

Surviving Recurrence: Coping with the First and Second

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Abstract

Objective: Of the 230,000 annual cases of breast cancer, 20% of patients will recur at least once. There are no data examining psychological responses to 2nd recurrence. Available data point to differences between initial diagnosis and 1st recurrence, with patients with recurrence having lower functional status and reporting more pain, fatigue and relationship problems (Frost et al., 2000; Northouse et al., 2002; Sarenmalm, Öhlén, Odén, & Gaston-Johansson, 2008). Data documenting patients' psychological responses to initial and 1st and 2nd recurrence breast cancer diagnoses is provided.

Methods: Breast cancer patients (N=215) newly diagnosed with initial disease (n=90), or a 1st (n=108) or 2nd recurrence (n=17) were assessed at diagnosis and 4 months later. Measures of stress (IES), mood (POMS), quality of life (QoL; SF-36), sexual satisfaction (SEX), and nurse-rated Karnofsky Performance Status (KPS) were used. Linear regressions tested whether (1) recurrence status (none, 1st, 2nd), (2) time (baseline, 4 months), and (3) the interaction (recurrence status by time) predicted psychological outcomes.

Results: All patients had reduced cancer stress, reduced negative mood, and improved mental QoL, but poorer physical QoL by 4 months (all $ps < .05$). Recurrence status significantly predicted lower SEX and lower KPS across time points ($ps < .01$). Across time, SEX and KPS were highest for initial diagnosis (SEX: $M=4.4$, KPS: $M=86$, respectively), middling for 1st recurrence (SEX: $M=3.4$, KPS: $M=75$), and lowest for 2nd recurrence patients (SEX: $M=3.0$, KPS: $M=73$).

Conclusions: New data is provided showing that 2nd recurrence patients report lower sexual satisfaction and nurse rated performance status, but the level and change in their other psychological/QoL responses were comparable to those of other diagnosis groups. These data suggest that existing interventions to reduce stress and enhance coping might be applicable for all newly diagnosed patients, with any alterations focused on the unique problem areas within a group.

Key words: cancer; recurrence; performance status; sexual satisfaction; quality of life

Introduction

Considerable advances have been made in our understanding of the physical and psychological reactions to the diagnosis and treatment of cancer. However, this research has been primarily limited to the experience of the initial cancer diagnosis. Yet the initial cancer diagnosis is only the beginning of the survivorship trajectory. Many patients will experience a recurrence, defined as the return of cancer after treatment, after a period of time during which the cancer cannot be detected (American Cancer Society, 2013). The experience of cancer recurrence is a qualitatively different and more emotionally intense experience from most stressors, including the initial diagnosis of cancer (Thornton et al., 2014). The diagnosis of cancer recurrence requires mobilization for coping in the long term, i.e., viewing cancer as chronic condition rather than an acute one, coping with maintenance (i.e., continuous) cancer therapy or having stable (or increasing) symptoms rather than a recovery trajectory. The patient is now faced with a chronic illness, the outcome of which cannot be guaranteed even with adherence to medical treatments and healthy lifestyle. In addition, patients may have multiple recurrences, punctuated by discrete periods of time without cancer.

Our knowledge of the response to the diagnosis of cancer recurrence is inadequate, especially in light of the prevalence of cancer recurrence. For example, there are 230,000 new diagnoses of breast cancer annually; of these cases, 20% will recur at least once (American Cancer Society, 2014). Thus, the physical and psychological reactions to the diagnosis and treatment of cancer recurrence are a particularly important topic to address. The aim of the present study is to compare patients' psychological response to cancer diagnosis across time and by recurrence status.

Although there are no data examining psychological responses across multiple

recurrences, differences between the initial diagnosis of cancer and first recurrence have been examined. In the physical domain, prognosis following recurrence is generally poor and associated with high symptom burden. Patients report negative physical sequelae, including lower functional status and greater role limitations (Frost et al., 2000), increased pain (Sarenmalm et al., 2008), high levels of fatigue (Mahon & Casperson, 1995), and difficulty sleeping (Sarenmalm et al., 2008). Compared to those with newly diagnosed disease, patients with recurrent cancer also experience poorer overall physical functioning, more pain, more physical symptoms, and worse symptom severity (H. C. Yang, Thornton, Shapiro, & Andersen, 2008). Finally, recurrent cancer patients evaluate their personal health more poorly than newly diagnosed patients do (Oh, Heflin, & Meyerowitz, 2004). For many patients, cancer becomes a chronic illness that they must cope with for the rest of their lives. Thus, the diagnosis of recurrence presents a significant physical burden for patients.

The psychological response to cancer recurrence also differs from the initial diagnosis of cancer. Patients typically find the recurrence diagnosis more upsetting than initial diagnosis (Hanson Frost et al., 2000). They have been diagnosed with a chronic and life-limiting disease, and must now relinquish or alter cherished life goals, contend with difficult and changing medical treatments, experience effects on intimate relationships, and confront mortality (Stanton & Low, 2012). Hope for cure must be revised and optimism is tempered (Worden, 1989). Research demonstrates that patients with recurrence cancer have poorer perceptions of their health, less hope, and more problems in relationships (Northouse et al., 2002). At recurrence, prospective, controlled research shows patients' cancer-related traumatic stress symptoms are significant, and when compared to their responses at their initial diagnosis, the stress is comparable (B. L. Andersen, Shapiro, Farrar, Crespin, & Wells-Di Gregorio, 2005). Controlled

longitudinal data also show distress remains high for the next year (Andersen et al., 2010; Bull et al., 1999; H.-C. Yang, Brothers, & Andersen, 2008).

While the extant research has led to a wealth of knowledge of patients' physical and emotional responses at the time of initial diagnosis, further information is needed to understand such responses across multiple recurrences. Therefore, hierarchical linear regressions were used to examine differences in physical and psychological variables across samples of patients at different points in the cancer survivorship trajectory. Breast cancer patients (N=215) with initial disease (n=90), or a first (n=108) or second recurrence (n=17) were assessed at diagnosis and 4 months later. At both time points, participants completed measures of cancer-related stress (Impact of Events Scale), mood (Profile of Mood States), quality of life (36-item Medical Outcomes Study Short Form), and sexual satisfaction (Sexual Experience Scale). In addition, oncology nurses rated patients' performance status (Karnofsky Performance Status). Our hypotheses were threefold. First, all patients would see reductions in symptoms from the time of diagnosis to the 4-month follow-up. Second, higher levels would be present with each successive recurrence diagnosis, such that initial diagnosis patients would have the best outcomes, followed by first recurrence patients, with worst outcomes for second recurrence patients. Third, the interaction of time and recurrence status would significantly predict outcomes, such that initial diagnosis patients would demonstrate the steepest symptom recovery, followed by first recurrence patients, and second recurrence patients would have the slowest symptom recovery slope.

Methods

Design

A three group, repeated measures design was used. A total of 215 female breast cancer

patients with initial disease ($n = 90$), or a first ($n = 108$) or second recurrence ($n = 17$) participated. Assessments occurred at diagnosis and 4 months later.

Procedures

Data were obtained from two sources. Patients were recruited from the oncology clinics of a National Cancer Institute-designated Comprehensive Cancer Center affiliated with a large Midwestern university or were self- and physician-referred patients from the community. Women with newly diagnosed, surgically treated regional breast carcinoma were eligible. The sample is similar to those in the Ohio Cancer Incidence Surveillance System (Ohio Department of Health, 2002) and the Surveillance, Epidemiology, and End Results program (Howlander et al., 2014) databases for patients with breast carcinoma.

The first source of data for the present study was a randomized clinical trial (RCT; $N=227$) which followed their diagnosis of Stage II/III breast cancer. Women were then randomized to a psychological intervention plus assessment ($n = 114$) or assessment only ($n = 113$) arms. Details of the RCT, including procedures for informed consent, accrual, and randomization have been published elsewhere (Andersen et al., 2004). Women were followed and while a subset of patients remained disease-free ($n = 90$), a subset of patients were diagnosed with recurrence ($n = 66$).

As these 66 women were diagnosed with cancer recurrence, they were approached for accrual to a secondary study on coping with recurrence. Recurrence was classified by the development of metastatic disease in the same area, adjacent to, or distant from the original disease (American Joint Committee on Cancer, 2002; Lenhard & Osteen, 2001). Of the 66 patients, 20 (30%) were not available for substudy accrual, 6 patients (9%) progressed rapidly and died, and 14 (21%) had previously discontinued assessments. Of the remaining 46, 5 (8%)

patients declined participation. Thus, a total of 41 women participated and are included in this analysis. These 41 women were assigned to either the first recurrence group or the second recurrence group. Twenty-nine women (71%) had only one recurrence and were included in the first recurrence group. Twelve women (29%) subsequently experienced a disease-free period, followed by a second recurrence diagnosis. Thus, these women were not included in the first recurrence group, but were instead included in the second recurrence group for the purposes of these analyses.

The second source of data for the present study was a longitudinal study of coping with recurrent breast cancer. New, consecutive cases of recurrent breast cancer were identified. Recurrence was classified as described above. Exclusion criteria included diagnosis of prior or current second primary tumor, prior or current refusal of cancer treatment, mental retardation, severe or untreated psychiatric diagnoses (e.g., schizophrenia), or neurological disorders (e.g., dementia). A total of 108 women who were approached to participate; 24 declined and 84 (78%) were accrued. Women were followed and a subset of patients ($n = 5$, 6%) experienced a disease-free period, followed by a second recurrence diagnosis.

Combining Groups 1 and 2, a total of 215 women participated. The initial diagnosis group included 90 women, the first recurrence group included 108 women, and the second recurrence group included 17 women. Preliminary data analyses demonstrated no statistically significant differences in sociodemographic, disease, treatment, or outcome variables between women in group 1 and women in group 2 (all $ps > 0.05$).

All participants were provided with oral and written informed consent. Following informed consent, a female RA assisted women with completing an assessment consisting of self-reports of cancer stress, depressive symptoms, health behaviors, and other areas.

Participants were compensated \$50.00 to \$100.00 per assessment.

Figure 1 provides information about the flow of study participants. The initial assessment was performed an average of 8.4 months (S.D. = 22.2) after receiving the cancer diagnosis. A follow-up assessment was completed 4 months following the baseline assessment. Thirty-one (14%) women did not complete the 4 month follow-up assessment because they were unavailable [too sick to participate (n=3), scheduling difficulties (n=13), study dropout (n=7), death (n=8)].

Participants

Sociodemographic, disease, and treatment characteristics are presented in Table 1. The sample was primarily Caucasian (89.8%), middle aged ($M = 53.5$, $SD = 11.2$ years), partnered (70.2%), and had, on average, some college education ($M = 14.5$, $SD = 2.8$ years). For the recurrence samples, 69.6% had distant rather than loco-regional metastases. Since the most recent diagnosis, most (91.6%) had received some type of cancer treatment by the time of initial assessment.

Measures

Cancer-specific Stress. The impact of events scale (IES; Horowitz, Wilner, & Alvarez, 1979) assesses traumatic stress, both intrusive thoughts (i.e., “Other things kept making me think about cancer”) and avoidant thoughts and behaviors concerning cancer (e.g., “I tried not to talk about it”) and is used as an indicator of individual differences in treatment outcome (Andersen, et al., 2004). The frequency of 15 feelings or events is rated during the previous week, using a 5-point Likert scale (0 = not at all to 4 = often). Items are summed for a total score, which can range from 0 to 75, with higher scores reflecting greater stress. Scores above 19 reflect clinically relevant levels of traumatic stress (Zilberg, Weiss, & Horowitz, 1982).

Mood. The Profile of Mood States (POMS; McNair, Lorr, & Droppleman, 1971) was used to assess negative mood. Participants rate how they have been feeling in the last week by responding to a list of 65 adjectives on a 5-point scale (0=not at all to 4=extremely). The POMS has six subscales: 1) Tension-Anxiety; 2) Depression-Dejection; 3) Anger-Hostility; 4) Vigor-Activity; 5) Fatigue-Inertia; and 6) Confusion-Bewilderment. A Total Mood Disturbance Score can be calculated from the six abovementioned scales. The score can range from -32 to 200, with higher scores representing greater disturbance.

Quality of life. The Medical Outcomes Study 36-Item Short Form Health Survey (SF-36; Ware & Sherbourne, 1992) has 36 items contributing to eight subscales for assessing psychological and physical quality of life over the past month. These subscales yield a Physical Component score (PCS) and a Mental Component score (MCS) that summarize quality of life. The PCS and MCS are computed by summing all subscales but using differential weights. The component score is converted to a T score relative to the population, with a mean of 50 and standard deviation of 10. Higher scores reflect better quality of life.

Sexual Satisfaction. Global sexual satisfaction was assessed by one item drawn from a factor analytic study of the Derogatis and Melisaratos Sexual Experience Scale (SEX; Derogatis & Melisaratos, 1979). Patients rated their overall level of sexual activity on a ten-point Likert scale from “could not be worse” to “could not be better.”

Karnofsky Performance Status. Karnofsky Performance Status (KPS; Karnofsky & Burchenal, 1949) is a functional status scale ranging from 100 (normal, no complaints, no evidence of disease) to 0 (dead) with 10-point intervals. KPS ratings were made by oncology research nurses based on patient interview, medical chart review, and, if needed, physician consultation.

Analytic Strategy

To test the relationship between recurrence status and the outcomes of interest (cancer stress, mood, quality of life, sexual satisfaction, and performance status), hierarchical multiple linear (HLM) regression analyses were conducted using IBM SPSS 22. Recurrence status at baseline and time of assessment were specified as the predictors. Empirical selection of control variables is described below. Variables were entered in the following order: 1) controls, if any 2) recurrence status (none, first, second), 2) time (baseline, 4 months), and 3) the interaction of recurrence status and time. Significance was specified at the 0.05 level.

Results

Descriptive and Preliminary Analyses

Summary statistics for measures at baseline are reported in Table 2. Of the sociodemographic, disease, and treatment variables considered as controls, only age ($r_s = -0.15$ to -0.22 , all $p_s < 0.003$) and receipt of surgery since diagnosis (0 = no surgery, 1 = received surgery; $r_s = -0.12$ to 0.39 , all $p_s < 0.01$) were significantly correlated with the outcome variables and were thus considered as potential control variables. However, both age and receipt of surgery were correlated with recurrence status ($r = 0.14$, $p = 0.006$, and -0.76 , $p < 0.001$, respectively). Because our focus was on the role of recurrence status as a unique predictor, we chose to eliminate age and receipt of surgery from the analyses.

Primary Analyses

Time of assessment significantly predicted cancer-related stress ($\beta = -0.260$, $p < 0.001$), negative mood ($\beta = -0.147$, $p = 0.045$), physical quality of life ($\beta = 0.176$, $p = 0.013$), and mental health quality of life ($\beta = 0.267$, $p < 0.001$). Neither recurrence status nor the interaction of recurrence status and time predicted these outcomes. Thus, by four months all patients had

reduced cancer stress, reduced negative mood, improved mental quality of life, and poorer physical quality of life, regardless of recurrence status.

Recurrence status significantly predicted sexual satisfaction ($\beta = -0.246$, $p = 0.003$) and performance status ($\beta = -0.456$, $p < 0.001$). This relationship was such that sexual satisfaction and performance status were highest for initial diagnosis patients (SEX: $M = 4.4$, KPS: $M = 86$), middling for first recurrence patients (SEX: $M = 3.4$, KPS: $M = 75$), and lowest for second recurrence patients (SEX: $M = 3.0$, KPS: $M = 73$) (Figures 2 and 3). Neither time nor the interaction of recurrence status and time were significant. Thus, sexual satisfaction and performance status was progressively lower across groups .

Discussion

The present study is the first to examine physical and psychological responses to the diagnosis and treatment of a second recurrence of breast cancer. There are three central findings regarding differences in the trajectory of such symptoms between patients diagnosed with initial disease, or a first or second recurrence. First, although levels of stress, mood, and mental health quality of life improved over time as hypothesized, trajectories for sexual satisfaction and performance status were stable, and all patients demonstrated reduced physical health quality of life from baseline to four months. Second, no group differences were found for cancer stress, mood, or mental or physical quality of life. The only differences by recurrence status found were lower sexual satisfaction and lower nurse rated performance status. Third, the interaction of recurrence status and time did not significantly predict any of the outcomes of interest. These three findings each have significant theoretical and clinical implications.

For all patients there was no statistically significant change in sexual satisfaction or performance status from baseline to four months. Furthermore, all patients actually

demonstrated worse physical quality of life at four months compared to their baseline levels. This was contrary to our hypothesis that all patients would see reductions in symptoms from the time of diagnosis to the 4-month follow-up. The stability of performance status and the decrease in physical symptoms might be attributed to the adjuvant treatments that these individuals were receiving for their cancers at the 4-month follow-up time point. Although there were few differences between time points in receipt of radiation therapy or tamoxifen use, there were differences in receipt of chemotherapy. Compared to the baseline assessment, when 28.8% were receiving chemotherapy, 37.0% were receiving chemotherapy at the 4-month follow up. Although this was not a statistically significant difference, it might be clinically significant in its impact on physical symptoms among these patients.

A second notable finding from the present study was that patients with more recurrences had worse sexual satisfaction and lower performance status; however, recurrence status had no effect on stress, mood, or quality of life. Thus, our second hypothesis, that higher levels would be present with each successive recurrence diagnosis, was only partially supported. We believe that there are two possible explanations for this finding. First, it may speak to the resilience of patients. Second, it could merely reflect the lack of power inherent in our small sample size. Though the cell sizes for the initial diagnosis ($n = 90$) and first recurrence ($n = 108$) patients were reasonable, there were very few second recurrence diagnoses in this sample ($n=17$). Although this is typically of the cancer survivorship trajectory, as it is often difficult to determine a discrete period without cancer following a first recurrence, it may certainly affect our ability to find results in the present study.

Finally, there were no differences in symptom recovery over time based on recurrence status. All patients improved at similar rates, rejecting our hypothesis that initial diagnosis

patients would demonstrate the steepest symptom recovery, followed by first recurrence patients, and that second recurrence patients would have the slowest symptom recovery slope. The positive trajectory of psychological symptoms following cancer diagnosis is one that has been previously established in the psycho-oncology literature (Andersen et al., 2004; Yang et al., 2008). The present study adds to the literature by demonstrating that this upward slope is true of patients with a second recurrence as well.

In all, these findings certainly have implications for intervention research. Given the similarities in levels of stress, mood, and quality of life across samples of patients with varying recurrence statuses, existing interventions to reduce stress and enhance coping might be applicable for all newly diagnosed patients. However, there appear to be unique problem areas, specific to patients with recurrent cancer. Similar to treatment tailoring for individuals with cancer located at a specific disease site (Myers et al., 1999; Andersen et al., 2004; Northouse et al., 2007; Carpenter et al., in press), perhaps intervention developers and clinicians should also consider treatment tailoring for patients at different points along the cancer survivorship trajectory. Intervention alterations should be focused on the unique problem areas within a group.

The present study has strengths. Our sample is fairly unique, in that patients were followed over the course of several years. Thanks to our rigorous follow-up, we have confirmed the recurrence status for each participant within that time frame. Thus, we are very confident about the classification of our recurrence status groups. This allows us to look at the differences between women who never recurred, women who recurred once, and women who had a second recurrence, rather than examining women at one diagnostic time point who might recur in the future. In addition, the repeated measures nature of the data allows for us to examine not only

mean level of symptoms upon diagnosis, but also the change in symptoms over the course of the first few months afterwards. As mentioned above, our results also have implications for interventions within the context of recurrent cancer, speaking to the clinical needs of this unique and understudied population. Finally, to our knowledge this is the first study to examine psychological and physical responses to a second diagnosis of cancer recurrence and furthers our scant knowledge about the psychological processes involved in this sample.

Limitations must also be acknowledged. While our sample is unique in its composition, there were very few women with a second recurrence diagnosis, limiting our power to find statistically significant differences between groups. Additionally, the sample was predominantly Caucasian, educated, and with above-average income. The generalizability of the findings to other ethnic and minority groups or to the underserved is unknown. As socioeconomic disparities covary with cancer outcomes (American Cancer Society, 2014), the findings presented here may underestimate adverse effects of cancer diagnosis for the underserved.

In conclusion, repeated measures data from breast cancer patients recently diagnosed with initial disease, or first or second recurrence were compared. These results highlight the many similarities in physical and psychological outcomes in patients at all points along the cancer survivorship continuum. However, treatment tailoring may be effective to address the specific problem areas for patients of different diagnosis statuses. Further research is still needed in order to replicate these preliminary results; research on the unique experience of patients with recurrence cancer may lead to the development of more focused interventions to improve patients' physical and psychological quality of life.

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Table 1. *Sample (N = 215) sociodemographic, disease/prognostic, and treatment characteristics at baseline.*

Variable	Mean (SD) or N (%)			
	Total (N = 215)	Initial (n = 90)	1 st Recurrence (n = 108)	2 nd Recurrence (n = 17)
Sociodemographics				
Age (years)	53.5 (11.2)	51.3 (10.8)	55.0 (11.6)	55.3 (9.8)
Education (years)	14.5 (2.8)	14.3 (2.6)	14.6 (2.9)	14.9 (3.0)
Income (thousand dollars/year)	66.3 (74.2)	66.5 (91.6)	69.0 (59.9)	49.4 (34.7)
Race: Caucasian	193 (89.8%)	80 (89.9%)	98 (90.7%)	15 (88.2%)
Partner Status: Partnered	151 (70.2%)	65 (72.2%)	75 (69.4%)	11 (64.7%)
Extent of Disease				
Present Distant Metastases	87 (40.5%)	N/A	74 (68.5%)	13 (76.5%)
Months Since Current Diagnosis	8.4 (22.2)	2.1 (4.6)	14.2 (29.7)	2.9 (1.9)
Months Between Initial Diagnosis and 1 st Recurrence	N/A	N/A	55.5 (61.9)	37.8 (30.0)
Months Between 1 st Recurrence and 2 nd Recurrence	N/A	N/A	N/A	25.3 (17.5)
Treatment(s) Received Since Current Diagnosis				
None	18 (8.4%)	0 (0.0%)	17 (15.7%)	1 (5.9%)
Surgery	120 (55.8%)	90 (100.0%)	28 (25.9%)	2 (11.8%)
Chemotherapy	62 (28.8%)	2 (2.2%)	54 (50.0%)	6 (35.3%)
Radiation Therapy	69 (32.1%)	48 (53.3%)	20 (18.5%)	1 (5.9%)
Hormonal Therapy	115 (53.5%)	74 (82.2%)	28 (25.9%)	13 (76.5%)

Table 2. *Summary statistics for measures of stress, mood, quality of life, sexual satisfaction, and performance status.*

Measure	Total (N = 215)		Initial (n = 90)		1 st Recurrence (n = 108)		2 nd Recurrence (n = 17)	
	Mean (SD)	Observed Range	Mean (SD)	Observed Range	Mean (SD)	Observed Range	Mean (SD)	Observed Range
Cancer Stress (IES)	24.8 (14.8)	0 – 59	25.7 (13.8)	0 – 59	24.5 (15.6)	0 – 58	21.0 (15.3)	0 – 45
Total Mood Disturbance (POMS)	25.6 (28.3)	-26 – 112	30.4 (32.3)	-26 – 112	21.0 (23.5)	-18 – 98	28.2 (29.2)	-14 – 95
SF-36: Mental Component Summary	44.7 (10.6)	20.3 – 67.1	43.9 (10.6)	23.1 – 62.3	45.2 (10.8)	20.3 – 67.1	45.5 (10.7)	26.6 – 59.9
SF-36: Physical Component Summary	38.1 (10.2)	12.1 – 68.0	40.7 (8.9)	18.4 – 68.0	36.5 (10.5)	12.7 – 62.9	34.1 (12.1)	12.1 – 51.9
Sexual Satisfaction (SEX)	3.9 (2.1)	0 – 8	4.4 (2.0)	0 – 8	3.4 (2.1)	0 – 8	3.0 (2.2)	0 – 6
Functional Status (KPS)	80.0 (10.7)	40 – 100	86.4 (6.9)	70 – 100	75.5 (10.1)	40 – 90	72.5 (12.9)	50 – 90

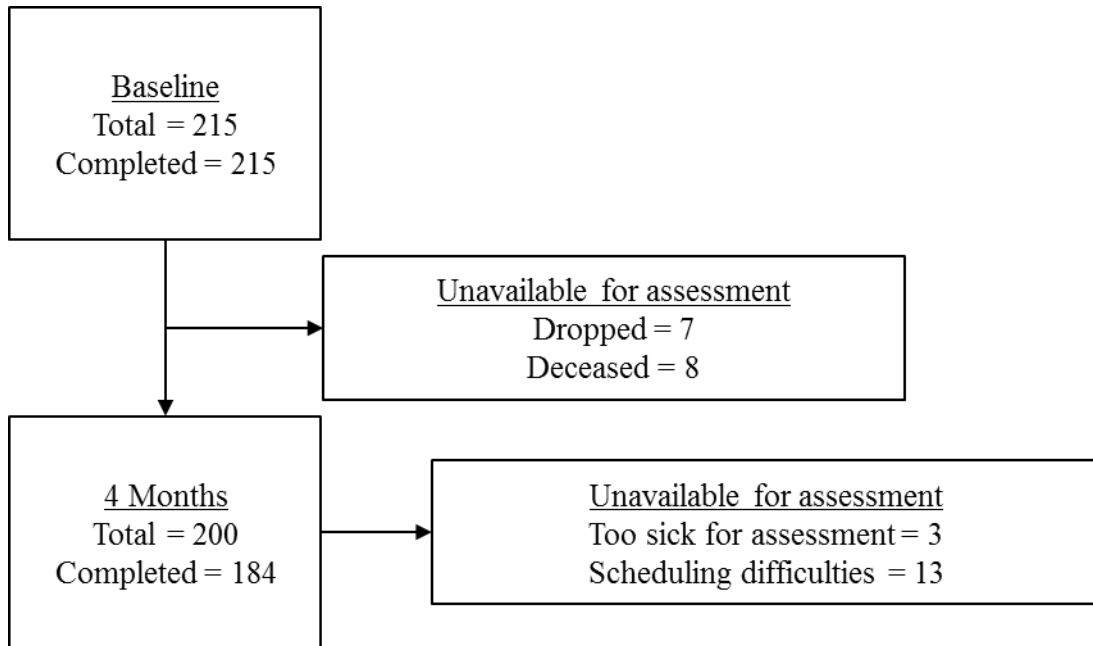


Figure 1. Study flow.

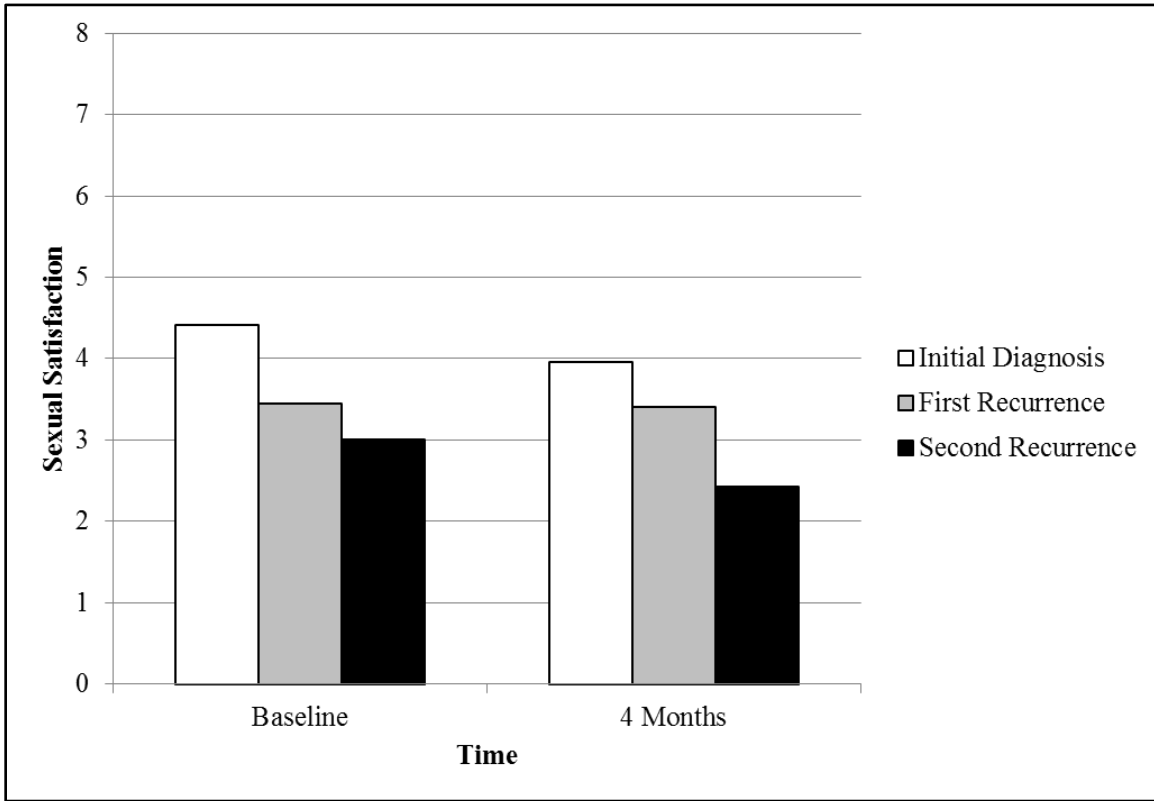


Figure 2. Mean levels of Sexual Satisfaction (SEX) by diagnostic status.

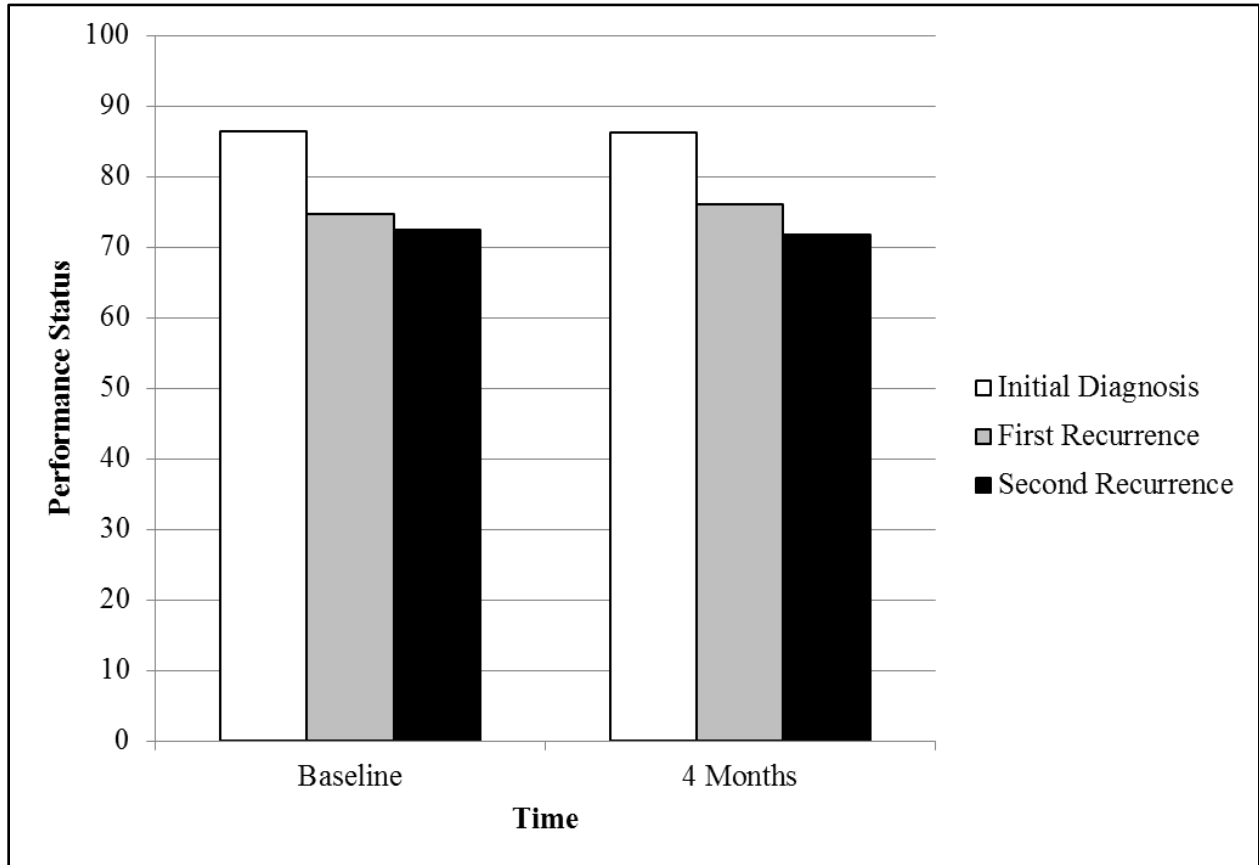


Figure 2. Mean levels of Karnofsky Performance Scale (KPS) by diagnostic status.