (9%)	1,107 (7%)	9,242 (9%)	660 (6%)	9,617 (9%)	285 (8%)	9,831 (9%)	71 (7%)
Dual Medicaid insurance								
No	76,039 (78%)	10,243 (68%)	78,423 (78%)	7,859 (70%)	84,283 (78%)	1,999 (56%)	85,688 (77%)	594 (56%)
Yes	21,153 (22%)	4,848 (32%)	22,680 (22%)	3,321 (30%)	24,406 (22%)	1,595 (44%)	25,543 (23%)	458 (44%)

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eAppendix 5. Secondary Analysis: Investigating Depressive, Anxiety, Psychotic, and Bipolar Disorder Diagnoses (cont.)

eTable 8. Patient Characteristics According to Early Depressive, Anxiety, Psychotic, and Bipolar Disorder Status (cont.)								
	Depressive Disorder ^a		Anxiety Disorder ^a		Psychotic Disorder ^a		Bipolar Disorder ^a	
	None n (%)	Diagnosed n (%)	None n (%)	Diagnosed n (%)	None n (%)	Diagnosed n (%)	None n (%)	Diagnosed n (%)
Charlson comorbidity score								
0	44,512 (46%)	4,886 (32%)	45,152 (45%)	4,246 (38%)	48,499 (45%)	899 (25%)	49,103 (44%)	295 (28%)
1	24,650 (25%)	3,879 (26%)	25,641 (25%)	2,888 (26%)	27,729 (26%)	800 (22%)	28,295 (25%)	234 (22%)
2	13,323 (14%)	2,541 (17%)	14,107 (14%)	1,757 (16%)	15,206 (14%)	658 (18%)	15,657 (14%)	207 (20%)
≥3	14,707 (15%)	3,785 (25%)	16,203 (16%)	2,289 (20%)	17,255 (16%)	1,237 (34%)	18,176 (16%)	316 (30%)
Cancer stage								
Locals	42,590 (44%)	6,568 (44%)	44,340 (44%)	4,818 (43%)	47,492 (44%)	1,666 (46%)	48,670 (44%)	488 (46%)
Regional	39,036 (40%)	6,410 (42%)	40,714 (40%)	4,732 (42%)	43,961 (40%)	1,485 (41%)	45,022 (40%)	424 (40%)
Distant	15,566 (16%)	2,113 (14%)	16,049 (16%)	1,630 (15%)	17,236 (16%)	443 (12%)	17,539 (16%)	140 (13%)

All comparisons were significant at the $P < .0001$ level aside from those appearing in bold. Cells with small numbers are not shown.

eAppendix 5. Secondary Analysis: Investigating Depressive, Anxiety, Psychotic, and Bipolar Disorder Diagnoses (cont.)

eTable 9. Multivariate Logistic Regression Analysis of Characteristics Associated With Early Depressive, Anxiety, Psychotic, and Bipolar Disorders

	Depressive Disorder		Anxiety Disorder		Psychotic Disorder		Bipolar Disorder	
	Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)	P Value
Disease subsite								
Colorectal	Ref		Ref		Ref		Ref	
Pancreatic	1.22 (1.15–1.30)	<.0001	1.15 (1.08–1.23)	<.0001	0.80 (0.70–0.92)	.001	1.03 (0.83–1.29)	.78
Gastric	1.08 (1.01–1.16)	.02	1.09 (1.01–1.18)	.02	0.75 (0.65–0.86)	<.0001	0.95 (0.75–1.22)	.71
Hepatic/Biliary	0.99 (0.93–1.06)	.76	0.89 (0.83–0.97)	.005	0.91 (0.80–1.03)	.13	0.78 (0.61–0.99)	.04
Esophageal	1.12 (1.03–1.22)	.01	1.19 (1.08–1.31)	.0005	0.80 (0.66–0.96)	.017	1.04 (0.77–1.41)	.779
Anal	1.20 (1.06–1.36)	.004	1.10 (0.96–1.26)	.18	0.99 (0.78–1.28)	.96	1.22 (0.83–1.79)	.31
Age group								
65–74 y	Ref		Ref		Ref		Ref	
75–84 y	0.90 (0.87–0.94)	<.0001	0.85 (0.82–0.89)	<.0001	1.36 (1.25–1.47)	<.0001	0.68 (0.60–0.78)	<.0001
≥85 y	0.93 (0.88–0.99)	.01	0.77 (0.72–0.82)	<.0001	1.74 (1.57–1.92)	<.0001	0.44 (0.35–0.55)	<.0001
Sex								
Male	Ref		Ref		Ref		Ref	
Female	1.78 (1.71–1.85)	<.0001	2.19 (2.10–2.29)	<.0001	0.97 (0.90–1.04)	.40	1.39 (1.22–1.59)	<.0001
Race								
White	Ref		Ref		Ref		Ref	
Black	0.51 (0.48–0.55)	<.0001	0.49 (0.45–0.53)	<.0001	0.91 (0.81–1.01)	.08	0.52 (0.41–0.65)	<.0001
Asian/Pacific Islander	0.37 (0.34–0.41)	<.0001	0.37 (0.34–0.42)	<.0001	0.42 (0.35–0.50)	<.0001	0.23 (0.16–0.35)	<.0001
North American Native	0.67 (0.50–0.89)	.006	0.55 (0.38–0.79)	.001	1.01 (0.64–1.60)	.96	0.15 (0.02–1.07)	.06
Unknown	0.85 (0.62–1.16)	.30	0.65 (0.44–0.97)	.03	0.81 (0.43–1.53)	.51	1.40 (0.62–3.18)	.42
Ethnicity								
Non-Hispanic	Ref		Ref		Ref		Ref	
Hispanic	0.76 (0.70–0.81)	<.0001	0.76 (0.70–0.83)	<.0001	0.62 (0.53–0.71)	<.0001	0.50 (0.38–0.65)	<.0001
Marital status								
Married/Domestic partner	Ref		Ref		Ref		Ref	
Widowed	1.20 (1.15–1.26)	<.0001	1.05 (1.00–1.11)	.0499	1.30 (1.19–1.43)	<.0001	1.14 (0.96–1.36)	.13
Single	1.21 (1.13–1.29)	<.0001	1.05 (0.98–1.13)	.18	1.93 (1.72–2.15)	<.0001	2.14 (1.78–2.59)	<.0001
Separated/Divorced	1.32 (1.24–1.41)	<.0001	1.21 (1.13–1.30)	<.0001	1.71 (1.52–1.93)	<.0001	1.92 (1.58–2.33)	<.0001
Unknown	1.22 (1.12–1.33)	<.0001	1.12 (1.01–1.23)	.03	1.54 (1.32–1.81)	<.0001	1.41 (1.05–1.89)	.02
Area income								
Highest	Ref		Ref		Ref		Ref	
Third	1.00 (0.95–1.06)	.92	1.02 (0.96–1.08)	.62	1.12 (1.01–1.25)	.03	0.90 (0.75–1.08)	.27
Second	1.03 (0.98–1.09)	.20	1.06 (1.00–1.12)	.07	1.25 (1.13–1.39)	<.0001	0.88 (0.74–1.06)	.17
Lowest	1.01 (0.96–1.07)	.69	1.19 (1.12–1.26)	<.0001	1.23 (1.11–1.37)	<.0001	0.79 (0.66–0.96)	.02
Unknown	0.83 (0.77–0.89)	<.0001	0.67 (0.61–0.73)	<.0001	1.08 (0.93–1.25)	.31	0.69 (0.53–0.91)	.007
Dual Medicaid insurance								
No	Ref		Ref		Ref		Ref	
Yes	1.68 (1.61–1.75)	<.0001	1.49 (1.42–1.57)	<.0001	2.34 (2.17–2.53)	<.0001	2.45 (2.13–2.81)	<.0001

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eAppendix 5. Secondary Analysis: Investigating Depressive, Anxiety, Psychotic, and Bipolar Disorder Diagnoses (cont.)

eTable 9. Multivariate Logistic Regression Analysis of Characteristics Associated With Early Depressive, Anxiety, Psychotic, and Bipolar Disorders (cont.)

	Depressive Disorder		Anxiety Disorder		Psychotic Disorder		Bipolar Disorder	
	Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)	P Value
Charlson comorbidity score								
0	Ref		Ref		Ref		Ref	
1	1.41 (1.35–1.48)	<.0001	1.19 (1.14–1.26)	<.0001	1.46 (1.33–1.61)	<.0001	1.37 (1.15–1.63)	.0003
2	1.70 (1.61–1.79)	<.0001	1.32 (1.25–1.40)	<.0001	2.06 (1.86–2.29)	<.0001	2.17 (1.81–2.60)	<.0001
≥3	2.32 (2.21–2.43)	<.0001	1.53 (1.45–1.62)	<.0001	3.18 (2.90–3.48)	<.0001	2.73 (2.32–3.23)	<.0001
Cancer stage								
Local	Ref		Ref		Ref		Ref	
Regional	1.10 (1.06–1.15)	<.0001	1.08 (1.03–1.13)	.0005	1.05 (0.98–1.13)	.16	0.98 (0.86–1.12)	.80
Distant	0.94 (0.89–0.99)	.03	0.96 (0.90–1.02)	.16	0.91 (0.82–1.02)	.11	0.86 (0.70–1.04)	.12

eAppendix 5. Secondary Analysis: Investigating Depressive, Anxiety, Psychotic, and Bipolar Disorder Diagnoses (cont.)

Figure 3. Development of a subsequent depressive disorder following a gastrointestinal cancer diagnosis among patients (A) without and (B) with another early mental disorder.

Figure 4. Development of a subsequent anxiety disorder following a gastrointestinal cancer diagnosis among patients (A) without and (B) with another early mental disorder.

eAppendix 5. Secondary Analysis: Investigating Depressive, Anxiety, Psychotic, and Bipolar Disorder Diagnoses (cont.)

eFigure 5. Development of a subsequent psychotic disorder following a gastrointestinal cancer diagnosis among patients (A) without and (B) with another early mental disorder.

eFigure 6. Development of a subsequent bipolar disorder following a gastrointestinal cancer diagnosis among patients (A) without and (B) with another early mental disorder.

eAppendix 5. Secondary Analysis: Investigating Depressive, Anxiety, Psychotic, and Bipolar Disorder Diagnoses (cont.)

eTable 10. Multivariate Analysis of Characteristics Associated With Development of a Subsequent Depressive, Anxiety, Psychotic, or Bipolar Disorder

	Depressive Disorder Hazard Ratio (95% CI)	Anxiety Disorder Hazard Ratio (95% CI)	Psychotic Disorder Hazard Ratio (95% CI)	Bipolar Disorder Hazard Ratio (95% CI)
Disease subsite				
Colorectal	Ref	Ref	Ref	Ref
Pancreatic	1.41 (1.29–1.54)	1.37 (1.24–1.51)	1.32 (1.14–1.53)	1.22 (0.86–1.71)
Gastric	1.24 (1.15–1.34)	1.07 (0.98–1.17)	0.91 (0.80–1.04)	0.96 (0.72–1.28)
Hepatic/Biliary	1.18 (1.08–1.28)	1.14 (1.03–1.25)	1.38 (1.21–1.56)	1.13 (0.85–1.52)
Esophageal	1.73 (1.58–1.91)	1.50 (1.34–1.68)	1.01 (0.83–1.22)	1.18 (0.79–1.75)
Anal	1.09 (0.95–1.25)	1.15 (1.00–1.33)	0.97 (0.78–1.22)	1.36 (0.90–2.07)
Age group				
65–74 y	Ref	Ref	Ref	Ref
75–84 y	1.15 (1.10–1.20)	0.96 (0.91–1.00)	1.54 (1.44–1.64)	0.95 (0.82–1.10)
≥85 y	1.22 (1.15–1.30)	0.95 (0.89–1.03)	2.22 (2.03–2.43)	1.01 (0.81–1.25)
Sex				
Male	Ref	Ref	Ref	Ref
Female	1.30 (1.25–1.36)	1.69 (1.61–1.77)	1.02 (0.95–1.09)	1.12 (0.97–1.30)
Race				
White	Ref	Ref	Ref	Ref
Black	0.68 (0.63–0.73)	0.60 (0.55–0.66)	0.78 (0.69–0.87)	0.72 (0.57–0.92)
Asian/Pacific Islander	0.49 (0.45–0.54)	0.42 (0.38–0.48)	0.47 (0.40–0.55)	0.37 (0.25–0.53)
North American Native	0.72 (0.51–1.03)	0.79 (0.55–1.14)	1.18 (0.77–1.82)	0.24 (0.03–1.70)
Unknown	0.71 (0.50–1.02)	0.71 (0.48–1.06)	0.37 (0.17–0.83)	1.10 (0.41–2.96)
Ethnicity				
Non-Hispanic	Ref	Ref	Ref	Ref
Hispanic	0.89 (0.82–0.96)	0.86 (0.78–0.93)	0.53 (0.46–0.61)	0.79 (0.61–1.03)
Marital status				
Married/Domestic partner	Ref	Ref	Ref	Ref
Widowed	0.98 (0.94–1.04)	1.00 (0.95–1.06)	1.07 (1.00–1.16)	1.15 (0.97–1.38)
Single	1.03 (0.95–1.11)	1.04 (0.96–1.13)	1.07 (0.96–1.20)	1.43 (1.14–1.80)
Separated/Divorced	1.07 (0.99–1.15)	1.13 (1.04–1.22)	1.24 (1.11–1.39)	1.59 (1.27–1.99)
Unknown	1.09 (0.99–1.19)	0.99 (0.89–1.10)	0.95 (0.82–1.11)	1.23 (0.89–1.69)
Area income				
Highest	Ref	Ref	Ref	Ref
Third	0.99 (0.93–1.05)	1.06 (0.99–1.13)	1.06 (0.97–1.16)	1.20 (0.98–1.47)
Second	1.00 (0.94–1.06)	1.10 (1.03–1.18)	1.24 (1.13–1.35)	1.01 (0.82–1.24)
Lowest	0.99 (0.93–1.05)	1.16 (1.09–1.24)	1.29 (1.17–1.41)	1.09 (0.88–1.34)
Unknown	0.91 (0.85–0.98)	0.92 (0.85–0.99)	1.05 (0.94–1.18)	0.81 (0.62–1.06)
Dual Medicaid insurance				
No	Ref	Ref	Ref	Ref
Yes	1.49 (1.42–1.56)	1.36 (1.29–1.43)	1.71 (1.60–1.84)	2.25 (1.93–2.63)

(continued on next page)

eAppendix 5. Secondary Analysis: Investigating Depressive, Anxiety, Psychotic, and Bipolar Disorder Diagnoses (cont.)

eTable 10. Multivariate Analysis of Characteristics Associated With Development of a Subsequent Depressive, Anxiety, Psychotic, or Bipolar Disorder (cont.)

	Depressive Disorder Hazard Ratio (95% CI)	Anxiety Disorder Hazard Ratio (95% CI)	Psychotic Disorder Hazard Ratio (95% CI)	Bipolar Disorder Hazard Ratio (95% CI)
Charlson comorbidity score				
0	Ref	Ref	Ref	Ref
1	1.23 (1.17–1.29)	1.21 (1.15–1.28)	1.26 (1.17–1.36)	1.61 (1.36–1.91)
2	1.43 (1.35–1.52)	1.30 (1.22–1.39)	1.49 (1.37–1.63)	1.78 (1.46–2.18)
≥3	1.63 (1.54–1.72)	1.50 (1.41–1.60)	2.00 (1.85–2.18)	2.30 (1.90–2.78)
Cancer stage				
Local	Ref	Ref	Ref	Ref
Regional	1.11 (1.06–1.15)	1.02 (0.98–1.07)	1.02 (0.96–1.09)	1.01 (0.88–1.16)
Distant	1.34 (1.25–1.44)	1.17 (1.08–1.27)	1.35 (1.20–1.51)	1.02 (0.77–1.36)

These patients did not have an early mental disorder, and hazard ratio estimates were determined from a subdistribution hazard model. Early mental disorder is defined as 12 months prior to up to the date of cancer diagnosis.