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Presence and predictors of anxiety disorder onset following cancer diagnosis among anxious cancer survivors

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Abstract

Purpose: Despite cancer survivors' frequent endorsement of anxiety symptoms, assessing the full range of anxiety *disorders* (AD), their timing of onset relative to cancer diagnosis, co-morbidity with mood disorder, and predictors of post-cancer onset, is rare or absent to date. This study provides a step toward addressing these gaps.

Methods: Cancer survivors at re-entry after primary treatment completion who screened positively for anxiety symptoms (*N*=133) and sought care through an intervention trial completed standardized diagnostic interviews, dimensional assessment of disorder severity, and timing of disorder onset relative to cancer diagnosis. We evaluated sociodemographic and medical predictors of developing a first AD after cancer diagnosis.

Results: Most ADs began after cancer diagnosis (58%), for 68% of affected patients, this represented their first AD episode. The most common was generalized anxiety disorder (GAD; 41%), where "cancer-focused GAD" was distinguished from "typical GAD"; the next most common were specific phobia (14%) and social anxiety disorder (13%). A minority (31%) of ADs were comorbid with major depression. Relative to having no AD, experiencing more lingering treatment side effects predicted developing a first AD after cancer diagnosis. Relative to having an AD that began before cancer diagnosis, reporting a higher cancer stage predicted developing a first AD after diagnosis.

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Conflict of Interest

The authors declare no conflicts of interest. The authors have primary control of all primary data and agree to allow the journal to review the data if requested.

Conclusions: Cancer survivors at re-entry seeking care for anxiety symptoms manifested a broad range of ADs which most commonly developed after cancer diagnosis and were prompted by the experience of cancer. Such disorders represent an unusually late-life, cancer-linked etiology that warrants further investigation and clinical attention.

Keywords

Cancer Survivors; Cancer; Anxiety; Anxiety Disorders; Phobia Disorders; Mental Health

Background

Among post-treatment cancer survivors, anxiety represents one of the most common and unaddressed symptoms [1–3]. For many, elevated anxiety persists for a decade or more after cancer treatment [3]. Elevated anxiety predicts nonadherence to recommended chemotherapy [4], higher use and costs of medical care [5], unacceptability of survivorship care plan [6], lower quality of life [7], and possibly breast cancer recurrence [8] and earlier death following recurrence [9]. These negative outcomes underscore the importance of accurately assessing the presence, topography, and onset of anxiety relative to cancer diagnosis.

Despite cancer survivors' frequent endorsement of anxiety *symptoms,* characterization of the full range of anxiety *disorders* is rare to date [10]. Most studies have used DSM-IV criteria to assess single anxiety disorders believed to be more common among cancer survivors or linked to the cancer experience: generalized anxiety disorder (GAD), characterized by enduring, difficult-to-control, excessive (most or all day) worry and accompanying physical and cognitive symptoms; posttraumatic stress disorder (PTSD) [11], characterized by a broad array of distressing cognitive, affective, and physiological responses to trauma, and occasionally panic disorder (PD), characterized by unexpected panic attacks and intense fear and avoidance thereof. However, without evaluating the full range of anxiety disorders or their onset relative to cancer diagnosis, the assumption that certain anxiety disorders are more common following cancer or more etiologically linked to cancer remains untested. Moreover, as demonstrated by large epidemiologic studies [12,13], the most common anxiety disorders in the US and Europe are specific phobia (SP), characterized by persistent marked fear of specific objects or situations (e.g., heights) and social anxiety disorder (SAD), characterized by persistent marked fear of social or performance situations involving exposure to unfamiliar people or possible scrutiny by others. In the US, SP and SAD are two to three times more prevalent than the anxiety disorders most commonly assessed among cancer survivors [13].

One of the few studies to assess SP and SAD among cancer survivors [14] found that SP was 1.6 times more common among cancer survivors than community controls; the other anxiety disorders did not differ between groups. This study, however, focused on long-term cancer survivors (≥5 years from diagnosis) and did not directly assess for cancer-related onset. A study [15] of German adults with diverse types and stages of cancer similarly showed high rates of SP compared to population norms. Another study [7] diagnosed GAD, PD, or "phobia" among patients at various points during kidney cancer, lymphoma, or melanoma

survivorship, but did not distinguish among phobia types (SP or SAD) or base diagnoses on DSM or ICD criteria. Notably, the study showed that more than two-thirds of the disorders began within 6 months of cancer diagnosis, suggesting a potential link between learning that one has cancer and developing an anxiety disorder. However, the study did not distinguish between anxiety disorders that began within 6 months before vs. after cancer diagnosis, thwarting knowledge of whether anxiety disorders developed after diagnosis. Other studies have assessed “anxiety disorders” among pre-treated, actively treated, and post-treatment cancer survivors but do not distinguish among anxiety disorders (apart from PTSD [16,17]); one of these studies in early post-treatment cancer survivors reported that anxiety disorders overwhelmingly began before cancer diagnosis [17] whereas the other study reported that at 6 months after diagnosis, half the patients with anxiety disorders were experiencing new-onset anxiety disorders that occurred for the first time, that is, without a history of anxiety disorder [16]. Thus, the few studies to assess timing of onset are mixed regarding whether anxiety disorders among cancer survivors reflect a preexisting vulnerability, develop for the first time following cancer diagnosis, or represent some combination of both. Clarifying these mixed findings requires reporting on the full range of anxiety disorders, evaluating whether onset occurred before or after cancer diagnosis, and assessing the extent to which being diagnosed with cancer contributed to the anxiety disorder. In addition, most anxiety disorders in community samples begin very early in life, with a median age at onset of 11 years [18] whereas the median age at cancer diagnosis is 66 years [19]. Cancer-linked onset of an anxiety disorder in later adulthood would thus underscore the considerable anxiety that cancer triggers for some.

In the case that a portion of anxiety disorders begins after cancer diagnosis, it is critical to elucidate predictors of this risky event, particularly among individuals without a history of anxiety disorder prior to cancer diagnosis. In that regard, one study showed that female sex and past psychiatric history predicted anxiety disorders [7], two studies showed associations between anxiety disorders and greater physical symptoms [7,15], and a meta-analysis showed that higher anxiety symptoms were associated with younger adult patient age [20]. Finally, it remains vital to understand whether the high comorbidity of anxiety and mood disorders in the general population [13] is mirrored in cancer survivors, with implications for intervention.

To address these gaps, during the early post-treatment period (i.e., the re-entry phase [21]) we conducted standardized diagnostic and dimensional assessment of anxiety disorders, evaluated the timing of anxiety disorder onset among cancer survivors (relative to diagnosis), and examined predictors of a first anxiety disorder onset after cancer. We focused on the cancer survivors at highest risk of anxiety disorders: those screening positively for anxiety symptoms and seeking help by enrolling in an intervention study designed to address the needs of anxious cancer survivors. Our goal was *not* to provide general prevalence rates of anxiety disorders among cancer survivors, as such rates will certainly be higher in this high-risk group. Rather, the goal was to leverage this high-risk sample to explore the extent to which the full range of anxiety disorders was present (vs. the few anxiety disorders focused upon in the literature to date: GAD and PTSD) and more importantly, their timing of onset relative to cancer diagnosis. We were particularly interested in identifying cancer survivors who were experiencing an anxiety disorder after cancer diagnosis for the first time,

and evaluating predictors thereof, toward the aim of identifying those at greatest risk of developing significant anxiety-related sequelae following the experience of cancer.

Methods

Participants

Adult post-treatment cancer survivors (*N*=139) were recruited from community cancer centers in the Denver metropolitan area. To be eligible, adults (age 21+) were required to: (1) have completed active cancer treatment (apart from anti-hormonal therapy) 6 weeks to 24 months prior; (2) show no current evidence of disease for solid tumor cancer or for hematologic cancer, be in remission or asymptomatic (under surveillance); (3) endorse at least moderate anxiety about cancer, indicated by a rating of 5+ on a 0–10 scale probing "your current anxiety about cancer or the effects of cancer treatment"; (4) endorse anxiety or depressive symptoms in daily life by meeting an evidence-based screening cut-off of 3+ on the Patient Health Questionnaire-2 [22] or Generalized Anxiety Disorder Scale-2 [23], or 14+ on the short form of the State-Trait Anxiety Inventory [24] and (5) consent to participate in a study comparing a behavioral intervention to enhanced usual care to address the needs of anxious cancer survivors.[1] Patients were excluded (*n*=3) and referred to more intensive resources if they reported a psychiatric hospitalization or suicide attempt within the past 5 years, moderate to high risk of suicide on the interview, or chronic trauma symptoms unrelated to cancer diagnosis/treatment.

Participants completing the baseline diagnostic interview (133/139) were included in the current study (see Table 1 for participant characteristics). The University of Colorado Boulder Institutional Review Board (#15–0313) and University of Colorado Cancer Center approved the study and all participants provided written informed consent.

Assessment

Categorical diagnostic assessment—Psychological symptoms were assessed with the full Mini-International Neuropsychiatric Interview (MINI) for DSM-5 [25] enhanced with more detailed diagnostic questions developed previously in large-scale anxiety disorder studies [26]. The MINI has excellent interrater reliability (70% of Cohen's $\kappa > 0.90$) and good test-retest reliability (61% of Cohen's $\kappa > 0.70$) [27].

Dimensional diagnostic assessment—Following previous research [28] and calls for dimensional assessment [29], interviewers rated past-month symptom interference and distress based on detailed questions from the gold-standard Anxiety Disorder Interview Schedule for DSM-5 [30], which were used to make overall clinical severity ratings (CSR) that reflected past-month symptom severity, distress, and functional impairment for each disorder on a 0 to 8 dimensional scale with anchors: 0=none, 2=subclinical, 4=clinically significant, 6=severe, and 8=highest severity possible for the disorder. CSRs are widely-used and validated for anxiety disorder assessment [31]; CSRs of ≥4 signify that the disorder is above threshold for clinical significance; CSRs <4 indicate sub-threshold.

[1]This trial was registered in clinicaltrials.gov #NCT02550925; results will be reported elsewhere.

Assessing Links to Cancer—For each diagnostic module with endorsed symptoms, interviewers first assessed the approximate date and timing of symptom onset and only subsequently asked about timing relative to cancer diagnosis, e.g., if the date of [psychological] symptom onset occurred before or after their date of cancer diagnosis. For GAD, participants rated from 0–100% the extent to which their worry focused on cancer domains (e.g., recurrence, treatment cost, family/work strain from cancer), other health domains (e.g., spouse's health, fear of illness beyond cancer), and non-health domains (e.g., family relationships). We distinguished "typical GAD", in which >50% of uncontrollable/excessive worry focused on domains unrelated to cancer from "cancer-focused GAD", in which >50% uncontrollable/excessive worry focused on cancer domains.

Predictors of Post-Cancer Diagnosis Onset of Anxiety Disorders—Based on the literature, we examined patient age [20], side effects during treatment (total count from 15 commonly reported side effects, plus one write-in option), side effects experienced currently (total count), reported cancer stage [15], past depressive episode, treatment with chemotherapy or radiation [32], and given treatment costs, household income. As the sample was predominantly female and white/non-Latino (Table 1), we could not assess sex/gender or race/ethnicity as predictors.

Interview Training and Supervision

The enhanced MINIs were administered by phone by clinical psychology doctoral students and post-baccalaureate research assistants trained and supervised by a licensed psychologist (J.J.A.) and trained based on materials developed by a leading anxiety disorder research lab [33] and multiple supervised interviews. Diagnoses and ratings were reviewed weekly by a licensed psychologist or doctoral student with Master's degree in clinical psychology; disagreements were resolved by consensus. Interviewers were unaware of condition (participants were not yet randomized).

Analytic Approach

Full disorders ("Full") were defined as disorders that met DSM-5 diagnostic criteria and had a CSR of 4 or greater [31]. Sub-threshold ("Sub") disorders in Supplemental Table 1 were defined as symptom clusters that had a CSR of <4 (i.e., CSRs from 1 to 3) or did not meet full diagnostic criteria.

In that SP is often considered the least impactful anxiety disorder [13] that does not require treatment in cancer populations [15], we used it to assess the minimal potential cancer impact of an anxiety disorder diagnosis. Specifically, we categorized each SP as: 1) directly medically relevant: phobia could impact common oncology procedures, such as needle phobia and claustrophobia (for MRIs); 2) indirectly medically relevant: phobia related to the environment that could potentially interfere with receiving oncology care such as an elevator phobia; 3) non-medically relevant: phobia that does not affect care, such as dog phobia.

For predictors of first anxiety disorder onset after cancer, we used multinomial logistic regression, with a dependent variable of post-cancer onset of the first anxiety disorder as the reference category vs. pre-cancer onset or no anxiety disorder.

Results

Individual Anxiety Disorder Presence and Characteristics

GAD was the most common anxiety disorder, with 41% of the sample meeting typical or cancer-focused (full) GAD criteria and 85% meeting full or subthreshold GAD criteria (Table 2 and Supplemental Table 1). Most GAD cases began after cancer diagnosis. Typical GAD and cancer-focused GAD had similar rates. Though typical GAD had a marginally higher CSR than cancer-focused GAD, p=.051, it did not cause more distress, p=.94. Most (82%) individuals with cancer-focused GAD worried about more than one cancer-related domain (and endorsed all other required symptoms), thereby meeting full DSM-5 GAD criteria, which require that intensive worry occur in multiple domains [34]. Cancer worry foci included: cancer recurrence, treatment side effects, family consequences, financial burden of treatment, dying, treatment decisions, medical appointments, and more. The 18% with cancer-focused GAD who did not worry about multiple cancer-related domains worried exclusively about recurrence, dying, or side effects.

SP and SAD were the next most common anxiety disorders (Table 2). Though SAD most commonly developed after cancer diagnosis and SP before, nonetheless, 43% of specific phobia cases had the potential to directly (29%) or indirectly (14%) affect cancer treatment. OCD, PD, PTSD, and agoraphobia occurred less commonly, reflecting their lower community base rates [13] (apart from PTSD).

Comorbidity with Other Mood and Anxiety Disorders

Averaging across all anxiety disorders, 31% co-occurred with a major depressive episode (MDE). Anxiety disorders more frequently co-occurred with other anxiety disorders, in 58% of cases. Of GAD cases (n=55), 20% co-occurred with MDE, though GAD usually began first, and an additional half (47%) reported sub-threshold depressive symptoms. For SP and SAD, 42% and 41% met criteria for current MDE, respectively.

Post-cancer onset with vs. without a history of anxiety disorder

Nearly 60% (77/133) of the sample met criteria for at least one current anxiety disorder (AD); 58% of total ADs reflected post-cancer onset (Table 2). Among patients with a post-cancer AD onset, 68% (30/46) reported **no** pre-cancer history of another AD.

Predictors of first anxiety disorder onset post-cancer

Prior to testing predictors, we examined their bivariate correlations to evaluate collinearity risk. All were below r=.36, indicating low collinearity risk, except for the number of current side effects vs. side effects during treatment, r=.65, and the latter vs. receipt of chemotherapy, r=.70; the latter reached collinearity concern threshold [35]. As presence of side effects was the stronger predictor individually, we omitted chemotherapy from the models to reduce collinearity risk.

Table 3 presents the combined models. Greater likelihood of developing a first AD after cancer compared to no AD was predicted only by having more current side effects from treatment. Greater likelihood of developing a first AD after cancer, compared to before

cancer, was predicted by higher reported cancer stage and radiation receipt (the latter reached but did not exceed p=.05).

The Relative Severity of Pre- vs. Post-Cancer GAD

As GAD was the most prevalent anxiety disorder in the sample, we compared the overall severity (CSR), distress, and interference ratings of GAD that began pre- vs. post-cancer diagnosis; no differences emerged on any variable, ps >.24.

Discussion

This study illuminates the relative presence of individual anxiety disorders among anxious post-treatment cancer survivors, their timing of onset relative to cancer diagnosis, and their comorbidity with mood disorder. We identified the phenomenon of cancer-focused GAD and the portion of anxiety symptoms attributed to the experience of cancer, and categorized SP's potential cancer treatment impacts. Importantly, we differentiated newly vulnerable individuals who developed their first anxiety disorder after cancer diagnosis from those with anxiety disorder histories prior to diagnosis, and we identified predictors of this vulnerability.

The most common anxiety disorders were GAD, SP, and SAD; the latter have neither been evaluated regularly in cancer samples nor considered linked to the cancer experience. Yet most cases of SAD, along with most other current anxiety disorders, typically evidenced onset after cancer diagnosis. Furthermore, apart from SP and PTSD, cancer survivors attributed the majority of their anxiety disorder symptoms to the cancer experience. They reported that SAD was often triggered by cancer-related changes in their appearance, self-perception, and sense of social connectedness, whereas GAD was often triggered by cancer-related changes in perceived health and vulnerability to misfortune. The sample's median age was 58 years, which is far greater than the median age-of-onset for anxiety disorders in community samples of 11 years [18], underscoring the potential for the cancer experience to trigger anxiety disorders later in life. Over two-thirds of cancer survivors with post-cancer onset of an anxiety disorder reported no lifetime history of anxiety disorder prior to cancer diagnosis. Thus, the experience of cancer appeared to render a substantial portion vulnerable to developing an anxiety disorder for the first time in their lives. Earlier findings by Stark et al. [7] and Kangas et al. [16] indicate that one-half to two-thirds of anxiety disorders among cancer survivors began around or within 6 months after cancer diagnosis. The current study extends those findings by more precisely noting whether anxiety disorder onset was before or after cancer diagnosis, reporting on the full range of anxiety disorders, and directly assessing patient-perceived links between their experience of cancer and anxiety symptoms. The current findings also contradict an early study reporting that nearly all anxiety disorders among cancer survivors began prior to cancer diagnosis [17].

This study contributes novel findings to understanding the predictors of developing a first anxiety disorder after cancer diagnosis. First, compared to having an anxiety disorder that began *before* cancer diagnosis, cancer survivors with the first anxiety disorder onset *after* cancer reported higher cancer stage and marginally greater likelihood of radiation treatment, suggesting that more advanced disease and arduous treatment distinguished risk for

developing an anxiety disorder after cancer diagnosis, relative to before. Future studies in more diverse samples should also evaluate gender/sex [36] and race/ethnicity as predictors of anxiety disorders [37,1].

Second, this study replicated and extended the previously found association between physical symptoms and anxiety levels in cancer populations [7,15] by demonstrating that current side effects predicted the first anxiety disorder onset after cancer diagnosis. Specifically, a greater number of ongoing treatment side effects predicted greater risk of developing a first-time anxiety disorder after cancer diagnosis, relative to no anxiety disorder (past or present). This finding is consistent with established relationships between mental health and physical health, particularly as perceived by the patient [38,39], and if replicated, suggests that ongoing side effects should cue cancer providers to assess for anxiety symptoms.

Finally, this study extended previous work by examining the potential treatment-related impacts of SP and found that nearly half of cases posed potential direct or indirect obstacles to cancer treatment. Direct obstacles included phobias of blood/injury/injection and claustrophobia that could interfere with cancer care (blood draws and MRIs, respectively). Indirect obstacles included phobias of crowds, driving, elevators that could present obstacles to attending cancer care appointments, for example, in crowded, distant, or multi-story hospitals. Thus, even a comparatively mild anxiety disorder [13] can create barriers to oncology care, challenging the assertion that SP does not require timely treatment in cancer populations [15].

PTSD was uncommon, consistent with relatively low diagnostic interview-based rates of PTSD in other samples of post-treatment, early stage cancer survivors (e.g., paralleling most of the current sample) [40,41]. The current rates could have been somewhat reduced by exclusion criteria for untreated PTSD not related to cancer and by two participants who declined to describe their trauma symptoms.

Cancer-focused GAD

We defined symptoms that otherwise met full criteria for GAD apart from a dominant focus on cancer as “cancer-focused GAD”. Three reasons justify characterizing this phenomenon as GAD. First, the content, breadth, number, duration, and severity of cancer-focused GAD symptoms was most fully captured by GAD rather than by potential alternative diagnoses such as Adjustment Disorder or Hypochondriasis (Illness Anxiety Disorder in DSM-5), or by labeling the symptoms solely as fear of cancer recurrence, though characterizing fear of cancer recurrence is important nonetheless. Second, a possible alternative diagnosis is Hypochondriasis/Illness Anxiety Disorder, but the focus therein is on having the disease itself. In contrast, cancer survivors with cancer-focused GAD often worried more about the difficulties of re-experiencing oncologic treatments or cancer’s consequences for finances, work, and family than about having the disease per se. Third, among a minority, cancer-focused GAD overlapped with Hypochondriasis/Illness Anxiety Disorder in that vigilance and reactivity to bodily symptoms were common; however, their psychological symptoms extended beyond to include full GAD symptoms.

Study Limitations

Generalizability is limited to post-treatment cancer survivors who have some indication of anxiety and are open to associated intervention. However, participants all knew that they had qualified for the trial when anxiety disorders were assessed, precluding motivated over-reporting as an explanation for the findings. In addition, the sample was primarily female, white and non-Latino/a, and well educated. Findings thus require replication in consecutively-recruited, larger, and more diverse samples. Including cancer survivors across cancer type was both a study strength, in that findings may better generalize to clinics that treat across cancer type, and a study limitation, in that some studies suggest that anxiety and distress levels vary by cancer type [3,42]. Larger future studies will want to compare findings by cancer type. Participants' report of onset of anxiety symptoms relative to cancer diagnosis was retrospective; however, assessing timing relative to a distinct, relatively recent, and personally significant event strongly improves accuracy of recall [43]. Further, anxiety disorders typically begin early in life and often endure for decades [44], rendering it unlikely that patients had major anxiety symptoms prior to cancer but were completely unaware of them. Nonetheless, it will be important to replicate the current findings in prospective, longitudinal future studies.

Clinical Implications

Recent cancer survivors seeking care for anxiety symptoms suffered from a broad range of anxiety disorders, the majority of which occurred independently of mood disorders. The most common was GAD; half of cases had a predominantly cancer focus. The next most common anxiety disorders were SP and SAD, which rarely have been examined in relation to cancer. The majority of anxiety disorders began after cancer diagnosis, representing an unusually late-life, disease-linked etiology that warrants clinical attention. Findings suggest that anxiety is multifaceted and debilitating among many anxious cancer survivors and that most first-time anxiety disorders are directly related to patients' experience of cancer, specifically, having more advanced disease, arduous treatment, and ongoing side effects. A sizable minority are experiencing clinically significant levels of anxiety for the first time in their lives. For oncology care providers, these findings demonstrate the importance of understanding that cancer can trigger serious, debilitating, and diverse forms of anxiety for some patients that can endure into the post-treatment survivorship period and extend beyond fear of cancer recurrence. Future prospective, consecutively-recruited, cancer survivor studies are now needed to evaluate fully the general prevalence rates of all anxiety disorders, including cancer-focused (forms of) GAD, and their onset relative to cancer. For providers, this underscores the potential need to screen for multiple forms of anxiety symptoms and the degree to which they cause impairment in patients' ability to engage in daily life and in cancer and survivorship care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Koch L, Jansen L, Brenner H, Arndt V (2013) Fear of recurrence and disease progression in long-term (≥ 5 years) cancer survivors-a systematic review of quantitative studies. Psycho-Oncology 22:1–11
2. Harrison SE, Watson EK, Ward AM, Khan NF, Turner D, Adams E, Forman D, Roche MF, Rose PW (2011) Primary health and supportive care needs of long-term cancer survivors: A questionnaire survey. Journal of Clincal Oncology 29 (15):2091–2098
3. Mitchell AJ, Ferguson DW, Gill J, Paul J, Symonds P (2013) Depression and anxiety in long-term cancer survivors compared with spouses and healthy controls: A systematic review and meta-analysis. The Lancet Oncology 14 (8):721–732 [PubMed: 23759376]
4. Greer JA, Pirl WF, Park ER, Lynch TJ, Temel JS (2008) Behavioral and psychological predictors of chemotherapy adherence in patients with advanced non-small cell lung cancer. Journal of psychosomatic research 65 (6):549–552 [PubMed: 19027443]
5. Marciniak MD, Lage MJ, Dunayevich E, Russell JM, Bowman L, Landbloom RP, Levine LR (2005) The cost of treating anxiety: the medical and demographic correlates that impact total medical costs. Depression and Anxiety 21 (4):178–184 [PubMed: 16075454]
6. Thomas SF, Glynne-Jones R, Chait I, Marks DF (1997) Anxiety in long-term cancer survivors influences the acceptability of planned discharge from follow-up. Psycho-Oncology 6 (3):190–196 [PubMed: 9313284]
7. Stark D, Kiely M, Smith A, Velikova G, House A, Selby P (2002) Anxiety disorders in cancer patients: Their nature, associations, and relation to quality of life. Journal of Clinical Oncology 20 (14):3137–3148 [PubMed: 12118028]
8. De Brabander B, Gerits P (1999) Chronic and acute stress as predictors of relapse in primary breast cancer patients. Patient education and counseling 37 (3):265–272 [PubMed: 14528552]
9. Weihs KL, Enright TM, Simmens SJ, Reiss D (2000) Negative affectivity, restriction of emotions, and site of metastases predict mortality in recurrent breast cancer. Journal of psychosomatic research 49 (1):59–68 [PubMed: 11053605]
10. Roy-Byrne PP, Davidson KW, Kessler RC, Asmundson GJ, Goodwin RD, Kubzansky L, Lydiard RB, Massie MJ, Katon W, Laden SK (2008) Anxiety disorders and comorbid medical illness. Focus 6 (4):467–485
11. Mitchell AJ, Chan M, Bhatti H, Halton M, Grassi L, Johansen C, Meader N (2011) Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. The lancet oncology 12 (2):160–174 [PubMed: 21251875]
12. Wittchen H-U, Jacobi F, Rehm J, Gustavsson A, Svensson M, Jönsson B, Olesen J, Allgulander C, Alonso J, Faravelli C (2011) The size and burden of mental disorders and other disorders of the brain in Europe 2010. European neuropsychopharmacology 21 (9):655–679 [PubMed: 21896369]
13. Kessler RC, Chiu WT, Demler O, Walters EE (2005) Prevalence, Severity, and Comorbidity of 12-Month DSM-IV Disorders in the National Comorbidity Survey Replication. Archives of General Psychiatry 62 (6):617–627 [PubMed: 15939839]
14. Greer JA, Solis JM, Temel JS, Lennes IT, Prigerson HG, Maciejewski PK, Pirl WF (2011) Anxiety disorders in long-term survivors of adult cancers. Psychosomatics 52 (5):417–423 [PubMed: 21907059]
15. Härter M, Reuter K, Aschenbrenner A, Schretzmann B, Marschner N, Hasenburg A, Weis J (2001) Psychiatric disorders and associated factors in cancer: results of an interview study with patients in inpatient, rehabilitation and outpatient treatment. European Journal of Cancer 37 (11):1385–1393 [PubMed: 11435069]

16. Kangas M, Henry JL, Bryant RA (2005) The course of psychological disorders in the 1st year after cancer diagnosis. Journal of consulting and clinical psychology 73 (4):763 [PubMed: 16173866]
17. Green BL, Rowland JH, Krupnick JL, Epstein SA, Stockton P, Stern NM, Spertus IL, Steakley C (1998) Prevalence of posttraumatic stress disorder in women with breast cancer. Psychosomatics 39 (2):102–111 [PubMed: 9584535]
18. Kessler RC, Berglund P, Demler O, Jin R, Walters EE (2005) Lifetime Prevalence and Age-of-Onset Distributions of DSM-IV Disorders in the National Comorbidity Survey Replication. Archives of General Psychiatry 62 (6):593–602 [PubMed: 15939837]
19. Noone A, Howlader N, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis D, Chen H, Feuer E, Cronin K, (eds). SEER Cancer Statistics Review 1975–2015 National Cancer Institute, Bethesda, MD doi:bsased on November 2017 SEER data submission, posted to the SEER web site, 4 2018
20. van't Spijker A, Trijsburg RW, Duivenvoorden HJ (1997) Psychological sequelae of cancer diagnosis: a meta-analytical review of 58 studies after 1980. Psychosomatic medicine 59 (3):280–293 [PubMed: 9178339]
21. Mullan F (1984) Re-entry: The educational needs of the cancer survivor. Health Education Quarterly 10:88–94 [PubMed: 6706620]
22. Lowe B, Kroenke K, Grafe K (2005) Detecting and monitoring depression with a two-item questionnaire (PHQ-2). Journal of psychosomatic research 58 (2):163–171 [PubMed: 15820844]
23. Kroenke K, Spitzer RL, Williams JBW, Monahan PO, Lowe B (2007) Anxiety disorders in primary care: Prevalance, impairment, comorbidity, and detection. Annals of Internal Medicine 146:317–325 [PubMed: 17339617]
24. Tluczek A, Henriques JB, Brown RL (2009) Support for the reilability and validity of a six-item state anxiety scale derived from the State-Trait Anxiety Inventory. Journal of Nursing Measurement 17 (1):19–28 [PubMed: 19902657]
25. Sheehan DV (2014) MINI International Neuropsychiatric Interview, English Version 7.0.0 for DSM-5.
26. Roy-Byrne P, Craske MG, Sullivan G, Rose RD, Edlund MJ, Lang A, Bystritsky A, Welch SS, Chavira DA, Golinelli D, Campbell-Sills L, Sherbourne C, Stein MB (2010) Delivery of evidence-based treatment for multiple anxiety disorders in primary care: a randomized controlled trial. Journal of the American Medical Association 19 (303):1921–1928
27. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, J.J, Weiller E, al. e (1998) The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. Journal of Clinical Psychiatry 59 (Suppl 20):22–33
28. Arch JJ, Ayers CR, Baker A, Almklov E, Dean DJ, Craske MG (2013) Randomized clinical trial of adapted mindfulness based stress reduction versus group cognitive behavioral therapy for heterogeneous anxiety disorders. Behaviour Research and Therapy 51:185–196 [PubMed: 23419887]
29. Shear MK, Bjelland I, Beesdo K, Gloster AT, Wittchen HU (2007) Supplementary dimensional assessment in anxiety disorders. International journal of methods in psychiatric research 16 (S1):S52–S64 [PubMed: 17623395]
30. Brown TA, Barlow DH (2014) Anxiety Disorders Interview Schedule for DSM-5 (ADIS-5) - Adult Version. Oxford University Press, Oxford, England
31. Brown TA, DiNardo PA, Lehman CL, Campbell LA (2001) Reliability of DSM-IV anxiety and mood disorders: Implications for the classification of emotional disorders. Journal of Abnormal Psychology 110:49–58 [PubMed: 11261399]
32. Yao C, Bernstein LJ, Rich JB (2017) Executive functioning impairment in women treated with chemotherapy for breast cancer: a systematic review. Breast cancer research and treatment 166 (1):15–28 [PubMed: 28707202]
33. Craske MG, Stein MB, Sullivan G, Sherbourne C, Bystritsky A, Rose RD, Lang AJ, Welch S, Campbell-Sills L, Golinelli D, Roy-Byrne P (2011) Disorder-specific impact of coordinated anxiety learning and management treatment for anxiety disorders in primary care. Archives of General Psychiatry 68 (4):378–387. doi:10.1001/archgenpsychiatry.2011.25 [PubMed: 21464362]

34. American Psychiatric Association (2013) Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub,

35. Dormann CF, Elith J, Bacher S, Buchmann C, Carl G, Carré G, Marquéz JRG, Gruber B, Lafourcade B, Leitão PJ (2013) Collinearity: a review of methods to deal with it and a simulation study evaluating their performance. Ecography 36 (1):27–46

36. Craske MG (2003) Origins of phobias and anxiety disorders: Why more women than men? Elsevier Ltd, Oxford, UK

37. Janz NK, Hawley ST, Mujahid MS, Griggs JJ, Alderman A, Hamilton AS, Graff JJ, Jagsi R, Katz SJ (2011) Correlates of worry about recurrence in a multiethnic population-based sample of women with breast cancer. Cancer 117 (9):1827–1836 [PubMed: 21445916]

38. Pinquart M (2001) Correlates of subjective health in older adults: a meta-analysis. Psychology and aging 16 (3):414 [PubMed: 11554520]

39. Murray SA, Kendall M, Mitchell G, Moine S, Amblàs-Novellas J, Boyd K (2017) Palliative care from diagnosis to death. BMJ(Clinical research ed) 356:j878

40. Voigt V, Neufeld F, Kaste J, Bühner M, Sckopke P, Wuerstlein R, Hellerhoff K, SztroKay-Gaul A, Bruan M, von Koch FE, Silva-Zurcher E, Hasmuller S, Bauerfeind I, Debus G, Herschbach P, Mahner S, Harbeck N, Hermelink K (2016) Clinically assessed posttraumatic stress in patients with breast cancer during the first year after diagnosis in the prospective, longitudinal, controlled COGNICARES study. Psycho-Oncology 1–7 [PubMed: 26929207]

41. Abbey G, Thompson SB, Hickish T, Heathcote D (2015) A meta-analysis of prevalence rates and moderating factors for cancer-related post-traumatic stress disorder. Psycho-Oncology 24 (4):371–381 [PubMed: 25146298]

42. Admiraal J, Reyners A, Hoekstra-Weebers J (2013) Do cancer and treatment type affect distress? Psycho-Oncology 22 (8):1766–1773 [PubMed: 23109282]

43. Loftus EF, Marburger W (1983) Since the eruption of Mt. St. Helens, has anyone beaten you up? Improving the accuracy of retrospective reports with landmark events. Memory & Cognition 11 (2):114–120 [PubMed: 6865744]

44. Yonkers KA, Bruce SE, Dyck IR, Keller MB (2003) Chronicity, relapse, and illness—course of panic disorder, social phobia, and generalized anxiety disorder: Findings in men and women from 8 years of follow-up. Depression and Anxiety 17 (3):173–179 [PubMed: 12768651]

Table 1.

Sample sociodemographic and medical characteristics

Sociodemographics	
Female	87.97% (117/133)
Age	*M*=56.21 (*SD*=11.59); *Md*=58.00 Range=21–75
Race/Ethnicity	White/Caucasian & Not Latino/a: 84.21% (112/133) Hispanic/Latino/a: 9.77% (13/133) Biracial: 2.26% (3/133) Other: 1.50% (2/133) Asian American: 1.50% (2/133) Black/African American:.75% (1/133)
Education (median)	Bachelor's degree
Household income (median)	$61,000-$80,000
Married or partnered	68.42% (91/133)
Cancer treatment history	
Months between end of active cancer treatment and study enrollment	*M*=8.70 (*SD*=6.33)
% of each who received: 1) Surgery 2) Chemotherapy 3) Radiation	 1) 77.44% (103/133) 2) 68.42% (91/133) 3) 55.64% (74/133)
Cancer type	
Breast	59.40% (79/133)
Lymphoma	10.53% (14/133)
Gastrointestinal	9.02% (12/133)
Gynecologic	4.51% (6/133)
Lung	3.76% (5/133)
Prostate or testicular	3.01% (4/133)
Head and neck	3.76% (5/133)
Multiple myeloma	3.01% (4/133)
Other	3.01% (4/133)
Cancer stage (solid tumor cancers only)	
0	2.63% (3/114)
I	36.84% (42/114)
II	29.82% (32/114)
III	25.44% (29/114)
IV	5.26% (6/114)
Current medication use[1]	
% on psychiatric medication	44.26% (54/122)
% on sleep medication	FDA-regulated=26.23% (32/122) Alternative (herbal)=14.75% (18/122)
% on pain medication	33.61% (41/122)
% on anti-hormonal medication (includes ovarian suppression medication)	40.98% (50/122)

% on maintenance chemotherapy or immunotherapy	9.02% (11/122)

[1] Data are unavailable for 11 participants, as we did not initially assess medication use.

Table 2.

Anxiety disorder rate, relation to cancer experience, and severity

Anxiety Disorder	Rate	Onset After Cancer Diagnosis[1]	% symptoms triggered by cancer experience		Clinical Severity Rating (0–8)	
	% (*n*)	% (*n*)	*M (SD)*	*Md*	*M (SD)*	*Md*
Generalized anxiety disorder (all)[2]	41.35% (55/133)	67.39% (31/46)	73.77% (21.94%)	80.00%	5.06 (.93)	5.00
Typical GAD	21.05% (28/133)	60.87% (14/23)	65.76% (23.31%)	70.00%	5.30 (.99)	5.00
Cancer-focused GAD	20.30% (27/133)	73.91%[2] (17/23)	81.09% (18.15%)	80.00%	4.79 (1.75)	5.00
Specific phobia (most severe phobia for each individual)	14.29% (19/133)	17.65% (3/17)	24.41% (39.13%)	.00%	4.89 (1.10)	4.00
Social Anxiety Disorder	12.78% (17/133)	62.50% (10/16)	70.33% (38.19%)	100.00%	5.06 (.97)	5.00
Agoraphobia[3]	3.79% (5/132)	75.00% (3/4)	85.00% (30.00%)	100.00%	5.60 (.55)	6.00
Post-traumatic stress disorder[3]	3.05% (4/131)	33.33% (1/3)	45.00% (30.41%)	30.00%	5.50 (.58)	5.50
Obsessive compulsive disorder	3.01% (4/133)	66.67% (2/3)	30.00% --	30.00%	4.75 (.96)	4.50
Panic disorder[3]	3.79% (5/132)	60.00% (3/5)	100.00%[4] (.00%)	100.00%[4]	4.20 (.45)	4.00

[1] Data are unavailable for *n*=11 participants as we did not initially assess this.

[2] Pre-cancer cases reflected typical GAD that became cancer-focused after diagnosis.

[3] Missing data for those declining to discuss PD and AG (n=1) or PTSD (n=2)

[4] Missing data for *n*=2 with PD onset before diagnosis.

Table 3.

Combined predictive model of developing a first anxiety disorder (AD) after cancer diagnosis

Comparison	Predictor	β	SE β	Odds Ratio Exp(β)
No AD vs.Post-Cancer AD	Age	−.01	.03	.99
	Side effects during cancer treatment	.03	.11	1.03
	Current side effects from treatment	−.42**	.14	.66
	Reported cancer stage	−.43	.29	.65
	Received radiation	−.54	.60	.65
	Previous depression episode	.43	.56	1.53
First AD onset Pre-Cancer vs. Post-Cancer	Age	−.02	.03	.98
	Number of side effects during cancer treatment	.00	.11	.98
	Number of current side effects from treatment	−.19	.13	.83
	Reported cancer stage	−.76*	.30	.47
	Received radiation	−1.16[a]	.60	.31
	Previous depression episode	.91	.57	2.48
No AD vs.Post-Cancer AD	Model Intercept	4.49*	1.96	
Pre-Cancer vs. Post-Cancer AD	Model Intercept	5.55**	1.99	
Overall model fit: −2 Log Likelihood χ^2=37.03***, *df*=12 Cox and Snell R^2=.26, Nagelkerke=.30				

[a] p=.05;

* p<.05

** p<.01

*** p<.001

Post-Cancer AD=reference category (coded 2)