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Advanced cancer as a risk for major depressive episodes

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Abstract

Objective—Major depression adversely affects health communication, quality of life, and survival in patients with advanced cancer. Prior research provides limited insight into how advanced cancer patients differ from the general population in risk for developing a major depressive episode (MDE). This study aims to determine whether advanced cancer poses distinct risks for initial and recurrent MDEs.

Methods—Advanced cancer patients (N=628) from Coping with Cancer were compared to propensity-weighted general population controls (N=9,282) from the National Comorbidity Survey Replication.

Results—Advanced cancer patients were more likely than comparisons to have an initial MDE [OR=27.3, 95% CI = (14.8 – 50.4); p<0.001], but no more likely than comparisons to have a recurrent MDE [OR=1.5, 95% CI = (0.9 – 2.6); p=0.160]. Nearly two-thirds (64.4%) of current MDEs in patients were initial onset; the vast majority (91.8%) of current MDEs in comparisons were recurrent.

Conclusions—Advanced cancer increases risk of an initial MDE, but appears not to enhance risk of a recurrent MDE. This suggests the importance of screening widely for depression in patients with advanced cancer as opposed to targeting screening to presumably high-risk subgroups of those with psychiatric histories.

Keywords

Cancer; oncology; depression; etiology; epidemiology

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Conflict of interest:

The authors declare no conflicts of interest and no financial interests in this investigation.

BACKGROUND

There is a growing interest in the mental health of cancer patients generally [1–3], and in connections between cancer and depression more specifically [4, 5]. Cancer patients with major depressive episodes (MDEs) exhibit maladaptive thoughts and behaviors that may result in poor patient-physician communication, reduced treatment adherence, and longer hospitalizations [3, 6]. Furthermore, depression adversely affects quality of life and overall survival in advanced cancer [7–10], defined as incurable, life-limiting oncologic illness.

Despite the clinical significance of MDEs in this population, it is unclear how advanced cancer affects the risk of developing a MDE. The majority of studies examining prevalence of depressive symptoms in advanced cancer patients have utilized measures that are not validated for making DSM-IV diagnoses of MDEs. Twelve studies with sample sizes of $N \geq 100$ that examined the prevalence of MDEs in advanced cancer patients using a structured diagnostic interview yielded a mean prevalence of 15.8% [5]. Although these pooled results suggest that advanced cancer patients have higher rates of MDEs than the general population (for which 1-month point prevalence is closer to 5%), none of these studies directly compared the frequency of MDEs in advanced cancer patients to a control sample.

Two studies have compared rates of DSM-IV MDEs between cancer patients (without reference to stage) and the general population. Using data from the National Comorbidity Study Replication, Honda and Goodwin [11] found that individuals who were diagnosed with cancer in the year prior to a screening interview were 3.6 times more likely to have experienced a MDE in that year compared to general population comparisons. However, this study included a relatively small number of individuals recently diagnosed with cancer (N=45) and did not include data on cancer stage. Harter *et al.* [12] pooled a sample of German individuals diagnosed with cancer in the year prior to being screened for a MDE in the German National Health Interview and Examination Survey Mental Health Supplement (GHS-MHS) with a sample of inpatient cancer patients from the Epidemiology of Mental Disorders in Medical Rehabilitation Study (EMDMR). This pooled sample of individuals with cancer (N=174) was compared to healthy controls (N=1,083) matched for age and gender from the GHS-MHS, revealing that cancer patients were 2.4 times more likely to have an unspecified mood disorder than healthy comparisons. Unfortunately, this study also lacked information on cancer stage and did not provide data related to risk of a MDE specifically.

Major depression is a highly recurrent disorder, and risks for initial MDEs may be distinct from those for recurrent MDEs. Experiencing a stressful life event places an individual at greater risk of an initial onset as opposed to a recurrent MDE [13, 14]. Numerous studies suggest that cancer constitutes a life stressor which results in clinically significant emotional distress [15–18]. Therefore, as a stressful life event, advanced cancer may pose a greater risk for an initial onset than for a recurrent MDE.

This study aims to determine how advanced cancer affects the risk for developing a MDE. Given that life stressors pose greater risks for a first episode and lesser risks for recurrent

episodes of major depression [13, 14, 19, 20], we hypothesized that advanced cancer would pose greater risk for an initial MDE and lesser risk for a recurrent MDE.

METHODS

Study samples

The Coping with Cancer (CwC) study is a prospective, multi-institutional cohort investigation of advanced cancer patients and their caregivers funded by the National Institute of Mental Health (MH63892) and the National Cancer Institute (CA106370). Participants were recruited between September 2002 and February 2008 at six comprehensive cancer centers: Yale Cancer Center (New Haven, CT), Veterans Affairs Connecticut Healthcare System Comprehensive Cancer Clinics (West Haven, CT), Parkland Hospital (Dallas, TX), Simmons Comprehensive Cancer Center (Dallas, TX), Dana-Farber Cancer Institute (Boston, MA), and New Hampshire Oncology-Hematology (Hooksett, NH). Criteria for patient eligibility included diagnosis of advanced cancer (presence of distant metastases and disease refractory to first-line chemotherapy); estimated life expectancy of 6 months or less; age ≥ 20 years; and presence of an informal caregiver. Participants were identified by reviewing outpatient clinic rosters, and initial ascertainment of eligibility occurred via medical record extraction. Research staff subsequently confirmed each patient's diagnosis, treatment, and performance status with the physician. Patients with obvious signs of cognitive impairment (e.g., dementia/delirium) based on the evaluations of trained interviewers and clinicians and/or patients who made more than 6 errors on the Short Portable Mental Status Questionnaire (SPMSQ; [21]) were excluded because their responses were considered unlikely to be reliable or valid. Review boards of all participating institutions approved study procedures; all participants provided written, informed consent. Patients and caregivers received $25 as compensation for participating in the study.

Of 939 eligible patients, 661 (70.4%) participated in the survey. Common reasons for non-participation were "not interested" (n=106), "caregiver refuses" (n=32), and "too upset" (n=21). Patient participants and non-participants did not differ significantly in age, gender, race/ethnicity, and education. No patient participants resided in a nursing home or other institution. The present study includes data from 628 CwC participants (95.0% of all CwC participants) with complete diagnostic assessments for major depression. Patients included in the present study did not differ significantly from those not included with respect to age, gender, race/ethnicity, education, or marital status.

The National Institute of Mental Health sponsored National Comorbidity Survey Replication (NCS-R; MH60220) is a nationally representative community household survey conducted between February 2001 and December 2002, designed to evaluate the prevalence and correlates of mental disorders in the US [22]. The NCS-R sample includes 9,282 respondents aged 18 years or older. Respondents were selected from a multistage area probability sample of the non-institutionalized civilian population in the 48 contiguous states. The overall participation rate was 74.6%. Complete NCS-R survey methodology is described elsewhere [23].

Measures

Patient Characteristics—Patients provided information regarding age, gender, race/ethnicity, education, marital status, and primary cancer diagnosis. A patient's functional status was determined by the Karnofsky score [24] as assessed by a trained interviewer or physician. The Charlson Comorbidity Index [25] evaluated the number and severity of the patient's comorbid illnesses.

Major Depression—Both CwC and the NCS-R used DSM-IV compliant tools and face-to-face interviews to assess for MDEs. Trained non-clinician research assistants administered the Structured Clinical Interview for DSM-IV (SCID) modules for current and lifetime MDEs to patients in the CwC sample. The NCS-R utilized the Composite International Diagnostic Interview Version 3.0 (CIDI 3.0), administered by trained lay interviewers, to assess for 12-month and lifetime episodes of major depression. As supported by prior literature suggesting good concordance of the CIDI with standardized clinical assessments [26], the current study considered a MDE occurring within the last 12 months according to the CIDI 3.0 to be equivalent to a current MDE as measured by the SCID. Notably, the diagnostic criteria for MDE used by the CIDI and the SCID are identical.

Statistical Analysis

Chi-square tests and t-tests were used to compare clinical characteristics, i.e., recruitment site, primary cancer diagnosis, Karnofsky score, and Charlson Comorbidity Index, between CwC patients with and without a current MDE.

Chi-square tests and t-tests were also used to compare demographic characteristics, i.e., age, gender, race/ethnicity, education and marital status, between the CwC patient group and the NCS-R comparison group. These between-group comparisons were made using two sets of weights applied to the NCS-R sample: one set of weights included in the NCS-R data set used to reflect the general US population, and another set of weights based on propensity scores, a common method of matching samples to facilitate causal inference for between-group effects [27], calculated to make the NCS-R sample demographically similar to the CwC sample. The propensity weights match the NCS-R sample to the CwC sample in terms of age, gender, race/ethnicity, education and marital status, and in their use eliminate these factors as potential confounds in the analysis of patient-comparison group differences in MDEs.

Chi-square tests were used to compare rates of past and current MDEs between the CwC advanced cancer patient sample and the propensity-weighted NCS-R comparison sample. Odds ratios for current MDE associated with prior MDE, advanced cancer, and the interaction between prior MDE and advanced cancer (used to compare cancer-related risks for a recurrent as opposed to an initial onset MDE) were estimated using multiple logistic regression analysis using the CwC advanced cancer patient sample combined with the propensity-weighted NCS-R sample.

Statistical analysis was conducted using SAS statistical software, version 9.2 (Cary, NC). Statistical inferences were based on two-sided tests with $p<0.05$ taken to be statistically significant.

RESULTS

Clinical characteristics of advanced cancer patients, i.e., recruitment site, primary cancer diagnosis, Karnofsky score, and Charlson Comorbidity Index, were unrelated to current MDE (Table 1). Advanced cancer patients in the CwC sample were more likely to be older, black, less well educated, and separated/widowed/divorced as opposed to never married, than comparisons in the NCS-R sample weighed to reflect the general population (Table 2). However, advanced cancer patients did not differ from comparisons in the NCS-R sample weighed to be demographically similar to the CwC sample using propensity score weights (Table 2).

Advanced cancer patients and demographically similar comparisons did not significantly differ in rates of prior MDE (OR 0.9; 95% CI 0.7–1.2; p=0.440), but patients with advanced cancer were significantly more likely to have a current MDE (OR 3.5; 95% CI 2.5–4.9; p<0.001) than demographically similar comparisons (Table 3). Based on multiple logistic regression analysis using the propensity-weighted NCS-R sample, prior MDE modified the association between advanced cancer and current MDE [interaction OR=0.055, 95% CI = (0.024 – 0.127); p<0.001]. Among individuals without prior MDE, advanced cancer patients were more likely to have an initial onset MDE than comparisons [OR=27.3, 95% CI = (14.8 – 50.4); p<0.001]. Among individuals with prior MDE, advanced cancer patients were no more likely than comparisons to have a recurrent MDE [OR=1.5, 95% CI = (0.9 – 2.6); p=0.160]. The association between prior MDE and current MDE for advanced cancer patients [OR=4.2, 95% CI = (2.2 – 8.2); p<0.001] was significantly lower than that for comparisons [OR=77.3, 95% CI = (46.4 – 128.7); p<0.001] (Table 4).

Notably, nearly two-thirds of current MDEs in patients with advanced cancer were first onset episodes (29/45=64.4%). By contrast, in demographically similar individuals from the general population, over 90% (183/199=91.8%) of current MDEs were recurrent episodes. Still, advanced cancer patients with a previous history of MDE were at greater risk of a current MDE than advanced cancer patients without a history of MDE. Within cancer patients, 16/83 (19.3%) of those with a previous MDE had a current MDE and 29/545 (5.3%) of those with no previous MDE had a current MDE. In demographically similar comparisons, 183/1330 (13.8%) of those with a previous MDE had a current MDE and 16/7952 (0.2%) of those with no prior history of MDE had a current MDE.

DISCUSSION

Results indicate that, as compared to demographically similar population comparisons, advanced cancer patients have an elevated risk of initial episodes of major depression, but no increased risk for recurrent episodes. Among individuals with no prior history of MDEs, advanced cancer presented a high risk for an initial MDE. Among those with a prior history of MDE, advanced cancer did not pose an additional risk for a recurrent MDE. Viewing

advanced cancer as a major stressor, these findings are consistent with the "kindling" model of depression [13, 14], in which the association between stressful life events and depressive episodes diminishes as the number of lifetime depressive episodes increases.

Two distinct factors – the psychosocial stress of an advanced cancer diagnosis and the physical symptom burden accompanying advanced cancer – could contribute to increased risk for initial onset MDE in the present study. Although many cancer patients experience psychosocial stress throughout the course of their illnesses [15–18], distress and depressive symptoms often peak shortly after a cancer diagnosis [28–32], suggesting that it is the actual event of being diagnosed with a life-threatening illness, as opposed to the physical burden of disease (which tends to increase as the cancer progresses and death nears), which causes a cancer patient to experience higher levels of distress. Although the evidence is mixed, several prior studies have likewise found that increasing physical symptom burden and/or proximity to death do not predict higher rates of depression [2, 33]. Furthermore, physical symptoms are generally associated with more medical comorbidities and lower performance status. Our data revealed no significant association between either physical functioning, as measured by Karnofsky score, or medical comorbidity, as measured by the Charlson Comorbidity Index, and current MDE. Indeed, in the present study, advanced cancer patients with MDE had relatively high mean Karnofsky performance status, in a range (between 60–70) indicating inability to work but ability to live at home and independently attend to many personal care needs. Interpreted in this context, our results suggest that cancer as a psychological stressor is more likely than physical symptom burden to be the primary risk for an initial onset episode of major depression in this population. This interpretation is concordant with that of other recent studies showing that a cancer diagnosis, conceptualized as a major stressor, increases an individual's immediate risks of suicide and cardiovascular death [34, 35]. Because a cancer diagnosis can trigger severe psychological stress, clinicians must ensure that their communication methods inflict as little emotional harm as possible.

Results also indicate that there is no association between prior history of MDEs and advanced cancer. On the one hand, this suggests that there is no common etiology between major depression and cancer, which presents a contrast to the bidirectional links between major depression and other somatic illnesses such as cardiovascular disease [36]. On the other hand, it appears that advanced cancer induces incident MDEs that might not otherwise occur, suggesting cancer biology may play a role in enhancing risk for depression due to stress. A plausible mechanism might be that acute psychological stress associated with diagnosis of an advanced cancer exacerbates biological features of the patient's cancer such as impairments in micro-immunity and elevations in tumor- or treatment-derived inflammatory cytokines, which in prior studies have been associated with depression [37, 38].

Limitations and Strengths

Several limitations of the present study must be acknowledged. Our sample of advanced cancer patients likely comprised two distinct populations: those who were diagnosed initially with advanced disease; and those who developed advanced disease after previously completing treatment for an early stage cancer. We did not have data on the proportion of

advanced cancer patients in each subgroup; however, the psychological impact of advanced cancer may differ between these subgroups, potentially leading to distinct patterns of depressive episode onset. Further, we lacked data on the amount of time that had elapsed between a patient's advanced cancer diagnosis and initial administration of the SCID for MDEs. Therefore, no firm conclusions can be drawn regarding the period of vulnerability for a MDE associated with receiving an advanced cancer diagnosis. This concern is somewhat mitigated by the fact that study participants had been refractory to first-line chemotherapy (suggesting a poor prognosis) and were estimated to have an average life-expectancy of 6 months or less, suggesting that for most participants initial assessment and diagnosis of MDE had occurred approximately within the last year.

Another methodological limitation is that CwC utilized the SCID to assess MDEs, whereas the NCS-R used the CIDI. Although both measures are DSM-compliant, and a clinical reappraisal study in the NCS-R population revealed that the measures are concordant in detecting major depression (AUC 0.7–0.8) [26], it is possible that CIDI may slightly underestimate the prevalence of MDEs. In light of this concern, it is reassuring that the prevalence of prior MDE is similar between the two samples, 13% in advanced cancer patients versus 14% in comparisons. Additionally, the OR of 3.6 between cancer and MDE that Honda and Goodwin [11] observed using common NCS-R MDE assessments in both cancer and non-cancer groups is nearly identical to the OR of 3.5 between advanced cancer and MDE observed in the present study, suggesting that differences between SCID and CIDI MDE assessments may have little influence on the present findings. Still, future research should assess MDEs in advanced cancer patients and members of the general population with identical measures.

A related concern is that clinicians sometimes experience difficulty distinguishing major depression from adjustment disorder in advanced cancer patients, since symptoms such as sleep disturbance, fatigue, and anorexia may constitute side-effects of advanced cancer and its treatment. Although it is possible that these physical symptoms could bias the rate of MDE among patients in our study, this seems unlikely given that advanced cancer patients with histories of prior MDE were not shown to have significantly higher risks of recurrent MDE as compared to non-cancer comparisons. In addition, measures of lifetime diagnosis are subject to recall bias; questions about prior depressive episodes may have limited salience to a depressed cancer patient in the midst of a current situational crisis. Again, the nearly equivalent prevalence of prior MDEs in the two samples mitigates against this problem. It is worth noting that, in a post-hoc analysis, we found that CwC participants were nearly three times more likely than NCS-R participants to be on an antidepressant medication. This greater antidepressant use in advanced cancer patients may reflect not only the greater likelihood that advanced cancer patients experience MDEs, but also a greater likelihood that advanced cancer patients receive medical attention and treatment more generally. CwC patients with and without prior depression were similarly more likely to be on an antidepressant than their respective NCS-R counterparts. Finally, despite rigorously controlling for major demographic confounders utilizing propensity weights, we cannot eliminate the possibility of residual or unmeasured confounders (e.g. social supports, personality disorders, or anxiety disorders across cases and comparisons) that may be associated with initial onset or recurrent MDEs.

There are several key strengths of the present study as compared to prior investigations in this area. Both the CwC and NCS-R featured large, diverse samples and employed precise, SCID-based definitions of psychiatric diagnoses; both studies were comparable in their utilization of trained lay as opposed to clinician interviewers to conduct face-to-face interviews with community-residing, non-institutionalized participants. Utilizing the CwC sample allowed analysis of MDE in advanced cancer (an understudied population) increasing the specificity of our findings. Indeed, given the psychosocial and existential implications of having incurable as opposed to curable disease, advanced cancer may be a qualitatively different stressor than early stage cancer. The use of an objective cognitive screening measure (SPSMQ) to exclude patients with probable dementia or delirium increased the validity and reliability of depression diagnoses in these patients. Most importantly, the current study adds to a body of literature on depression and cancer as the first to compare differences in risk for MDE between advanced cancer patients and comparable general population comparisons in the context of prior depression history. This permitted the original finding that advanced cancer patients are primarily at greater risk for MDE because they are more likely to experience initial episodes of major depression.

Clinical Implications

Our results are of fundamental interest to clinicians who prescribe antidepressants to advanced cancer patients. Busy clinicians who have limited time to administer structured DSM-based interviews often experience difficulty in distinguishing adjustment disorders from major depression in advanced cancer patients. Coupled with the knowledge that major depression is generally a highly recurrent disorder, this sometimes leads clinicians to recommend antidepressants for advanced cancer patients with prior histories of depression who present with sadness or tearfulness and are no longer on antidepressants. Our results suggest the need for rigorous application of diagnostic criteria in order to mitigate against the tendency to overprescribe medications which, while often safe, are likely ineffective for adjustment disorders, sometimes costly, and occasionally accompanied by side-effects such as sedation, gastrointestinal distress, akathisia, hyponatremia, and QTc prolongation. Over-prescription may also exert a negative psychological effect in this vulnerable population, by conveying that justified emotional responses are aberrant.

The fact that advanced cancer patients are at higher risk of MDE than demographically similar individuals in the general population supports the importance of implementing distress screening including validated depression measures in oncology practices. Given the higher prevalence of initial onset episodes, screening should be universal as opposed to targeted to particular subgroups of patients with mental health histories who are presumed to be at higher risk. Patients with initial onset depression and their families may be less familiar with the condition and its treatment than those who have previously experienced depression, suggesting the importance of providing high quality psycho-education in the advanced cancer setting.

Finally, this study underscores the importance of early detection and treatment of depression in advanced cancer patients in order to mitigate its effects on end-of-life communication between patients, families, and oncologists. Irritability, social withdrawal, and poor

treatment adherence associated with depression can erode patient-family as well as patient-oncologist relationships and delay discussions about treatment preferences and goals of care. Notably, these delays occur in a subgroup of cancer patients who may have worse survival [39]; therefore, they may have a particularly high impact on the aggressiveness of care at the end of life and associated health care costs.

CONCLUSIONS

The present study sheds considerable light on the epidemiology of major depression, specifically the issue of incidence versus recurrence, in patients with advanced cancer. Advanced cancer poses a large risk for an initial MDE, and, somewhat surprisingly, no increase in risk for a recurrent MDE. Further research is indicated to confirm these findings in various subgroups of advanced cancer patients, and to ascertain the relative effects of psychological stress versus biological parameters in inducing MDEs. A future longitudinal study might compare MDE incidence among newly diagnosed advanced cancer patients and patients whose cancer recurred as metastatic disease, as well as assess advanced cancer patients for MDE shortly after initial diagnosis and re-assess them later in the disease process in order to determine if MDE tends to remit as patients psychologically adapt to their cancer diagnosis.

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Table 1

Clinical characteristics of the Coping with Cancer sample (N=628) in relation to current MDE

Patient Characteristic	Full Sample		Current MDE						
	(N=628)		Yes (N=45)		No (N=583)		Yes vs. No		
	n	%	n	%	n	%	χ^2	df	p
Recruitment Site									
Yale Cancer Center	153	24.4%	11	24.4%	142	24.6%	4.69	5	0.455
West Haven VA Cancer Center	24	3.8%	2	4.4%	22	3.8%			
Simmons Comprehensive Cancer Center	55	8.8%	2	4.4%	53	9.2%			
Parkland Hospital	186	29.6%	12	26.7%	174	30.2%			
Partners (DFCI, MGH) Cancer Centers	50	8.0%	7	15.6%	43	7.5%			
New Hampshire Oncology-Hematology	154	24.5%	11	24.4%	143	24.8%			
Cancer Diagnosis									
Lung	146	23.2%	6	13.3%	140	24.5%	7.48	5	0.187
Colon	76	12.1%	4	8.9%	72	12.6%			
Pancreatic	49	7.8%	6	13.3%	43	7.5%			
Other Gastrointestinal	65	10.4%	4	8.9%	61	10.7%			
Breast	72	11.5%	9	20.0%	63	11.0%			
Other	209	33.3%	16	35.6%	193	33.7%			
	mean	sd	mean	sd	mean	sd	t	df	p
Karnofsky Performance Score	67.36	16.38	63.64	14.16	67.65	16.51	−1.57	617	0.117
Charlson Comorbidity Index	8.34	2.69	8.23	2.47	8.35	2.71	−0.28	609	0.779

Table 2

Demographic comparisons between the Coping with Cancer (CwC) sample and National Comorbidity Survey Replication samples without (NCS-R) and with (NCS-R*) propensity weights

Characteristic	CwC (N=628)		NCS-R (N=9282)		CwC vs. NCS-R			NCS-R* (N=9282)		CwC vs. NCS-R*		
	mean	sd	mean	sd	t	df	p	mean	sd	t	df	p
Age in years	59.5	13.1	44.8	17.6	20.58	9908	0.000	60.3	18.1	−1.04	9908	0.297
	n	%	n	%	χ^2	df	p	n	%	χ^2	df	p
Gender												
Male	319	50.8%	4445	47.9%	2.00	1	0.158	4697	50.6%	0.01	1	0.927
Female	309	49.2%	4837	52.1%				4585	49.4%			
Race/Ethnicity												
Hispanic	72	11.5%	1007	10.8%	14.59	3	0.002	1055	11.4%	0.03	3	0.998
Black	94	15.0%	1073	11.6%				1413	15.2%			
Other	12	1.9%	404	4.4%				176	1.9%			
White	450	71.7%	6798	73.2%				6639	71.5%			
Education Level												
0–11 years	157	25.0%	1498	16.1%	41.38	3	0.000	2393	25.8%	0.20	3	0.978
12 years	172	27.4%	2993	32.2%				2535	27.3%			
13–15 years	135	21.5%	2568	27.7%				1967	21.2%			
16+ years	164	26.1%	2223	23.9%				2388	25.7%			
Marital Status												
Married/Cohabitating	379	60.4%	5182	55.8%	77.91	2	0.000	5565	60.0%	0.34	2	0.844
Separated/Widowed/Divorced	188	29.9%	1897	20.4%				2863	30.8%			
Never Married	61	9.7%	2202	23.7%				854	9.2%			

Table 3

Comparison of rates of past and current major depressive episodes between the Coping with Cancer (CwC) sample and National Comorbidity Survey Replication sample with propensity weights (NCS-R*)

Diagnosis	CwC (N=628)		NCS-R* (N=9282)		CwC vs. NCS-R*				
	n	%	n	%	OR	(95% CI)	χ^2	df	p
Past MDE									
Yes	83	13.2%	1330	14.3%	0.9	(0.7 – 1.2)	0.60	1	0.440
No	545	86.8%	7952	85.7%					
Current MDE									
Yes	45	7.2%	199	2.1%	3.5	(2.5 – 4.9)	54.63	1	0.000
No	583	92.8%	9083	97.9%					

Table 4

Current major depressive episodes in relation to advanced cancer and past major depressive episodes

Current MDE associated with	for group	OR	(95% CI)	χ^2	df	p
Advanced Cancer	without Past MDE	27.3	(14.8 – 50.4)	111.86	1	0.000
	with Past MDE	1.5	(0.9 – 2.6)	1.97	1	0.160
Past MDE	without Advanced Cancer	77.3	(46.4 – 128.7)	279.13	1	0.000
	with Advanced Cancer	4.2	(2.2 – 8.2)	18.38	1	0.000

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