Published in final edited form as:

Death Stud. 2010 March ; 34(3): 257–273. doi:10.1080/07481180903559303.

Distinguishing Symptoms of Grief and Depression in a Cohort of Advanced Cancer Patients

Juliet C. Jacobsen, M.D.^{1,2}, Baohui Zhang, M.S.³, Susan D. Block, M.D.^{1,3,4}, Paul K. Maciejewski, Ph.D.^{3,4}, and Holly G. Prigerson, Ph.D.^{1,3,4}

¹ Harvard Medical School Center for Palliative Care

² Department of Medicine, Massachusetts General Hospital, 55 Fruit Street, Founders 600, Boston, MA 02114

³ Center for Psycho-oncology and Palliative Care Research, Dana Farber Cancer Institute, 44 Binney St., Boston, MA 02115.

⁴ Department of Psychiatry, Brigham and Women's Hospital

Abstract

Several studies have shown that the symptoms of grief are different from symptoms of depression among bereaved family members. This study is an attempt to replicate this finding among advanced cancer patients and examine clinical correlates of patient grief and depression. Analyses were conducted on data from interviews with 123 advanced cancer patients. Grief was measured using symptoms from the patient version of the Inventory of Complicated Grief-Revised (ICG-R) and symptoms of depression were assessed using the Structured Clinical Interview for DSM-IV (SCID). A factor analysis revealed that symptoms of patient grief formed a coherent factor that was distinct from a depression factor. Patient grief “caseness” (defined as being in the top 10% of the distribution of grief scores), but not MDD, was uniquely associated with the wish to die (OR 10.13 [0.108-95.06]). Both depression and grief were significantly associated with mental health service use (OR 16.07 [1.68, 153.77] vs. 4.82 CI=[1.09, 21.41]) and negative religious coping (OR 1.36 [1.06, 1.73] vs. 1.25 [1.05, 1.49]); neither was associated with terminal illness acknowledgement.

Keywords

grief; depression; end-of-life

Several studies have shown that symptoms of depression are distinct from those of grief in bereaved family members (Boelen, van den Bout, & de Keijser, 2003; Boelen & van den Bout, 2005; Horowitz et al., 1997; Latham & Prigerson, 2004; Ogrodniczuk et al., 2003; Prigerson et al., 1995; Prigerson et al., 1996). They have also shown that independent of symptoms of depression, severe and prolonged symptoms of grief are associated with mental and physical impairments such as an elevated risk of suicidal ideation and attempts, hypertension, cardiac events, functional impairments, hospitalization, adverse health behaviors, and reduced quality of life (Horowitz et al., 1997; Latham & Prigerson, 2004; Ogrodniczuk et al., 2003; Ott, 2003; Prigerson et al., 1995; Prigerson et al., 1996; Prigerson et al., 1997; Prigerson et al., 1999; Simon et al., 2005). Prolonged grief can be distinguished from normal grief by the severity and duration of symptoms and the marked distress and disability with which symptoms

of Prolonged Grief Disorder (PGD), but not normal manifestations of grief, are associated (Prigerson et al., 1999; Prigerson & Jacobs, 2001; Prigerson, Vanderwerker, & Maciejewski, 2008). Consensus criteria for PGD in bereaved individuals have been proposed for the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSMV) (Prigerson et al., 2008) but these symptom criteria have not been evaluated in patients with terminal illness. Patients who are dying cope with multiple losses including the loss of health, independence, function, role and the future loss of relationships, all of which may be sources of grief. We sought to determine whether grief over such losses formed a cluster of symptoms distinguishable from those of depression.

The diagnosis of depression in advanced cancer patients is often difficult to distinguish from grief and other forms of mental distress, as well as from symptoms associated with physical illness (Green & Austin, 1993) and its treatment (Besik, Kocabey, & Caliskan, 2003; Geinitz et al., 2004; Ito et al., 2003). For example, the neurovegetative symptoms of depression (poor appetite, loss of energy, difficulty sleeping, and diminished concentration) can be confused with the symptoms of terminal illness. Similarly, withdrawal from persons other than close family is often thought of as a symptom of depression, but in the setting of terminal illness, this behavior can be a normal part of the grieving process (Block, 2000). While grief shares some additional characteristics with depression such as an association with somatic distress, there are some important differences. Freud had postulated that self-esteem, self-loathing and suicidality would be associated with depression but not grief (Freud, 1917) whereas we find identity confusion and decrements in one's perceived self-worth are symptoms of PGD (Prigerson et al., 2008) and that post-loss grief is a strong predictor of suicidality (Latham & Prigerson, 2004; Szanto et al., 2006). The aim of this study was to examine the distinction between depressive and grief symptoms in terminally ill cancer patients.

The gold standard for diagnosing depression at the end of life is the clinical interview (Koenig, Cohen, Blazer, Meador, & Westlund, 1992). However, since the usual diagnostic features of depression do not apply, experts suggest assessing for alternative clinical indicators such as hopelessness, helplessness, intractable pain, excessive somatic preoccupation, disproportionate disability, poor cooperation or refusal of treatment, and hopelessness or aversion on the part of the clinician (Block, 2000). Endicott has recommended that the DSM IV Major Depressive Disorder (MDD) criteria be modified so that neurovegetative symptoms of depression are substituted with psychological symptoms (Endicott, 1984).

As cancer patients approach the end of life, the relief of mental suffering assumes heightened importance as a goal of cancer care. Providing appropriate treatment for psychological distress rests on clarity about diagnosis, thus differentiating symptoms of depression from those of grief will enhance efforts to provide specialized care. In this study, we set out to determine whether symptoms of grief are distinct from those of MDD in a cohort of advanced cancer patients who had metastatic disease and had not responded to first-line chemotherapy and who would die a median of 4 months from the baseline assessment.

Method

Sample

Patients were recruited from 8/1/2002 to 4/25/2007, as part of an ongoing multi-site longitudinal investigation (MH63892, CA106370) of advanced cancer patients and their primary, informal (unpaid) caregivers called the Coping with Cancer (CWC) study. Participating sites included the Yale Cancer Center (New Haven, CT), the Veterans Affairs Connecticut Healthcare System Comprehensive Cancer Clinics (West Haven, CT), Memorial Sloan-Kettering Cancer Center (New York, NY), Simmons Comprehensive Cancer Center (Dallas, TX), and the Parkland Hospital Palliative Care Service (Dallas, TX). Approval was

obtained from the human subjects committees of all participating centers; all enrolled patients provided written informed consent. Inclusion criteria were: 1) diagnosis of advanced cancer (presence of distant metastases and failure of first-line chemotherapy); 2) diagnosis at a participating site; 3) age greater than 20 years; 4) identified unpaid, informal caregiver; and 5) adequate stamina to complete the interview. Patient-caregiver dyads in which either the patient or caregiver met criteria for dementia or delirium (by neuro-behavioral cognitive status exam) or did not speak either English or Spanish were excluded. Potentially eligible patients were identified by oncology staff at each site. Research staff approached each identified patient to offer participation in the study. Once the patient's written informed consent was obtained, medical records and clinicians were consulted to confirm eligibility.

The most common reasons for nonparticipation included "not interested" (N=113), "caregiver refuses" (N=33), and "too upset" (N=27). Non-participants reported more distress (mean=2.84; S.D.=1.31) than participants (mean=2.42; S.D.=1.27) ($t=3.92$, $df=652$, $p\text{-value} < .0001$) on a 5-point Likert scale whose extremes ranged from 1 ("minimal/nonexistent") to 5 ("distracted"). They did not differ significantly from participants by age, gender, race or education.

Of the 998 contacted patients, 810 were eligible for inclusion into the study. Of these, 123 (12.3%) had complete information on a modified version of the rater-administered Inventory of Complicated Grief-Revised (ICG-R) (Prigerson & Jacobs, 2001), the refinements of which were added later in the course of the study. Compared to the other study participants, the 123 subjects included in the analyses were younger (mean= 56.1, S.D.=11.90 versus mean= 59.0 years S.D.=12.40;) ($t=2.35$, $df=591$, $p=0.02$); had fewer years of formal education (mean=12.1, S.D.= 4.13 versus mean=13.1 years S.D.=4.11 years;) ($t=2.38$, $df=591$, $p=0.02$); and were less likely to be White (59.35% versus 72.25%; $df=1$, chi-square statistic=7.67, $p=0.006$). However, they did not differ from the remaining participants in gender or rates of MDD.

Measures

The ICG-R is used for the diagnosis of Complicated Grief in bereaved subjects, now called Prolonged Grief Disorder (PGD) (Prigerson et al., 2008), and consists of 25 symptom criteria assessed at 0-12 months post-loss. Prior work using Item Response Theory (IRT) and Differential Item Functioning analysis (DIF) (Prigerson et al., 2008) suggests that 13 of the 25 items are biased or contribute little information compared to the most informative symptoms. These items (Prigerson et al., 2008) and the symptom duration criterion were eliminated given the multiple losses and difficulty in dating the index loss in the context of terminal cancer. The 12 unbiased, informative ICG-R symptoms were modified so that the loss referred to the patient's illness (i.e., loss of health and normal function) rather than the surviving caregiver's grief. Table 1 contains the 12 modified ICG-R symptoms.

In addition to the modified ICG-R, all subjects were required to have complete information on the items from the SCID Axis 1 Modules for MDD (Keller et al., 1995) and Endicott criteria for MDD (Endicott, 1984). The SCID has high test-retest reliability for these lifetime diagnoses, with an overall weighted Kappa of 0.68 (Williams et al., 1992). The Endicott criteria substitute biologic depressive symptoms likely to be confounded with cancer with four cognitive and emotional symptoms items. Using the Endicott criteria, weight loss was substituted with depressed appearance, insomnia was substituted with social withdrawal or decreased talkativeness, loss of energy was substituted with brooding, self pity, or pessimism, and poor concentration was substituted with lack of reactivity/can't be cheered up.

Other clinical correlates were examined because of their expected association with patient emotional distress. The Yale Evaluation of Suicidality scale was used to measure patient wish to live and wish to die. This scale has been found to be a useful measure of suicidality in bereaved subjects (Ogrodniczuk et al., 2003). Religious coping, assessed with Pargament's

Brief RCOPE (BRC) has shown to account for significant unique variance in measures of adjustment (stress-related growth, religious outcome, physical health, mental health, and emotional distress) after controlling for the effects of demographics and global religious measures (Koenig, Pargament, & Nielsen, 1998; Pargament et al., 1998; Pargament, Koenig, & Perez, 2000). We hypothesized that patients with lower levels of religious coping would have higher grief scores. We also hypothesized that higher grief scores would be correlated with terminal illness acknowledgement. Terminal illness acknowledgment was assessed by a question that asks patients to define their health status as “relatively healthy,” “seriously ill but not terminal,” or “seriously ill and terminal” whereby only those who endorse the latter are considered to acknowledge their terminal illness (Prigerson, 1992; Ray et al., 2006). Mental health service use was assessed with the question, “Have you accessed any type of mental health intervention to help you adjust to your illness since you were diagnosed with cancer?”

An exploratory factor analysis was performed to examine the number of underlying constructs that exist with the proposed patient items for PGD and the DSM-IV depression items for MDD. Once the scree plot identified the number of main factors, the analyses were rerun to determine the factor loadings when the analyses were restricted to the main factors. Fisher’s exact test was employed because of the small cells in the analysis of the association between patient grief “caseness” and depression defined by the SCID axis 1 Modules for MDD and the Endicott substitution criteria for depressive disorder. Logistic regression analyses regressed binary outcomes (MDD, PGD “caseness”) on clinical correlates, controlling for demographic variables of patients’ age, gender, education and race. Patient grief “caseness” was determined by dichotomizing a summary grief symptom severity score at the top 10% of scores. Ten percent was chosen to be comparable to the prevalence of MDD in the full sample of the CWC, which is 7.41% (Kadan-Lottick, Vanderwerker, Block, Zhang, & Prigerson, 2005), and because this percentile corresponds to the rate of PGD in community samples of the bereaved (Barry, Kasl, & Prigerson, 2002).

Results

The factor analysis revealed two distinct symptom clusters: one, a depression cluster, comprised entirely of SCID MDD items, and the other a patient grief symptom cluster (Table 1). The eigenvalues for factor 1 (MDD) and factor 2 (patient grief symptoms) were 5.22 and 4.88 and 33.7% and 14.4% of the variances were explained by factor 1 (MDD) and factor 2 (patient grief symptoms), respectively. They were the only eigenvalues much greater than 1; factor 3 resided at the elbow of the scree plot of the eigenvalues (see Figure 1) and no remaining factors account for a large amount of the variance in the data. The standardized Cronbach’s α was 0.86 for the twelve patient grief symptoms; it was 0.90 for the MDD symptoms.

Patient grief appeared to be relatively distinct from MDD but there was overlap between the syndromes (Table 2). Eighty-three percent of the 6 patients with MDD met criteria for patient grief “caseness” but only 38% of the 13 patients with patient grief “caseness” (i.e., those in the upper 10% of the ICG-R distribution) met diagnostic criteria for MDD. In other words, nearly two-thirds of cases of patient grief would have been missed by sole reliance on diagnostic criteria for MDD. As expected, the Fisher’s exact test showed a significant positive association between patient grief “caseness” and MDD ($P < 0.0001$). When MDD was assessed using the Endicott criteria, the results were the same.

Patient grief “caseness”, but not MDD, was uniquely associated with the wish to die (OR 10.13 [0.1.08-95.06]). Both depression and grief were significantly associated with mental health service use (OR Depression 16.07 [1.68, 153.77] vs. Grief 4.82 CI=[1.09, 21.41]) and negative religious coping (OR Depression 1.36 [1.06, 1.73] vs. Grief 1.25 [1.05, 1.49]); neither was associated with terminal illness acknowledgement.

Discussion

This study confirms that in patients with advanced cancer, a subset of patients have multiple symptoms of grief that are distinct from symptoms of depression and that, at syndromal (or “caseness”) levels, are significantly associated with morbidity such as wish to die and mental health service use. Future research will be needed to distinguish a more intensified and pathological grieving process from normal grief, to determine criteria for a grief disorder among patients, and to determine which symptoms of grief are severe, distressing and persistent enough to warrant treatment. However, the results of the factor analysis suggest that the underlying constructs and phenomenology of grief and depression are significantly different.

Our study lacked data to assess the duration of the symptoms of grief. Therefore it is difficult to determine whether our symptom cluster of patient grief is a transient phenomenon and a part of a normal reaction to a terminal diagnosis or is a part of a prolonged and pathological grieving process. Prolonged Grief Disorder (PGD), is distinguished from normal grief in the literature on bereaved subjects using duration (symptoms lasting longer than six months) and function (Prigerson et al., 2008). However, pathological grief has not been defined for terminally ill patients, and the criterion of duration is similarly difficult to define as the index event that triggers a grief reaction (e.g., a cancer diagnosis or discussion of a terminal prognosis) needs to be identified and the reaction to each examined for similarities and differences. Additionally, early in the course of their disease patients lose their health, later they lose function, independence, and control, and finally they confront losing life itself including the loss of significant relationships. There is a need for greater clarity as to what it is the patient is grieving.

It is also difficult to apply the PGD criteria of duration to dying patients because, unlike the case of bereavement following death, there is often *no* index event marking the beginning of the loss of health. Whereas family members may engage in anticipatory grief prior to the death of a loved one, their period of bereavement is clearly delineated by the death of the patient. In contrast, terminally ill cancer patients have often learned their prognosis in steps, making it more difficult to define when the patient experiences the loss of health. For example, patients with early disease (stage 1, 2, or 3) may begin to grieve the loss of health, but may not see themselves as facing mortality. Similarly, patients given a 10% chance of cure may partially grieve thinking that they will not survive, yet not fully grieve because of the chance of recovery. If arriving at a terminal diagnosis involves several steps, it is difficult to determine how long “normal” grief should last, and where pathological grief begins. In this context, the duration of symptoms seems less relevant than the intensity of symptoms and their impact on function. The associations of the grief symptoms in our study with a wish for death and mental health service use suggest that there is substantial distress and impairment associated with severe (but not necessarily prolonged) grief symptoms among patients. Future research on this topic should focus on distinguishing pathological grief from normal grief based on criteria other than duration such as the intensity of grief, disability, and decrements in ability to enjoy the time remaining.

In the bereaved, the symptoms clusters and treatments of grief and depression are different therefore this distinction may also be important in terminally ill patients. In the bereaved, antidepressant treatment alone (Jacobs, Nelson, & Zisook, 1987) and with interpersonal psychotherapy are effective in reducing depressive symptoms, but relatively ineffective for symptoms of bereavement-related grief (Pasternak et al., 1991; Reynolds et al., 1999). In contrast, randomized, controlled trials of psychotherapy designed specifically for PGD have demonstrated efficacy for PGD symptoms (Boelen, de Keijser, van den Hout, & van den Bout, 2007; Shear, Frank, Houck, & Reynolds, 2005). Future studies are needed to determine whether treatments that ameliorate symptoms of grief in the bereaved work equally well to reduce patient grief. In addition, future work should assess if patients with high levels of grief derive

particular benefit from psychotherapeutic interventions designed to address psychosocial and existential distress among the terminally ill such as Chochinov's Dignity Therapy (Chochinov et al., 2005) or Breitbart's meaning-centered group psychotherapy (Breitbart, 2003; Breitbart, Gibson, Poppito, & Berg, 2004; Greenstein & Breitbart, 2000). Similarly, the literature around traumatic loss and the reconstruction of meaning may offer guidance for how to assist grieving patients with the reconstruction of a meaningful narrative of self and world in the wake of ongoing loss (Neimeyer, van Dyke & Pennebaker, 2009).

Aside from depression, another mood disorder discussed in the literature on mental distress among dying patients is demoralization. Demoralization has been defined on the basis of case reports (Clarke & Kissane, 2002; de Figueiredo, 1993; Griffith & Gaby, 2005; Shader, 2005; Slavney, 1999) and factor analysis (Clarke, Kissane, Trauer, & Smith, 2005; Kissane et al., 2004), although a consensus definition has not been reached and the syndrome has not been accepted into the International Classification of Disease (ICD) or the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM) (Ganzini & Prigerson, 2004). Demoralization is generally described as a syndrome of hopelessness, despair, and subjective incompetence in the setting of repeated perceived failures or inability to meet expectations (Clarke & Kissane, 2002). Kissane (Kissane et al., 2004) used factor analysis to divide demoralization into five subscales: loss of meaning and purpose, dysphoria, disheartenment, helplessness, and sense of failure.

There is some overlap in our patient-grief scale and Kissane's concept of demoralization. Both grief and demoralization are characterized by symptoms of disillusionment such as a loss of meaning or disheartenment (emotional pain or sorrow on the patient grief scale), and sense of failure (confusion about role in life, significant reduction in ability to function on the patient grief scale). However, patient grief is different from demoralization in that grief also includes agitated psychological symptoms such as yearning, avoidance, and difficulty accepting one's illness and trusting others. And, whereas the definition of demoralization might include dysphoric feelings such as subjective incompetence and bitterness about one's illness, our grief symptoms of feeling shocked, dazed, and emotionally numb are more related to symptoms of traumatic distress than they are to symptoms of dysphoria.

Even though the work of bereavement and the work of dying both involve processing significant interpersonal loss, they are fundamentally different, so the criteria for one may not apply well to the other. The work of bereavement involves an acceptance of the loved-one's death followed by a reintegration into life. For the bereaved, symptoms of prolonged grief revolve around the deficiencies in acceptance (yearning, disbelief, bitterness) and withdrawal (decreased social functioning, difficulty trusting others, difficulty moving on with life, emotional numbness, or detachment from others). In contrast, the work of dying involves an acceptance of one's own death and ultimately a letting go of life. Grief symptoms such as confusion about one's role in life, decreased social functioning, difficulty concentrating, and detachment from others are not necessarily pathological and can all be normal parts of dying, where patients lose their abilities to function physically, cognitively, and emotionally and must adapt to new ways of living and relating to others. Future research should address how to distinguish the integrative, reinvestment work of grief related to bereavement from the disengaging and relinquishing work of grief related to dying. In addition, future work should explore common qualities of grief in the bereaved and the dying. For example, the process of grief for the bereaved may evoke growth-promoting qualities that eventually enable the bereaved to reengage and invest in life despite the loss. These growth-promoting qualities should be explored and defined both in the bereaved and the terminally ill, as they may have a significant impact on the experience of the terminally ill patients, and may either facilitate or inhibit growth at the end of life.

Acknowledgments

This research was supported in part by the following grants: MH56529 (HGP) from the National Institute of Mental Health and CA106370 (HGP) from the National Cancer Institute; a grant from the American Foundation for Suicide Prevention; and the Center for Psycho-oncology and Palliative Care Research, Dana-Farber Cancer Institute (HGP,BZ, PKM).

References

- Barry LC, Kasl SV, Prigerson HG. Psychiatric disorders among bereaved persons: The role of perceived circumstances of death and preparedness for death. *The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry* 2002;10(4):447–457. [PubMed: 12095904]
- Besik SK, Kocabay G, Caliskan Y. Major depression and psoriasis activation due to interferon-alpha in a patient with chronic myeloid leukemia; “overlooked and/or misdiagnosed adverse reaction in malignant disease”. *American Journal of Hematology* 2003;74(3):224. [PubMed: 14587060]
- 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. Annals of Internal Medicine* 2000;132(3):209–218. [PubMed: 10651602]
- Boelen PA, de Keijser J, van den Hout MA, van den Bout J. Treatment of complicated grief: A comparison between cognitive-behavioral therapy and supportive counseling. *Journal of Consulting and Clinical Psychology* 2007;75(2):277–284. [PubMed: 17469885]
- Boelen PA, van den Bout J. Complicated grief, depression, and anxiety as distinct postloss syndromes: A confirmatory factor analysis study. *The American Journal of Psychiatry* 2005;162(11):2175–2177. [PubMed: 16263861]
- Boelen PA, van den Bout J, de Keijser J. Traumatic grief as a disorder distinct from bereavement-related depression and anxiety: A replication study with bereaved mental health care patients. *The American Journal of Psychiatry* 2003;160(7):1339–1341. [PubMed: 12832252]
- Breitbart W. Reframing hope: Meaning-centered care for patients near the end of life. interview by karen S. heller. *Journal of Palliative Medicine* 2003;6(6):979–988. [PubMed: 14733692]
- Breitbart W, Gibson C, Poppito SR, Berg A. Psychotherapeutic interventions at the end of life: A focus on meaning and spirituality. *Canadian Journal of Psychiatry. Revue Canadienne De Psychiatrie* 2004;49(6):366–372. [PubMed: 15283531]
- Chochinov HM, Hack T, Hassard T, Kristjanson LJ, McClement S, Harlos M. Dignity therapy: A novel psychotherapeutic intervention for patients near the end of life. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology* 2005;23(24):5520–5525. [PubMed: 16110012]
- Clarke DM, Kissane DW. Demoralization: Its phenomenology and importance. *The Australian and New Zealand Journal of Psychiatry* 2002;36(6):733–742. [PubMed: 12406115]
- Clarke DM, Kissane DW, Trauer T, Smith GC. Demoralization, anhedonia and grief in patients with severe physical illness. *World Psychiatry : Official Journal of the World Psychiatric Association (WPA)* 2005;4(2):96–105. [PubMed: 16633525]
- de Figueiredo JM. Depression and demoralization: Phenomenologic differences and research perspectives. *Comprehensive Psychiatry* 1993;34(5):308–311. [PubMed: 8306640]
- Endicott J. Measurement of depression in patients with cancer. *Cancer* 1984;53(10 Suppl):2243–2249. [PubMed: 6704912]
- Freud, S. *The Freud reader*. W. W. Norton and Company, Inc.; New York, NY: 1917. Mourning and melancholia.
- Ganzini L, Prigerson H. The other side of the slippery slope. *The Hastings Center Report* 2004;34(4):3. [PubMed: 15379086]
- Geinitz H, Zimmermann FB, Thamm R, Keller M, Busch R, Molls M. Fatigue in patients with adjuvant radiation therapy for breast cancer: Long-term follow-up. *Journal of Cancer Research and Clinical Oncology* 2004;130(6):327–333. [PubMed: 15007642]
- Green AI, Austin CP. Psychopathology of pancreatic cancer. A psychobiologic probe. *Psychosomatics* 1993;34(3):208–221. [PubMed: 8493302]

- Greenstein M, Breitbart W. Cancer and the experience of meaning: A group psychotherapy program for people with cancer. *American Journal of Psychotherapy* 2000;54(4):486–500. [PubMed: 11109133]
- Griffith JL, Gaby L. Brief psychotherapy at the bedside: Countering demoralization from medical illness. *Psychosomatics* 2005;46(2):109–116. [PubMed: 15774948]
- Horowitz MJ, Siegel B, Holen A, Bonanno GA, Milbrath C, Stinson CH. Diagnostic criteria for complicated grief disorder. *The American Journal of Psychiatry* 1997;154(7):904–910. [PubMed: 9210739]
- Ito M, Onose M, Yamada T, Onishi H, Fujisawa S, Kanamori H. Successful lithium carbonate treatment for steroid-induced depression following bone marrow transplantation: A case report. *Japanese Journal of Clinical Oncology* 2003;33(10):538–540. [PubMed: 14623924]
- Jacobs SC, Nelson JC, Zisook S. Treating depressions of bereavement with antidepressants. A pilot study. *The Psychiatric Clinics of North America* 1987;10(3):501–510. [PubMed: 3684751]
- 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(12):2872–2881. [PubMed: 16284994]
- Keller MB, Klein DN, Hirschfeld RM, Kocsis JH, McCullough JP, Miller I, et al. Results of the DSM-IV mood disorders field trial. *The American Journal of Psychiatry* 1995;152(6):843–849. [PubMed: 7755112]
- Kissane DW, Wein S, Love A, Lee XQ, Kee PL, Clarke DM. The demoralization scale: A report of its development and preliminary validation. *Journal of Palliative Care* 2004;20(4):269–276. [PubMed: 15690829]
- Koenig HG, Cohen HJ, Blazer DG, Meador KG, Westlund R. A brief depression scale for use in the medically ill. *International Journal of Psychiatry in Medicine* 1992;22(2):183–195. [PubMed: 1517023]
- Koenig HG, Pargament KI, Nielsen J. Religious coping and health status in medically ill hospitalized older adults. *The Journal of Nervous and Mental Disease* 1998;186(9):513–521. [PubMed: 9741556]
- Latham AE, Prigerson HG. Suicidality and bereavement: Complicated grief as psychiatric disorder presenting greatest risk for suicidality. *Suicide & Life-Threatening Behavior* 2004;34(4):350–362. [PubMed: 15585457]
- Neimeyer, RA.; van Dyke, JG.; Pennebaker, JW. Narrative medicine: Writing through bereavement. In: Chochinov, H.; Breitbart, W., editors. *Handbook of psychiatry in palliative medicine*. Oxford; New York: 2009. p. 454–469.
- Ogrodniczuk JS, Piper WE, Joyce AS, Weideman R, McCallum M, Azim HF, et al. Differentiating symptoms of complicated grief and depression among psychiatric outpatients. *Canadian Journal of Psychiatry* 2003;48(2):87–93.
- Ott CH. The impact of complicated grief on mental and physical health at various points in the bereavement process. *Death Studies* 2003;27(3):249–272. [PubMed: 12703505]
- Pargament KI, Koenig HG, Perez LM. The many methods of religious coping: Development and initial validation of the RCOPE. *Journal of Clinical Psychology* 2000;56(4):519–543. [PubMed: 10775045]
- Pargament KI, Zinnbauer BJ, Scott AB, Butter EM, Zerowin J, Stanik P. Red flags and religious coping: Identifying some religious warning signs among people in crisis. *Journal of Clinical Psychology* 1998;54(1):77–89. [PubMed: 9476711]
- Pasternak RE, Reynolds CF 3rd, Schlernitzauer M, Hoch CC, Buysse DJ, Houck PR, et al. Acute open-trial nortriptyline therapy of bereavement-related depression in late life. *The Journal of Clinical Psychiatry* 1991;52(7):307–310. [PubMed: 2071562]
- Prigerson HG. Socialization to dying: Social determinants of death acknowledgement and treatment among terminally ill geriatric patients. *Journal of Health and Social Behavior* 1992;33(4):378–395. [PubMed: 1464721]
- Prigerson HG, Bierhals AJ, Kasl SV, Reynolds CF 3rd, Shear MK, Day N, et al. Traumatic grief as a risk factor for mental and physical morbidity. *The American Journal of Psychiatry* 1997;154(5):616–623. [PubMed: 9137115]
- Prigerson HG, Bierhals AJ, Kasl SV, Reynolds CF 3rd, Shear MK, Newsom JT, et al. Complicated grief as a disorder distinct from bereavement-related depression and anxiety: A replication study. *The American Journal of Psychiatry* 1996;153(11):1484–1486. [PubMed: 8890686]

- Prigerson HG, Bridge J, Maciejewski PK, Beery LC, Rosenheck RA, Jacobs SC, et al. Influence of traumatic grief on suicidal ideation among young adults. *The American Journal of Psychiatry* 1999;156(12):1994–1995. [PubMed: 10588419]
- Prigerson HG, Frank E, Kasl SV, Reynolds CF 3rd, Anderson B, Zubenko GS, et al. Complicated grief and bereavement-related depression as distinct disorders: Preliminary empirical validation in elderly bereaved spouses. *The American Journal of Psychiatry* 1995;152(1):22–30. [PubMed: 7802116]
- Prigerson, HG.; Jacobs, SC. Diagnostic criteria for traumatic grief: A rationale, consensus criteria, and preliminary empirical test. In: Hansson, RO.; Schut, H., editors. part II. theory, methodology, and ethical issues. American Psychological Association Press; Washington DC: 2001. p. 614-646.
- Prigerson HG, Shear MK, Jacobs SC, Reynolds CF 3rd, Maciejewski PK, Davidson JR, et al. Consensus criteria for traumatic grief. A preliminary empirical test. *The British Journal of Psychiatry : The Journal of Mental Science* 1999;174:67–73. [PubMed: 10211154]
- Prigerson, HG.; Vanderwerker, LC.; Maciejewski, PK. Prolonged grief disorder: A case for inclusion in DSM-V. In: Strobe, M.; Hansson, R.; Schut, H.; Stroebe, W., editors. *Handbook of bereavement research and practice: 21st century perspectives*. American Psychological Association Press; Washington DC: 2008. p. 165-186.
- Ray A, Block SD, Friedlander RJ, Zhang B, Maciejewski PK, Prigerson HG. Peaceful awareness in patients with advanced cancer. *Journal of Palliative Medicine* 2006;9(6):1359–1368. [PubMed: 17187544]
- Reynolds CF 3rd, Miller MD, Pasternak RE, Frank E, Perel JM, Cornes C, et al. Treatment of bereavement-related major depressive episodes in later life: A controlled study of acute and continuation treatment with nortriptyline and interpersonal psychotherapy. *The American Journal of Psychiatry* 1999;156(2):202–208. [PubMed: 9989555]
- Shader RI. Demoralization revisited. *Journal of Clinical Psychopharmacology* 2005;25(4):291–292. [PubMed: 16012269]
- Shear K, Frank E, Houck PR, Reynolds CF 3rd. Treatment of complicated grief: A randomized controlled trial. *JAMA : The Journal of the American Medical Association* 2005;293(21):2601–2608. [PubMed: 15928281]
- Simon NM, Pollack MH, Fischmann D, Perlman CA, Muriel AC, Moore CW, et al. Complicated grief and its correlates in patients with bipolar disorder. *The Journal of Clinical Psychiatry* 2005;66(9):1105–1110. [PubMed: 16187766]
- Slavney PR. Diagnosing demoralization in consultation psychiatry. *Psychosomatics* 1999;40(4):325–329. [PubMed: 10402879]
- Szanto K, Shear MK, Houck PR, Reynolds CF 3rd, Frank E, Caroff K, et al. Indirect self-destructive behavior and overt suicidality in patients with complicated grief. *The Journal of Clinical Psychiatry* 2006;67(2):233–239. [PubMed: 16566618]
- Williams JB, Gibbon M, First MB, Spitzer RL, Davies M, Borus J, et al. The structured clinical interview for DSM-III-R (SCID). II. multisite test-retest reliability. *Archives of General Psychiatry* 1992;49(8):630–636. [PubMed: 1637253]

Figure 1.

Table 1

Factor Loadings on Major Depressive Disorder and Patient Grief

Items	Factor 1: Major Depressive Disorder	Factor 2: Patient Grief
In the past month, how often have you felt yourself longing or yearning to be healthy again?	0.102	0.420
In the past month, how often have you had intense feelings of emotional pain, sorrow, or pangs of grief related to your illness?	0.083	0.400
In the past month, how often have you tried to avoid reminders of your illness?	-0.036	0.733
In the past month, how often have you felt stunned, shocked, or dazed by your illness?	0.191	0.715
In the past month to what extent have you felt confused about your role in life or a diminished sense of self (i.e., feeling that a part of yourself has died)?	0.093	0.725
In the past month to what extent have you had trouble accepting the illness?	0.038	0.677
In the past month to what extent have you had difficulty trusting people?	0.250	0.493
In the past month to what extent have you felt bitter over your illness?	0.219	0.626
In the past month to what extent have you felt hard to concentrate on anything else?	0.307	0.649
In the past month to what extent have you felt emotionally numb?	0.134	0.575
In the past month to what extent have you felt that life is unfulfilling, empty, or meaningless?	0.064	0.709
In the past month have you experienced a significant reduction in social, occupational, or other important areas of functioning (e.g., domestic responsibilities)?	0.207	0.554
In the past month, has there been a period of time when you were feeling depressed or down most of the day, nearly every day, for at least two weeks	0.733	0.275
What about being a lot less interested in most things or unable to enjoy the things you used to enjoy	0.768	0.274
For the worst two-week period during the past month, did you lose or gain any weight * Rater: Does the patient exhibit fearfulness, or depressed appearance in face or body posture?	0.818	0.124
For the worst two-week period during the past month, was your sleeping was poor * Do you also feel more socially withdrawn or less talkative?	0.734	-0.033
For the worst two-week period during the past month, were you so fidgety or	0.837	0.233

Items	Factor 1: Major Depressive Disorder	Factor 2: Patient Grief
restless that you were unable to sit still		
For the worst two-week period during the past month, were you tired all the time * Rater: Does the patient exhibit brooding, self-pity, or pessimism?	0.727	0.039
For the worst two-week period during the past month, did you feel worthless * Did you find that you can't be cheered up, you don't smile, and/or you feel no response to good news or funny situations?	0.685	0.193
For the worst two-week period during the past month, did you have trouble thinking or concentrating	0.783	0.146
For the worst two-week period during the past month, were things so bad at his time that you were thinking a lot about death or that you would be better off dead	0.491	0.173

* Indicates Endicott substitution question

Table 2

Patient Grief Disorder vs. Major Depression Disorder *

Frequency Percent Row Percent Column Percent		Patient Grief Disorder		
		No	Yes	Total
Major Depression Disorder	No	109 (88.6%) (93.2%) (99.1%)	8 (6.5%) (6.8%) (61.5%)	117 (95.1%)
	Yes	1 (0.8%) (16.7%) (0.9%)	5 (4.1%) (83.3%) (38.5%)	6 (4.9%)
	Total	110 (89.4%)	13 (10.6%)	123 (100.0%)

* Fisher's exact test p-value < 0.0001