Published in final edited form as:

Ann Behav Med. 2017 August ; 51(4): 519–531. doi:10.1007/s12160-017-9875-3.

Distress is Interdependent in Patients and Caregivers with Newly Diagnosed Incurable Cancers

Jamie M. Jacobs, PhD^{1,2}, Kelly M. Shaffer, MS^{2,3}, Ryan D. Nipp, MD⁴, Joel N. Fishbein, BA¹, James MacDonald, BA¹, Areej El-Jawahri, MD⁴, William F. Pirl, MD, MPH⁵, Vicki A. Jackson, MD, MPH⁶, Elyse R. Park, PhD, MPH^{1,2}, Jennifer S. Temel, MD⁴, and Joseph A. Greer, PhD^{1,2}

¹Center for Psychiatric Oncology and Behavioral Sciences, Massachusetts General Hospital Cancer Center & Harvard Medical School, Boston, MA

²Department of Psychiatry, Massachusetts General Hospital & Harvard Medical School, Boston, MA

³Department of Psychology, University of Miami, Coral Gables, FL

⁴Department of Medicine, Division of Hematology & Oncology, Massachusetts General Hospital & Harvard Medical School, Boston, MA

⁵Sylvester Cancer Center, University of Miami Miller School of Medicine, Miami, FL

⁶Department of Medicine, Division of Palliative Care, Massachusetts General Hospital & Harvard Medical School, Boston, MA

Abstract

Background—Individuals with advanced, incurable cancer often experience high physical and psychological symptom burden. Family and friend caregivers are at risk for emotional distress.

Purpose—To investigate the interrelationship of distress in patient-caregiver dyads at the time of newly diagnosed incurable cancer.

Methods—From May 2011 to July 2015, within 8 weeks of diagnosis of advanced lung or non-colorectal gastrointestinal cancer, 350 patients and 275 family caregivers were enrolled in a randomized controlled trial of early palliative care. Actor-Partner Interdependence Modeling was used to examine relationships between dyad's self-reported anxiety and depressive symptoms on the Hospital Anxiety and Depression Scale at baseline.

Correspondence: Jamie M. Jacobs, PhD, Massachusetts General Hospital Cancer Center, 55 Fruit Street, Yawkey Center, Suite 10B, Boston, MA 02114, jjacobs@mgh.harvard.edu, Phone: (617) 643-1777, Fax: (617) 643-9913.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Conflict of Interest: The authors declare that they have no conflict of interest.

Research involving Human Participants: The hospital's Institutional Review Board approved the study procedures prior to initiation. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Results—Comparing patients with caregivers, patients reported more depressive symptoms ($M_{diff}=.84$; $t[274]=3.17$, $p=.002$, $d=.22$) and caregivers reported more anxiety symptoms ($M_{diff}=1.62$, $t[274]=4.91$, $p<.001$, $d=.39$). Dyads' anxiety symptoms were positively associated, as were depressive symptoms ($r=.21$, $ps=.001$). Actor Partner Interdependence Modeling showed that patients' anxiety symptoms were positively associated with their own depressive symptoms, with an equal effect for caregivers (actor effect $\beta s=.52$, $ps<.001$). Patients' own anxiety was concurrently positively associated with their caregivers' depressive symptoms, with an equal effect for caregivers to patients (partner effect $\beta s=.08$, $ps=.008$).

Conclusions—In the context of newly diagnosed incurable cancer, caregivers experience more pronounced anxiety, while patients report greater depressive symptoms. Findings indicate that anxiety and depressive symptoms are interrelated among dyads facing newly diagnosed incurable disease. Results emphasize the importance of addressing distress in both patients and caregivers. Future research should discern when dyadic versus individual psychosocial interventions would be optimal.

Keywords

Advanced cancer; depression; anxiety; caregiver; dyadic modeling

Introduction

Lung and non-colorectal gastrointestinal cancer are leading causes of cancer-related deaths, and those with advanced disease have a 4% 5-year survival rate (1). Advanced stage cancer is considered to be incurable and treated as a chronic illness (2), requiring palliative care and exceptional support and involvement of friends and family caregivers (3). During treatment and at the end of life, patients and caregivers experience notable psychological distress (4,5).

For patients, anxiety and depressive symptoms are common and co-occurring (6), resulting from uncertainty, anticipation of suffering and losses, and fear of mortality (7). Distressed patients with incurable cancer experience a higher frequency and intensity of symptoms such as pain, fatigue, nausea, and dyspnea (5,8). Those with untreated psychological distress are less able to participate effectively in end of life planning (9) and report a desire for hastened death (10). Specifically, patients with cancer and anxiety have difficulty engaging in effective decision-making (11), report worse relationships with their physicians (12), experience disruptions in their cancer care (13), and have worse physical functioning (14), which may lead to poorer clinical outcomes (12). Those with depression have elevated risk for suicide (15,16) cancer-related death, and early overall mortality (17,18).

Caregivers play an essential role in supporting a loved one through treatment and at the end of life (3,19). With recent technologies, medical advances, and home health care services, the majority of cancer care is administered in the outpatient setting, and the involvement of caregivers ensures that patients receive optimal treatment (20). Caregiving demands increase as the disease progresses, and caregivers experience substantial burden that affects their physical, social, and emotional health (21–23). Caregivers struggle with difficulties related to sleep, health, immune function, and financial well-being (24), placing them at increased risk for depression, anxiety, and mortality (4,25). In fact, approximately 10–52% of

caregivers experience anxiety and/or depression (26). Anxiety, depression, and the overall stress of care giving lead to chronic physical health problems (27), emphasizing the need to support caregivers.

While evidence suggests that patients with advanced disease and their caregivers experience anxiety and depression during end of life (4), most studies of cancer caregivers have focused on earlier stages of cancer or acute survivorship (28,29). Overall, anxiety in advanced cancer has been understudied, though it may be prevalent in caregivers (12,25). The psychological needs of patients are greatest following diagnosis and while beginning treatment (30). However, patients' needs are largely unmet (31), and their caregivers often report a lack of preparedness, needed support, and minimal guidance from the health care system (32). Therefore, the weeks following a new diagnosis of incurable cancer represent an acute period of high stress. Further study is needed to gain an understanding of the prevalence and severity of patient and caregiver anxiety and depressive symptoms at this critical time.

While early theories examined the influence of stress on the individual and their well-being (33), recent theories account for the impact of stress on the couple as a dyadic process, considering both partners' mutual influence on one another (34). Dyadic stress theory concerns both partners, regardless of whether the stressor concerns one partner primarily, as in the case of a cancer diagnosis. Dyadic stress and coping are also influenced by social dynamics such as common concerns, emotional intimacy or closeness, and the maintenance of the relationship and relationship quality (35). Importantly, relatively few investigators examined the co-occurrence and interdependence of psychiatric symptoms in dyads of patients with advanced cancer and caregivers (36). Interdependence exists when the emotion, cognition, or behavior of one partner in the relationship affects that of the other partner (37,38). Investigators have documented interdependence in mood among patient-caregiver dyads with early and mixed stages of disease (39,40). To design and effectively implement psychosocial interventions that target distress in patient-caregiver dyads in the context of incurable cancer, it is important to understand the extent to which psychiatric symptoms in one partner affect the severity of psychiatric symptoms in the other (36). For example, if patients' distress is interdependent with their family members', interventions delivered exclusively to the patient may not attenuate distress (or maintain reductions) without addressing the family member's distress. Therefore, identifying the prevalence and interdependence of psychiatric symptoms in patients with incurable cancer and their caregivers will enhance the ability to effectively manage distress in both populations. The aims of the current study were: 1) to understand the prevalence of psychological symptoms (i.e., depressive and anxiety symptoms) in patients with newly diagnosed incurable cancer and their primary friend or family caregivers; and 2) to determine whether distress is interdependent, such that the presence of distress in one member is associated with the distress in the other.

Methods

Study Design

From May 2011 to July 2015, patients with newly diagnosed incurable lung or non-colorectal gastrointestinal cancer were recruited from the outpatient clinics at a major

medical center in Boston, MA. Patients were invited to participate in a non-blinded, randomized controlled trial of early palliative care integrated with standard oncology care compared with standard oncology care alone ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02349412) Identifier: NCT02349412). A caregiver (friend or relative) identified by the patient was also given the opportunity to enroll in the overall study, although caregiver enrollment was not mandatory for participation. For the purpose of examining distress post-diagnosis, only enrollment data, prior to study randomization, were examined. The hospital's Institutional Review Board approved the study procedures prior to initiation.

Participants

Patients were eligible to participate if they were within 8 weeks of being informed of their diagnosis of *incurable* lung (non-small cell, small cell, or mesothelioma) or gastrointestinal (hepatobiliary, esophageal, gastric) cancer being treated with non-curative intent at the institution. To identify the intent of treatment (i.e., curative versus non-curative), research staff reviewed the clinical documentation and chemotherapy or clinical trial consent forms. Participants were eligible if they had previously been diagnosed with early-stage cancer that progressed to incurable cancer within 8 weeks prior, or if they had been initially diagnosed with incurable cancer 8 weeks prior. Patients were required to: (1) have an Eastern Cooperative Oncology Group status ≤ 2 ; (2) be able to read and respond to questions in English or to complete patient-reported measures with minimal assistance from family or an interpreter; and (3) be at least 18 years of age. Patients were ineligible if they had received prior treatment for incurable disease, already received care from the palliative care service, or had significant psychiatric or other co-morbid disease that prohibited informed consent or participation based on clinician judgment. At the time of written informed consent, patients identified a caregiver; only one caregiver was enrolled per study patient. Patients for whom caregivers did not enroll were permitted to participate. Caregivers were eligible to participate if they were: (1) a relative or friend who would likely accompany the patient to clinic visits; (2) able to read and respond to questions in English or with minimal assistance from an interpreter; and (3) at least 18 years of age. Given that this data was collected within a patient-focused palliative care intervention study, additional eligibility for caregivers were not applied.

Procedure

Research staff screened patients from the outpatient thoracic and gastrointestinal oncology clinics for eligibility criteria using the electronic health record. The treating oncology clinicians (physicians and nurse practitioners) were notified of eligible patients and invited these patients to participate in the study during clinic visits. Interested and eligible patients provided written informed consent prior to enrollment. Identified caregivers were approached in clinic or by telephone to discuss the study. Caregivers who agreed to participate also provided written informed consent. Completion of baseline study measures occurred prior to random assignment for patients and within one month of patient enrollment for their caregivers. Both patients and caregivers completed the self-report assessments via either paper questionnaires or electronically with Research Electronic Data Capture (REDCap), a HIPAA compliant, web-based survey tool.

Measures

Sociodemographic and clinical factors—Patients and caregivers self-reported their race, ethnicity, religion, marital status, smoking history, income, and level of education via a demographic questionnaire at baseline. Caregivers also self-reported their age, gender, years they knew the patient, whether they were married to the patient, and whether they were living with the patient. Research staff collected data on patients' age, gender, cancer diagnosis, cancer therapy, and Eastern Cooperative Oncology Group performance status from the electronic health records.

Depression and anxiety—As part of the baseline assessment, patients and caregivers each completed the Hospital Anxiety and Depression Scale (41). Participants respond to 14 items assessing symptoms of anxiety and depression during the past week. Items are scored using a 4-point Likert scale with responses ranging from 0 (Not at all; Very rarely) to 3 (All of the time; Very often). Two subscales measure anxiety and depression symptoms (7 items each), with scores ranging from 0 to 21, and higher scores indicating greater distress. The anxiety subscale is comprised of items such as “I get sudden feelings of panic” and “Worrying thoughts go through my mind.” The depression subscale includes items such as “I feel as if I am slowed down” and “I still enjoy the things I used to enjoy.” A clinical cut-off of 8 or greater identifies individuals with clinically significant anxiety or depression symptoms (42). The scale has excellent psychometric evidence, has been validated in samples of patients with cancer (43,44), and is a recommended screening instrument for assessing distress in oncology settings (31,45).

Statistical Analyses

Patient and caregiver clinical, sociodemographic, and psychiatric characteristics were described with measures of central tendency (i.e., means, proportions) using the Statistical Package for the Social Sciences (version 22.0). Levels of patient and caregiver anxiety and depressive symptoms were compared using paired sample *t* tests and McNemar's tests for continuous and categorical variables with dyadic data, respectively. Comparisons were made between the study sample and a non-medical community sample (46) using independent samples *t* tests. Statistical significance was determined based on a two-sided alpha of .05.

Actor-Partner Interdependence Modeling (47,48) using structural equation modeling in Mplus, Version 7.0 (49) was used to examine relationships between patient and caregiver anxiety and depressive symptoms on the Hospital Anxiety and Depression Scale at baseline. Dyad members are considered distinguishable given their unique roles in this setting (e.g., patient as care recipient and family friend as care provider). In this study model, the “actor effect” is the relation of the individual's own psychiatric symptoms (e.g., patient's anxiety) with his/her *own* psychiatric symptoms (e.g., patient's depression). The “partner effect” is the relation of the individual's own psychiatric symptoms (e.g., patient's anxiety) with the *partner's* psychiatric symptoms (e.g., caregiver depression). Actor Partner Interdependence Modeling allows for the estimation of the unique contribution of the patient's own anxiety to their caregiver's depression (partner effects) over and above the effect of the caregiver's own anxiety to their own depression (actor effects). Interdependence is accounted for by allowing correlations between the patients' and caregivers' predictor variables and between the

residual variance in patients' and caregivers' outcome variables. Chi-square difference tests were performed to assess for differences in actor and partner effects by comparing model fit when paths were constrained to be equal versus unconstrained. In the absence of a significant difference, the effects were considered to be equivalent, and the constrained model was retained as the more parsimonious model.

Covariates known to influence depression in caregivers and patients were entered in the final model, including patient and caregiver age (50,51), gender (52,53), and dyad marital status (51,54). Younger and women patients and caregivers have been shown to report higher distress (Northouse, 2012). Data were first screened to ensure that univariate distributions were normal and for multivariate assumptions of normality. Age in years was converted to age in decades using a linear transformation to meet assumptions of normality. Variables were mean-centered prior to analyses. The Full Information Maximum Likelihood method was implemented within MPlus to estimate missing data values from relations among variables in the full sample for participants without an enrolled caregiver (55). Using this missing data method, the population parameters that would most likely produce the estimates found in the sample data are estimated within the analysis model. This method allows for estimation, rather than imputation, of the missing data values, and results in a balanced sample size for patients and caregivers ($N=350$). The following indices and criteria were used to examine model fit: (1) non-significant chi-square; (2) comparative fit index (CFI) $> .95$; (3) root-mean-square error of approximation (RMSEA) $< .06$; and (4) standardized root mean square residual (SRMR) $< .08$ (56). The standardized coefficients were interpreted as measures of effect size, with coefficients of 0.1 = small; 0.3 = medium; 0.5 = large (57). Estimates (including 95% confidence intervals) were considered statistically significant based on a two-sided alpha of .05.

Results

Patient and Caregiver Characteristics

Of 480 eligible patients identified, 350 (73%) enrolled in the study, 117 (24%) declined participation, and 13 (3%) were not offered participation by their oncology clinician. Of the 350 enrolled patients, one caregiver enrolled for each of 275 patients (79% had an enrolled caregiver), while a remaining 75 patients (21%) did not have an enrolled caregiver. Patients with an enrolled caregiver were more likely to be married than those without an enrolled caregiver ($\chi^2[1] = 14.73, p < .001$). Patients with and without an enrolled caregiver did not differ on symptoms of anxiety ($t[348] = .602, p = .80$), depression ($t[348] = .794, p = .43$), or other sociodemographic characteristics ($p > .06$). Sociodemographic and clinical characteristics are summarized in Table 1. On average, patients ($M = 64.86, SD = 10.86$) were significantly older than caregivers ($M = 57.37, SD = 13.61$). Both patients and caregivers were predominantly White, non-Hispanic, Catholic, and well educated. Caregivers were more likely to be female (69.1%) and the majority of caregivers (66.2%) were married to the patient. Twenty percent of the caregivers were also living with dependent children, and 75.7% were living with the patient. With respect to clinical characteristics, 45.4% of patients were diagnosed with incurable GI cancer, whereas 54.6% had lung cancer. Since the time of diagnosis of incurable disease, almost all patients had

received or were currently receiving palliative chemotherapy (79.4%) or radiation (19.1%). The majority of patients had an Eastern Cooperative Oncology Group performance status of 1 (66%), indicating that were limited in strenuous activity but still able to walk and carry out light or sedentary activities.

Anxiety and Depression

On the anxiety subscale (see Table 2), caregivers reported more anxiety symptoms ($M = 6.93$, $SD = 4.41$) than patients ($M = 5.31$, $SD = 3.92$ [$t(274) = 4.91$, $p < .001$]). In contrast, on the depression subscale, patients reported more depressive symptoms ($M = 4.65$, $SD = 4.01$) than caregivers ($M = 3.81$, $SD = 3.55$; [$t(274) = 3.17$, $p = .002$]). Using the clinical cutoff of 8 or greater on either subscale, dyads were grouped according to concordance of patients' and their caregivers' clinical severity. Among dyads, the majority of dyads showed concordance in their levels of clinical severity. Both patient and caregiver reported clinically significant anxiety and depressive symptoms in 20% and 6% of dyads, respectively. Among those patient-caregiver dyads discordant on clinical levels of anxiety (i.e., $N = 112$ dyads in which one partner met the clinical cutoff while the other did not), caregivers were more likely to be the partner who reported clinically elevated anxiety symptoms (*McNemar's* $\chi^2[1] = 12.22$, $p < .001$). However, among those dyads discordant on clinical levels of depression ($N = 72$), there was no difference in the likelihood that the partner reporting clinically elevated symptoms was the patient or the caregiver (*McNemar's* $\chi^2[1] = 2.35$, $p = .13$). Specifically, one or both partners reported clinically significant anxiety or depressive symptoms in 56% and 32% of the dyads, respectively.

Normative Comparisons

According to normative data on the Hospital Anxiety and Depression Scale (46), patients in this sample reported fewer anxiety symptoms than individuals in the non-medical community (normative anxiety $M = 6.14$, $SD = 3.76$, $t[2140] = 3.75$, $p < .01$; see Table 3). However, caregivers in this sample reported greater anxiety symptoms than those in the community ($t[2065] = 3.17$, $p < .01$). With regard to depressive symptoms, patients in this sample reported greater depressive symptoms than individuals in a non-medical community (normative depressive $M = 3.68$, $SD = 3.07$; $t[2140] = 5.12$, $p < .001$). However, depressive symptoms in this caregiver sample did not differ from those reported in the community ($t[2065] = 0.64$, $p = .52$).

Bivariate Correlations

As seen in Table 4, patients' own anxiety symptoms were positively related to their own depressive symptoms ($r = .46$; $p < .001$), and caregivers' own anxiety symptoms were positively related to their own depressive symptoms ($r = .71$; $p < .001$). Patients' own anxiety symptoms were also positively related to their caregivers' depressive symptoms ($r = .23$; $p < .001$), and caregivers' own anxiety symptoms were positively related to their patients' depressive symptoms ($r = .14$; $p = .02$).

Actor Partner Interdependence Modeling

Dyadic interdependence between patients' and their caregivers' anxiety and depressive symptoms was first tested without covariates. Patients' and caregivers' greater anxiety symptoms were associated with their *own* greater depressive symptoms (actor effects). Chi-square difference testing was used to determine whether corresponding actor effects significantly differed between patients and caregivers. Patients' and caregivers' actor effects of their own anxiety with their *own* depressive symptoms did not differ ($\chi^2(1)=2.68, p=.10$). Patients' greater anxiety symptoms were concurrently associated with caregivers' greater depressive symptoms beyond the contribution of caregivers' own anxiety, and similarly for caregivers to patients (partner effects). Chi-square difference testing revealed that patients' and caregivers' partner effects of their own anxiety on their *partner's* depressive symptoms also did not differ ($\chi^2(1)=1.26, p=.26$). Lastly, chi-square difference testing was used to determine whether actor and partner effects significantly differed. The actor effect of one's own anxiety on one's *own* depressive symptoms was stronger than the partner effect of one's own anxiety on one's *partner's* depressive symptoms ($\chi^2(1)=93.99, p<.001$). Thus, the model constraining actor and partner effects separately was retained; this model showed good fit to the data ($\chi^2[2]=3.94, p=.14$; RMSEA=0.05 [90% CI: 0 – 0.13]; CFI=0.99; SRMR=0.03). This model explained 26% and 47% ($ps<.001$) of the variance in patient and caregiver depressive symptoms, respectively.

Factors known to be associated with one's own reported distress [age (24); and gender (40)] and related to dyadic coping [dyad marital status (38,58)] were added to the model to help explain interdependence between patient and caregiver depressive symptoms (patient with caregiver depressive symptoms [$B = 1.04, SE = 0.52, p = .05$]). Individuals' own age and gender and the dyad's marital status were added to the existing model; all exogenous predictor variables were covaried. Among patients, older age and *not* being the caregivers' spouse were related to greater depressive symptoms. There were no associations between patient gender and their depressive symptoms, nor between caregiver age, gender, or spousal status (to the patient) with caregivers' depressive symptoms.

Chi-square difference testing was employed as described above. As with the first model, when adjusting for covariates, patients' and caregivers' own greater anxiety symptoms remained associated with their *own* greater depressive symptoms to an equal degree ($\chi^2(1)=1.63, p=.20$). Patients' and caregivers' own greater anxiety symptoms were also associated with their *partner's* greater depressive symptoms to an equal degree ($\chi^2(1)=0.40, p=.53$). The association between one's own anxiety and depressive symptoms also remained stronger than that between one's own anxiety and one's partner's depressive symptoms ($\chi^2(1)=80.73, p<.001$). Thus, the model constraining actor and partner effects separately was retained; this model adjusting for covariates showed good fit to the data (see Figure 1; $\chi^2(6)=7.21, p=.30$; RMSEA=0.02 (90% CI: 0 – 0.08); CFI=1; SRMR=0.02). This final model explained 28% and 48% ($ps<.001$) of the variance in patient and caregiver depressive symptoms, respectively (Table 5).

Discussion

This is the largest study to date of patient-caregiver dyads with incurable cancer in the U.S., and we showed that patients' and caregivers' anxiety and depressive symptoms are interdependent at the time of newly diagnosed incurable disease. Overall, caregivers reported greater anxiety symptoms than patients and relative to a general non-medical population. Patients reported greater depressive symptoms than caregivers as well as compared to a non-medical population. One or both partners reported clinically elevated anxiety in more than half of these dyads and clinically elevated depressive symptoms in approximately one third of dyads. Dyadic analysis showed that, although one's own anxiety symptoms were more strongly associated with one's own depressive symptoms, there was significant cross-over from one's own anxiety symptoms to one's *partner's* depressive symptoms beyond the effects of the partner's own anxiety symptoms. These effects were equally strong for patients and caregivers. Our findings underscore the need to address *both* patient and caregiver mental health in advanced cancer.

Psychiatric Symptom Prevalence

Anxiety—In the current study, caregivers reported more anxiety than patients, which may point to their experience of worry about their partner and future uncertainty. In a study of patients with advanced breast cancer and their caregivers (4), more caregivers reported clinically significant anxiety as compared to patients (35% vs. 19%), a pattern also observed in the present study (42% vs. 27%). In comparisons with normative data, patients in the current sample reported less anxiety symptoms than individuals in a non-medical community (46). However, more clinically informative is the fact that a similar proportion of patients met criteria for elevated anxiety in the current sample relative to the normative sample (27% vs. 33%, respectively). Caregivers in this sample reported significantly greater anxiety symptoms than those in the community, which may be explained by their anticipation of increasing caregiver demands or of losing a loved one in the future.

Depression—In the current study, patients reported more depressive symptoms than caregivers at the time of advanced cancer diagnosis. While this indicates that their response to the diagnosis is one of sadness, it is also possible that patients are already experiencing many of the neurovegetative symptoms of depression that strongly relate to the progression of advanced cancer, including fatigue, loss of appetite, sleep difficulties, and loss of interest in previously enjoyable activities. On the other hand, the Hospital Anxiety and Depression scale, specifically designed for use with medical populations, is sensitive to the overlap of symptoms of physical illness and depression. Of the sample, 21% of patients met criteria for clinically elevated depressive symptoms, which is greater than the rate in the study by Grunfeld et al. (2004) of patients with advanced breast cancer (12%). However, the rate of depressive symptoms for caregivers in the current study (16%) is similar to the rate observed in their study (11%). The current finding that patients' older age was associated with increased depressive symptoms is congruent with other studies showing a relationship between age and depressive symptoms in advanced cancer (59). In comparisons with normative data, patients in the current sample reported significantly greater depressive symptoms than individuals in a non-medical community (46), while caregivers reported

similar levels of depressive symptoms relative to those in the community. Many patients in the current study had earlier stage cancer that had progressed to advanced, incurable disease; therefore, it is possible that the initial response was one of feeling down and hopeless about their response to treatment, rather than feeling anxious about a new diagnosis. While this is speculation, it is consistent with the fact that patients reported greater depressive symptoms than those in a non-medical community.

Interdependence in Distress

This is among the largest studies to date examining interdependence among psychiatric symptoms in patient-caregiver dyads in cancer and one of the few conducted in the context of advanced, incurable disease. Our findings further the existing evidence suggesting mutuality among distress symptoms and provide important information about the cross-section of anxiety and depression in these dyads. Two studies in cancer showed that patients' depression or anxiety levels were related to caregivers' depression or anxiety levels (60,61). A recent study in patient-caregiver dyads with various advanced cancers found that the presence of an anxiety disorder in one partner was associated with an increased likelihood of an anxiety disorder in the other (36). Taken together, these studies confirm the bidirectional and interdependent associations in anxiety and depression among patients with cancer and their caregivers.

The interdependence of distress observed in these patient-caregiver dyads is best understood within theories surrounding interpersonal emotion dynamics, which assume that partners' emotions become interconnected and influence each other via emotional contagion (62) when they experience a shared stimulus (e.g., cancer diagnosis). Therefore, the interdependence of distress observed here may also be understood within the framework of co-regulation or co-dysregulation (63). Based on this conceptualization, patients' and caregivers' emotions are bi-directionally linked; however, the interdependence may serve either to mutually dampen emotion, causing a return to emotional stability (co-regulation), or mutually amplify emotion, such that there is a departure from emotional stability (co-dysregulation). Representing co-dysregulation, an increase in depression in one partner may amplify anxiety in the other, as our findings suggest. The current results extend and support theories of co-regulation/dysregulation and emotional contagion to settings with newly diagnosed incurable cancer. Finally, the finding that patients being cared for by their spouses had less depressive symptoms than patients with a non-spousal caregiver is consistent with the Relationship Intimacy Model of couples' psychosocial adaptation to cancer, a theoretical framework that views the marital relationship as a resource for the individual during stressful times and proposes that the closeness of the marital relationship is a determinant of adaption to cancer (58). Taken in this context, the finding suggests the importance of enhancing emotional closeness in times of stress, and highlights the possibility that patients without spousal caregivers may be at greater risk and benefit from additional resources to buffer against distress.

Strengths and Limitations

Previous studies of interdependence or mutuality of psychiatric disorders in cancer have been mostly focused in early-stage prostate or breast cancer. This study sample comprises

patients with incurable lung and gastrointestinal cancers, expanding knowledge of psychiatric symptoms in patient-caregiver dyads to these diseases. While most studies focus on time frames of acute diagnosis and survivorship, this study contributes to the understanding of psychiatric symptoms and distress at the time of newly diagnosed incurable disease. Successful recruitment of a large number of patients and caregivers to this study is due in part to the multidisciplinary research team (oncology, palliative care, psychology, and psychiatry), the strong collaborations with staff in the oncology clinics, the fact that caregivers were already in attendance at their loved ones' oncology visit, and that participation required minimal burden to caregivers. A methodological strength of the current study is the use of Actor Partner Interdependence Modeling, a rigorous form of dyadic modeling; however, analyses were conducted on cross-sectional baseline data from a larger randomized controlled trial at a single institution, limiting conclusions about the directionality, temporality of the relationships, and sensitivity to change over time. For example, with a cross-sectional design, we are not able to probe whether patient distress influences caregiver distress, or vice versa, which might inform intervention development. The vast majority of the sample was white, well-educated, and not in financial distress, limiting the generalizability of the findings. Importantly, as the current study questions were exploratory, relevant information about caregivers or relationship dynamics were not collected, which could inform interpretation of the findings or sensitivity analyses. Understanding the reasons that caregivers did not enroll would inform future iterations of this work; however, the only difference we uncovered between patients with and without an enrolled caregiver indicated that patients with an enrolled caregiver were more likely to be married. Given that patients without an enrolled caregiver had no greater anxiety or depressive symptoms than those with an enrolled caregiver, we speculate that these patients may still receive substantial and adequate support from friends and family despite being less likely to be married. Although the prevalence of clinical psychiatric diagnoses was not assessed in this study, the Hospital Anxiety and Depression Scale was used to measure anxiety and depression with a valid cut-off score to identify clinically elevated symptoms. As the American College of Surgeons Commission on Cancer now requires cancer centers to implement screening programs for psychosocial distress (64), it is noteworthy that a brief measure such as the Hospital Anxiety and Depression Scale is an efficient psychosocial distress screening tool that is more likely to be incorporated into a clinical oncology assessment than a structured diagnostic interview requiring trained assessors to administer. In this way, the use of this scale is perhaps more clinically informative for an oncology care setting than an instrument such as the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders used in prior research (65). Nonetheless, premorbid psychiatric functioning may influence distress at the time of diagnosis of incurable disease, and therefore would be important to collect in future studies.

Future Directions and Clinical Applications

The psychological needs of patients with cancer are not being adequately addressed (31). In line with psychosocial distress screening guidelines (64), more strategies are needed to identify at-risk dyads at the time of a new diagnosis of advanced disease (27). Identification of psychiatric distress in this vulnerable population through screening and referrals can enhance patients' quality of life, potentially improving cancer outcomes and reducing

suffering along the disease trajectory (66–68). Psychiatric symptoms complicate the management of physical symptoms associated with advanced disease (69), worsen quality of life, and increase risk for disease-related morbidity and mortality (31). While depression and anxiety symptoms may be common in patients with incurable cancer (70), approximately 40–90% of these patients are under- or untreated with regard to their mental health (71). In a multi-institutional study of patients with advanced cancer, 90% of participants meeting criteria for a psychiatric condition were willing to receive mental health services and treatment, yet 55% of these patients did not access services (72). In a study of caregivers of patients with advanced cancer, only 46% of caregivers with a psychiatric condition accessed mental health services (73). This low healthcare utilization underscores a need for oncology clinicians to discuss mental health concerns with their patients and families, especially in the case of advanced cancer care, in which they are less likely to be addressed (74). In addition, clinical priorities emphasize the importance of developing individual interventions to improve outcomes in caregivers alone (75). Few interventions focus on caregivers' mental health, and those that do are designed to target patient care with a secondary focus on the caregiver (27). Palliative care in and of itself may address caregivers needs by helping patients to manage symptoms, thereby relieving caregiver burden (76).

In addition, psychiatric symptoms are modifiable in the context of coping with cancer with therapy-based psychosocial and/or pharmacologically-based interventions (7,77,78). Interdependence among psychiatric symptoms indicates that interventions stemming from dyadic coping theory (Bodenmann, 2012) may be warranted, as shown among other diseases (79). Dyadic coping aims to restore both individual and dyadic well-being and functioning, build mutual trust, security, intimacy, and closeness (80). Studies have begun to show that patients with advanced cancer and their family caregivers can benefit from both brief and extensive dyadic informational and supportive interventions within 6 months of a new advanced cancer diagnosis (81). Treating patients and caregivers together may result in synergistic effects that are beneficial for each individual (27,40).

As family caregivers continue to provide more home-based healthcare for patients with cancer, it will be crucial to understand further the caregiver's reaction to the patient and vice versa (61). The current findings support and extend the conclusions of Bambauer, Zhang, Maciejewski, Sahay, Pirl, Block and Prigerson (36), suggesting that the presence of psychological distress in one partner should raise concerns about the possibility of psychological distress in the other partner. Consistent with emotional contagion theories (62), shared concerns underlying these psychiatric symptoms, such as impending death, can be addressed with targeted interventions to reduce distress as patients approach end of life (36).

Distress increases throughout the course of advanced disease and towards the end of life in patients with advanced breast cancer (4). Future studies can examine whether a similar pattern is observed in patients with incurable lung and gastrointestinal cancer and their caregivers. In accordance with dyadic stress theory (38), research in dyadic samples of early and mixed-stages of disease show that patients' and their caregivers' levels of distress grow closer over time (39). However, the extent to which interdependence strengthens between dyad members' distress towards the end of life has yet to be investigated and findings

warrant further exploration into the stability of interdependence. Longitudinal studies are therefore necessary to determine the directionality of the interdependent relationships among anxiety and depression in patient-caregiver dyads. In addition, future studies should assess dyadic relationship patterns, such as emotional closeness, satisfaction with the quality of the relationship, as well as additional contributing caregiver characteristics such as preparedness for care giving.

Conclusions

Caregivers reported greater anxiety at the time of newly diagnosed incurable disease, while patients reported greater depressive symptoms. Distress is interrelated among patients with newly diagnosed incurable cancer and their family caregivers. This study of patients with newly diagnosed incurable cancer and their caregivers furthers the understanding of psychiatric symptoms at the time of diagnosis. Findings justify the need to better understand shared concerns in an effort to determine the potential benefits of dyadic or individual psychosocial interventions to reduce distress and improve quality of life in both patients and caregivers.

Acknowledgments

This work was supported by funding from the National Institute of Nursing Research (R01 NR012735) and the National Cancer Institute (K24 CA181253). We would like to thank all of the patients and their family and friend caregivers for dedicating their time to this research.

Funding sources: NINR R01 NR012735 (Temel) and NCI K24 CA181253 (Temel)

References

1. Ferlay, J., Soerjomataram, I., Ervik, M., et al. Globocan 2012 v1.0, cancer incidence and mortality worldwide: Iarc cancerbase no. 11. Available at http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx?cancer=lung. Accessibility verified November 10, 2014
2. McCorkle R, Ercolano E, Lazenby M, et al. Self-management: Enabling and empowering patients living with cancer as a chronic illness. *CA Cancer J Clin.* 2011; 61:50–62. [PubMed: 21205833]
3. Nijboer C, Tempelaar R, Sanderman R, Triemstra M, Spruijt RJ, van den Bos GA. Cancer and caregiving: The impact on the caregiver's health. *Psychooncology.* 1998; 7:3–13. [PubMed: 9516646]
4. Grunfeld E, Coyle D, Whelan T, et al. Family caregiver burden: Results of a longitudinal study of breast cancer patients and their principal caregivers. *CMAJ.* 2004; 170:1795–1801. [PubMed: 15184333]
5. Delgado-Guay M, Parsons HA, Li Z, Palmer JL, Bruera E. Symptom distress in advanced cancer patients with anxiety and depression in the palliative care setting. *Support Care Cancer.* 2009; 17:573–579. [PubMed: 19005686]
6. Stark D, Kiely M, Smith A, Velikova G, House A, Selby P. Anxiety disorders in cancer patients: Their nature, associations, and relation to quality of life. *J Clin Oncol.* 2002; 20:3137–3148. [PubMed: 12118028]
7. Traeger L, Greer JA, Fernandez-Robles C, Temel JS, Pirl WF. Evidence-based treatment of anxiety in patients with cancer. *J Clin Oncol.* 2012; 30:1197–1205. [PubMed: 22412135]
8. Teunissen SC, de Graeff A, Voest EE, de Haes JC. Are anxiety and depressed mood related to physical symptom burden? A study in hospitalized advanced cancer patients. *Palliat Med.* 2007; 21:341–346. [PubMed: 17656411]

9. Block SD. Assessing and managing depression in the terminally ill patient. Acp-asim end-of-life care consensus panel. American college of physicians - american society of internal medicine. *Ann Intern Med.* 2000; 132:209–218. [PubMed: 10651602]
10. Breitbart W, Rosenfeld B, Pessin H, et al. Depression, hopelessness, and desire for hastened death in terminally ill patients with cancer. *JAMA.* 2000; 284:2907–2911. [PubMed: 11147988]
11. Latini DM, Hart SL, Knight SJ, et al. The relationship between anxiety and time to treatment for patients with prostate cancer on surveillance. *J Urol.* 2007; 178:826–831. discussion 831–822. [PubMed: 17632144]
12. Spencer R, Nilsson M, Wright A, Pirl W, Prigerson H. Anxiety disorders in advanced cancer patients: Correlates and predictors of end-of-life outcomes. *Cancer.* 2010; 116:1810–1819. [PubMed: 20187099]
13. Greer JA, Pirl WF, Park ER, Lynch TJ, Temel JS. Behavioral and psychological predictors of chemotherapy adherence in patients with advanced non-small cell lung cancer. *J Psychosom Res.* 2008; 65:549–552. [PubMed: 19027443]
14. Aass N, Fossa SD, Dahl AA, Moe TJ. Prevalence of anxiety and depression in cancer patients seen at the norwegian radium hospital. *Eur J Cancer.* 1997; 33:1597–1604. [PubMed: 9389921]
15. Beard CJ, Travis LB, Chen MH, et al. Outcomes in stage i testicular seminoma: A population-based study of 9193 patients. *Cancer.* 2013; 119:2771–2777. [PubMed: 23633409]
16. Schairer C, Brown LM, Chen BE, et al. Suicide after breast cancer: An international population-based study of 723,810 women. *J Natl Cancer Inst.* 2006; 98:1416–1419. [PubMed: 17018788]
17. Pinquart M, Duberstein PR. Depression and cancer mortality: A meta-analysis. *Psychol Med.* 2010; 40:1797–1810. [PubMed: 20085667]
18. Satin JR, Linden W, Phillips MJ. Depression as a predictor of disease progression and mortality in cancer patients: A meta-analysis. *Cancer.* 2009; 115:5349–5361. [PubMed: 19753617]
19. Schumacher KL, Stewart BJ, Archbold PG, Caparro M, Mutale F, Agrawal S. Effects of caregiving demand, mutuality, and preparedness on family caregiver outcomes during cancer treatment. *Oncol Nurs Forum.* 2008; 35:49–56. [PubMed: 18192152]
20. Smeenk FW, de Witte LP, van Haastregt JC, Schipper RM, Biezenmans HP, Crebolder HF. Transmural care. A new approach in the care for terminal cancer patients: Its effects on re-hospitalization and quality of life. *Patient Educ Couns.* 1998; 35:189–199. [PubMed: 9887851]
21. Stenberg U, Ruland CM, Miaskowski C. Review of the literature on the effects of caring for a patient with cancer. *Psychooncology.* 2010; 19:1013–1025. [PubMed: 20014159]
22. Haley WE, LaMonde LA, Han B, Narramore S, Schonwetter R. Family caregiving in hospice: Effects on psychological and health functioning among spousal caregivers of hospice patients with lung cancer or dementia. *Hosp J.* 2001; 15:1–18. [PubMed: 11876341]
23. Kim Y, Carver CS, Shaffer KM, Gansler T, Cannady RS. Cancer caregiving predicts physical impairments: Roles of earlier caregiving stress and being a spousal caregiver. *Cancer.* 2015; 121:302–310. [PubMed: 25209592]
24. Northouse LL, Katapodi MC, Schafenacker AM, Weiss D. The impact of caregiving on the psychological well-being of family caregivers and cancer patients. *Semin Oncol Nurs.* 2012; 28:236–245. [PubMed: 23107181]
25. Grov EK, Dahl AA, Moum T, Fossa SD. Anxiety, depression, and quality of life in caregivers of patients with cancer in late palliative phase. *Ann Oncol.* 2005; 16:1185–1191. [PubMed: 15849218]
26. Pitceathly C, Maguire P. The psychological impact of cancer on patients' partners and other key relatives: A review. *Eur J Cancer.* 2003; 39:1517–1524. [PubMed: 12855257]
27. Northouse LL, Katapodi MC, Song L, Zhang L, Mood DW. Interventions with family caregivers of cancer patients: Meta-analysis of randomized trials. *CA Cancer J Clin.* 2010; 60:317–339. [PubMed: 20709946]
28. Kim Y, Given BA. Quality of life of family caregivers of cancer survivors: Across the trajectory of the illness. *Cancer.* 2008; 112:2556–2568. [PubMed: 18428199]
29. PDQ Family caregivers in cancer. National Cancer Institute; website. https://www.cancer.gov/about-cancer/coping/family-friends/family-caregivers-hp-pdq#section/_1. Updated January 1, 2016. Accessed November 29, 2016.

30. Blomberg BB, Alvarez JP, Diaz A, et al. Psychosocial adaptation and cellular immunity in breast cancer patients in the weeks after surgery: An exploratory study. *J Psychosom Res.* 2009; 67:369–376. [PubMed: 19837199]
31. Andersen BL, DeRubeis RJ, Berman BS, et al. Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: An american society of clinical oncology guideline adaptation. *J Clin Oncol.* 2014; 32:1605–1619. [PubMed: 24733793]
32. Hudson PL, Aranda S, Kristjanson LJ. Meeting the supportive needs of family caregivers in palliative care: Challenges for health professionals. *J Palliat Med.* 2004; 7:19–25. [PubMed: 15008126]
33. Lazarus R, Deese J, Osler SF. The effects of psychological stress upon performance. *Psychol Bull.* 1952; 49:293–317. [PubMed: 12983450]
34. Revenson, TA., Kayser, K., Bodenmann, G. Couples coping with stress: Emerging perspectives on dyadic coping. Washington, DC: American Psychological Association; 2005.
35. Randall AK, Bodenmann G. The role of stress on close relationships and marital satisfaction. *Clin Psychol Rev.* 2009; 29:105–115. [PubMed: 19167139]
36. Bambauer KZ, Zhang B, Maciejewski PK, et al. Mutuality and specificity of mental disorders in advanced cancer patients and caregivers. *Soc Psychiatry Psychiatr Epidemiol.* 2006; 41:819–824. [PubMed: 16865636]
37. Kelly, HH., Holmes, JG., Kerr, NL., Reis, HT., Rusbult, CE., Van Lange, PAM. An atlas of interpersonal situations. New York, NY: Cambridge University Press; 2003.
38. Bodenmann, G. Dyadic coping and its significance for marital functioning. In: Revenson, TA., Kayser, K., Bodenmann, G., editors. *Couples coping with stress: Emerging perspectives on dyadic coping.* Washington, DC, US: American Psychological Association; 2005.
39. Hodges L, Humphris G, Macfarlane G. A meta-analytic investigation of the relationship between the psychological distress of cancer patients and their carers. *Soc Sci Med.* 2005; 60:1–12. [PubMed: 15482862]
40. Hagedoorn M, Sanderman R, Bolks HN, Tuinstra J, Coyne JC. Distress in couples coping with cancer: A meta-analysis and critical review of role and gender effects. *Psychological bulletin.* 2008; 134:1. [PubMed: 18193993]
41. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand.* 1983; 67:361–370. [PubMed: 6880820]
42. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res.* 2002; 52:69–77. [PubMed: 11832252]
43. Hopwood P, Howell A, Maguire P. Screening for psychiatric morbidity in patients with advanced breast cancer: Validation of two self-report questionnaires. *Br J Cancer.* 1991; 64:353–356. [PubMed: 1892763]
44. Moorey S, Greer S, Watson M, et al. The factor structure and factor stability of the Hospital Anxiety and Depression Scale in patients with cancer. *Br J Psychiatry.* 1991; 158:255–259. [PubMed: 1812841]
45. Carlson LE, Bultz BD. Cancer distress screening. Needs, models, and methods. *J Psychosom Res.* 2003; 55:403–409. [PubMed: 14581094]
46. Crawford JR, Henry JD, Crombie C, Taylor EP. Normative data for the HADS from a large non-clinical sample. *Br J Clin Psychol.* 2001; 40:429–434. [PubMed: 11760618]
47. Cook WL, Kenny DA. The actor–partner interdependence model: A model of bidirectional effects in developmental studies. *International Journal of Behavioral Development.* 2005; 29:101–109.
48. Kenny, DA., Kashy, DA., Cook, WL. *Dyadic data analysis.* The Guilford Press; 2006.
49. Muthén, LK., Muthén, BO. *Mplus user's guide.* 6th. Los Angeles, CA: Muthén & Muthén; p. 1998-2010.
50. Walsh D, Donnelly S, Rybicki L. The symptoms of advanced cancer: Relationship to age, gender, and performance status in 1,000 patients. *Support Care Cancer.* 2000; 8:175–179. [PubMed: 10789956]
51. Given B, Wyatt G, Given C, et al. Burden and depression among caregivers of patients with cancer at the end of life. *Oncol Nurs Forum.* 2004; 31:1105–1117. [PubMed: 15547633]

52. Salvo N, Zeng L, Zhang L, et al. Frequency of reporting and predictive factors for anxiety and depression in patients with advanced cancer. *Clin Oncol (R Coll Radiol)*. 2012; 24:139–148. [PubMed: 21652191]
53. Dumont S, Turgeon J, Allard P, Gagnon P, Charbonneau C, Vezina L. Caring for a loved one with advanced cancer: Determinants of psychological distress in family caregivers. *J Palliat Med*. 2006; 9:912–921. [PubMed: 16910806]
54. Wadhwa D, Burman D, Swami N, Rodin G, Lo C, Zimmermann C. Quality of life and mental health in caregivers of outpatients with advanced cancer. *Psychooncology*. 2013; 22:403–410. [PubMed: 22135229]
55. Enders CK, Bandalos DL. The relative performance of full information maximum likelihood estimation for missing data in structural equation models. *Struct Equ Modeling*. 2001; 8:430–457.
56. Kline, RB. Principles and practice of structural equation modeling. New York, NY: Guilford Publications; 2015.
57. Cohen, J. Statistical power analysis for the behavioral sciences. 2nd. New York, NY: Academic Press; 1998.
58. Manne S, Badr H. Intimacy and relationship processes in couples' psychosocial adaptation to cancer. *Cancer*. 2008; 112:2541–2555. [PubMed: 18428202]
59. Mystakidou K, Tsilika E, Parpa E, Katsouda E, Galanos A, Vlahos L. Assessment of anxiety and depression in advanced cancer patients and their relationship with quality of life. *Qual Life Res*. 2005; 14:1825–1833. [PubMed: 16155770]
60. Given CW, Stommel M, Given B, Osuch J, Kurtz ME, Kurtz JC. The influence of cancer patients' symptoms and functional states on patients' depression and family caregivers' reaction and depression. *Health Psychol*. 1993; 12:277–285. [PubMed: 8404801]
61. Kurtz ME, Kurtz JC, Given CW, Given B. Relationship of caregiver reactions and depression to cancer patients' symptoms, functional states and depression—a longitudinal view. *Soc Sci Med*. 1995; 40:837–846. [PubMed: 7747219]
62. Parkinson B, Simons G. Worry spreads: Interpersonal transfer of problem-related anxiety. *Cogn Emot*. 2012; 26:462–479. [PubMed: 22471852]
63. Reed RG, Barnard K, Butler EA. Distinguishing emotional coregulation from codysregulation: An investigation of emotional dynamics and body weight in romantic couples. *Emotion*. 2015; 15:45–60. [PubMed: 25664951]
64. Pirl WF, Fann JR, Greer JA, et al. Recommendations for the implementation of distress screening programs in cancer centers: Report from the american psychosocial oncology society (apos), association of oncology social work (aosw), and oncology nursing society (ons) joint task force. *Cancer*. 2014; 120:2946–2954. [PubMed: 24798107]
65. Bambauer KZ, Locke SE, Aupont O, Mullan MG, McLaughlin TJ. Using the hospital anxiety and depression scale to screen for depression in cardiac patients. *Gen Hosp Psychiatry*. 2005; 27:275–284. [PubMed: 15993261]
66. Andersen BL, Thornton LM, Shapiro CL, et al. Biobehavioral, immune, and health benefits following recurrence for psychological intervention participants. *Clin Cancer Res*. 2010; 16:3270–3278. [PubMed: 20530702]
67. Stagl JM, Lechner SC, Carver CS, et al. A randomized controlled trial of cognitive-behavioral stress management in breast cancer: Survival and recurrence at 11-year follow-up. *Breast Cancer Res Treat*. 2015; 154:319–328. [PubMed: 26518021]
68. Giese-Davis J, Collie K, Rancourt KM, Neri E, Kraemer HC, Spiegel D. Decrease in depression symptoms is associated with longer survival in patients with metastatic breast cancer: A secondary analysis. *J Clin Oncol*. 2011; 29:413–420. [PubMed: 21149651]
69. Lloyd-Williams M, Dennis M, Taylor F. A prospective study to compare three depression screening tools in patients who are terminally ill. *Gen Hosp Psychiatry*. 2004; 26:384–389. [PubMed: 15474638]
70. Wilson KG, Chochinov HM, Skirko MG, et al. Depression and anxiety disorders in palliative cancer care. *J Pain Symptom Manage*. 2007; 33:118–129. [PubMed: 17280918]
71. Singer S, Kuhnt S, Gotze H, et al. Hospital anxiety and depression scale cutoff scores for cancer patients in acute care. *Br J Cancer*. 2009; 100:908–912. [PubMed: 19240713]

72. Kadan-Lottick NS, Vanderwerker LC, Block SD, Zhang B, Prigerson HG. Psychiatric disorders and mental health service use in patients with advanced cancer: A report from the coping with cancer study. *Cancer*. 2005; 104:2872–2881. [PubMed: 16284994]
73. Vanderwerker LC, Laff RE, Kadan-Lottick NS, McColl S, Prigerson HG. Psychiatric disorders and mental health service use among caregivers of advanced cancer patients. *J Clin Oncol*. 2005; 23:6899–6907. [PubMed: 16129849]
74. Fisch MJ, Titzer ML, Kristeller JL, et al. Assessment of quality of life in outpatients with advanced cancer: The accuracy of clinician estimations and the relevance of spiritual well-being—a hoosier oncology group study. *J Clin Oncol*. 2003; 21:2754–2759. [PubMed: 12860955]
75. Kent EE, Rowland JH, Northouse L, et al. Caring for caregivers and patients: Research and clinical priorities for informal cancer caregiving. *Cancer*. 2016; 122:1987–1995. [PubMed: 26991807]
76. El-Jawahri, A., Jackson, VA., Greer, JA., et al. Effect of early integrated palliative care on family caregivers (FC) outcomes for patients with gastrointestinal and lung cancer. Paper presented at: 2016 Palliative Care in Oncology Symposium; September 9, 2016; San Francisco, CA. <http://meetinglibrary.asco.org/content/173286-180>. Accessed November 29, 2016
77. Jacobsen PB, Jim HS. Psychosocial interventions for anxiety and depression in adult cancer patients: Achievements and challenges. *CA Cancer J Clin*. 2008; 58:214–230. [PubMed: 18558664]
78. Roth AJ, Massie MJ. Anxiety and its management in advanced cancer. *Curr Opin Support Palliat Care*. 2007; 1:50–56. [PubMed: 18660725]
79. Martire LM, Schulz R, Helgeson VS, Small BJ, Saghaei EM. Review and meta-analysis of couple-oriented interventions for chronic illness. *Ann Behav Med*. 2010; 40:325–342. [PubMed: 20697859]
80. Bodenmann G, Randall AK. Common factors in the enhancement of dyadic coping. *Behav Ther*. 2012; 43:88–98. [PubMed: 22304881]
81. Northouse LL, Mood DW, Schafenacker A, et al. Randomized clinical trial of a brief and extensive dyadic intervention for advanced cancer patients and their family caregivers. *Psychooncology*. 2013; 22:555–563. [PubMed: 22290823]

Figure 1. Actor-Partner Interdependence Models Adjusting for Covariates

Note: Significant paths indicated by solid line. Hash marks indicate equivalent paths.

Table 1

Demographic and Medical Characteristics of Patients with Incurable Cancer and their Caregivers

Variable	Patients (N = 350)	Caregivers (N = 275)
	Mean (SD) or N (%)	Mean (SD) or N (%)
Age (years)	64.86 (10.86)	57.37 (13.61)
Gender		
Male	189 (54.0%)	85 (30.9%)
Female	161 (46.0%)	190 (69.1%)
Ethnicity		
Hispanic or Latino	9 (2.6%)	8 (2.9%)
Not Hispanic or Latino	339 (96.9%)	253 (92.0%)
Missing	2 (.5%)	14 (5.1%)
Race		
White	323 (92.3%)	256 (93%)
Other	5 (1.4%)	4 (1.5%)
African American/Black	10 (2.9%)	6 (2.2%)
Asian	8 (2.3%)	8 (2.9%)
American Indian/Alaskan Native	4 (1.1%)	1 (.4%)
Religion		
Catholic	201 (57.4%)	161 (58.5%)
Protestant	62 (17.7%)	45 (16.4%)
None	41 (11.7%)	27 (9.8%)
Other	26 (7.4%)	28 (10.2%)
Jewish	16 (4.6%)	11 (4.0%)
Muslim	3 (0.9%)	2 (0.7%)
Missing	1 (.3%)	1 (.4%)
Education		
High School	131 (37.4%)	73 (26.5%)
> High School	219 (62.6%)	201 (73.1%)
Missing	–	1 (.4%)
Income		
> 50,000	189 (54%)	–
50,000	133 (38%)	–
Missing	28 (8%)	–
Dependent children (lives with)		
No	306 (87.4%)	220 (80%)
Yes	44 (12.6%)	55 (20%)
Marital Status		
Married	245 (70.0%)	222 (80.7%)
Divorced/Separated	36 (10.3%)	8 (2.9%)
Widowed	35 (10.0%)	5 (1.8%)
Single	34 (9.7%)	30 (10.9%)

Variable	Patients (N = 350)	Caregivers (N = 275)
	<u>Mean (SD) or N (%)</u>	<u>Mean (SD) or N (%)</u>
Missing	–	10 (3.6%)
Caregiver employment	–	
Not Working	–	111 (40.4%)
Working	–	153 (55.6%)
Missing	–	11 (4.0%)
Caregiver lives with patient	–	
Yes	–	208 (75.7%)
No	–	57 (20.7%)
Missing	–	10 (3.6%)
Caregiver's relationship to patient	–	
Married or living as if married	–	182 (66.2%)
Child	–	51 (18.4%)
Sibling	–	12 (4.4%)
Friend	–	12 (4.4%)
Other	–	11 (4.0%)
Parent	–	6 (2.2%)
Missing	–	1 (.4%)
Cancer type		
Gastrointestinal cancer	159 (45.4%)	–
Lung cancer	191 (54.6%)	–
Treatment for advanced disease		
Chemotherapy	278 (79.4%)	–
Radiation	67 (19.1%)	–
Chemoradiotherapy	3 (.9%)	–
No chemotherapy or radiation	2 (.6%)	–
ECOG performance status		
0	88 (25.1%)	–
1	231 (66.0%)	–
2	31 (8.9%)	–

Note: ECOG= Eastern Cooperative Oncology Group

Table 2

Clinical Characteristics of Patients with Incurable Cancer and their Caregivers

	Patients (N=350)				Caregivers (N = 275)				Comparison	
	<u>M</u>	<u>SD</u>	<u>Range</u>		<u>M</u>	<u>SD</u>	<u>Range</u>		<i>t</i>	<i>df</i>
Continuous Scores										
Anxiety Symptoms	5.31	3.92	0 – 19		6.93	4.41	0 – 21		4.91***	274
Depressive Symptoms	4.65	4.01	0 – 20		3.81	3.55	0 – 18		3.17**	274
% Meeting Clinical Cut-Off	<u>N</u>	<u>%</u>			<u>N</u>	<u>%</u>			<i>McNemar's χ^2</i>	<i>df</i>
Anxiety Symptoms	94	27%			116	42%			12.22***	1
Depressive Symptoms	72	21%			45	16%			2.35	1

Notes. Anxiety symptoms measured with the Hospital Anxiety and Depression Scale-anxiety subscale; Depressive symptoms measured with the Hospital Anxiety and Depression Scale-depression subscale; Meeting clinical cut-off: > 8 (Hospital Anxiety and Depression Scale-anxiety or depression subscale)

* $p < .05$.

**

* $p < .01$.

* $p < .001$

Table 3

Comparison of Patients and Caregivers with a Non-Clinical Sample

	Current Study				Normative Sample				Comparisons			
	Patients (N=350)		Caregivers (N = 275)		Non-Clinical Sample (N=1,792)		Patients vs. NonClinical Sample		Caregivers vs. NonClinical Sample		NonClinical Sample	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>t</i>	<i>df</i>	<i>t</i>	<i>df</i>	<i>t</i>	<i>df</i>
Anxiety Symptoms	5.31	3.92	6.93	4.41	6.14	3.76	3.75**	2140	3.17**	2140		2065
Depressive Symptoms	4.65	4.01	3.81	3.55	3.68	3.07	5.12***	2140	0.64	2140		2065

Notes. Anxiety symptoms measured with the Hospital Anxiety and Depression Scale-anxiety subscale, Depressive symptoms measured with the Hospital Anxiety and Depression Scale-depression subscale.

* $p < .05$.

** $p < .01$.

*** $p < .001$

Table 4

Bivariate Correlations of Psychiatric Symptoms for Patients with Incurable Cancer and their Caregivers

	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>
1. Patient Depressive Symptoms	1.00			
2. Patient Anxiety Symptoms	.46***	1.00		
3. Caregiver Depressive Symptoms	.21***	.23***	1.00	
4. Caregiver Anxiety Symptoms	.14*	.21**	.71***	1.00

Notes. Anxiety symptoms measured with the Hospital Anxiety and Depression Scale-anxiety subscale. Depressive symptoms measured with the Hospital Anxiety and Depression Scale-depression subscale.

*
 $p < .05$.

**
 $p < .01$.

 $p < .001$

Table 5

Actor-Partner Interdependence Model Results Testing Effects of Own Anxiety Symptoms on Own and Partner Depressive Symptoms Adjusting for Age, Gender, and Dyad Marital Status

	Patients' Depressive Symptoms				Caregivers' Depressive Symptoms			
	<i>B</i>	<i>95% CI</i>	<i>p</i>	Standardized <i>β</i>	<i>B</i>	<i>95% CI</i>	<i>p</i>	Standardized <i>β</i>
Own Anxiety Symptoms (Actor Effects)	0.52	[0.46, 0.58]	<0.001	0.49	0.52	[0.46, 0.58]	<0.001	0.66
Partner Anxiety Symptoms (Partner Effects)	0.08	[0.02, 0.14]	0.008	0.09	0.08	[0.02, 0.14]	0.008	0.09
Covariates								
Own age	0.54	[0.20, 0.89]	0.002	0.14	-0.10	[-0.36, 0.16]	0.431	-0.04
Own gender	-0.31	[-0.71, 0.09]	0.128	-0.08	0.03	[-0.30, 0.24]	0.865	0.01
Dyad marital status	-0.49	[-0.95, -0.03]	0.035	-0.11	0.16	[-0.21, 0.53]	0.407	0.04

Notes. Anxiety symptoms measured with the Hospital Anxiety and Depression Scale-anxiety subscale. Depressive symptoms measured with the Hospital Anxiety and Depression Scale-depression subscale.