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Symptom experiences in post-treatment cancer survivors: Associations with acceptance and commitment therapy constructs

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Abstract

Purpose—Acceptance and commitment therapy (ACT) has improved symptom and quality-of-life outcomes in pilot research with post-treatment cancer survivors. To further test the ACT model, the present study examined relationships between ACT constructs and subgroups of post-treatment survivors based on the severity of common symptoms.

Methods—Survivors who had completed primary treatment for stage I or II cancer (N=203) participated in this one-time survey. Latent class analysis (LCA) was used to identify subgroups of survivors based on the severity of fatigue, sleep disturbance, pain, anxiety, and depressive symptoms. Multinomial logistic regressions employing Vermunt's 3-step approach were used to examine ACT constructs (e.g., mindfulness, acceptance, values progress) as correlates of survivor subgroups based on symptoms.

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Author contributions:

Shelley A. Johns and Catherine E. Mosher contributed to the study conception and design. Data collection was performed by Kelly Chinh, and data analyses were performed by Ellen Kreuger and Ashley B. Lewson. The first draft of the manuscript was written by Ashley B. Lewson and Catherine E. Mosher, and all authors reviewed, edited, and approved the final manuscript.

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

Declarations

Availability of data and material: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability: not applicable

Ethics approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Indiana University Institutional Review Board.

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

Results—LCA showed three survivor classes: (1) mild to moderate levels of all symptoms except for normal pain intensity, (2) mild anxiety, moderate fatigue, and normal levels of all other symptoms, and (3) normal levels of all symptoms. Lower mindfulness, acceptance, and values progress and higher cognitive fusion, psychological inflexibility, and values obstruction were associated with a greater likelihood of being in class 1 or 2 than class 3.

Conclusion—Findings are consistent with the ACT model. Survivors with greater symptom burden reported greater withdrawal from personally meaningful activities and less acceptance of their cancer diagnosis and internal experiences (e.g., thoughts, feelings, symptoms). Findings provide strong justification for further testing of ACT to reduce symptom-related suffering in cancer survivors.

Keywords

latent class analysis; symptoms; cancer survivors; acceptance and commitment therapy; mindfulness; psychological flexibility

Introduction

Many cancer survivors experience persistent, debilitating symptoms for months or years after cancer treatment [1]. Common symptoms include fatigue, sleep disturbance, pain, anxiety, and depressive symptoms. These symptoms tend to co-occur, with survivors showing heterogeneous clustering and severity of symptoms [2, 3]. Survivors' heightened symptoms have a substantial negative impact on their daily activities, functional status, and quality of life [4–6].

There is growing interest in mindfulness and acceptance-based interventions for cancer symptom management. Rather than focusing on symptom reduction, these interventions, such as acceptance and commitment therapy (ACT), aim to minimize the negative impact of symptoms on functioning [7]. The goal of ACT is to increase psychological flexibility so that internal experiences (e.g., symptoms, thoughts, feelings) do not impede engagement in meaningful activities. Psychological flexibility is comprised of commitment and behavior change processes as well as mindfulness and acceptance-based processes. Commitment and behavior change processes involve identifying and behaving in accordance with one's values, or personal guiding principles. Mindfulness and acceptance-based processes involve intentional and nonjudgmental attention to one's thoughts, feelings, and experiences of the present moment [8]. Thus, from an ACT perspective, cancer survivors with higher physical and psychological symptom interference are expected to show greater psychological inflexibility. This includes processes such as obstruction of value-based action and cognitive fusion, or allowing one's behavior to be overly influenced by one's thoughts [8].

Pilot studies of ACT have produced promising results in cancer populations, including improved emotional well-being, psychological flexibility, and quality of life [9, 10]. In a pilot randomized controlled trial (RCT) with post-treatment survivors, both ACT and Behavioral Activation groups were superior to a waitlist control group and showed comparable post-intervention reductions in anxiety and depressive symptoms [11]. Additionally, the ACT group showed greater reductions in avoidance/rumination and social

impairment than the other two groups. Another pilot RCT found that compared to survivorship education and enhanced usual care, group-based ACT was effective in reducing breast cancer survivors' fear of cancer recurrence, general anxiety, and depressive symptoms at 6-month follow-up [12]. Both studies demonstrated moderate to large effects of ACT on psychological outcomes [11, 12].

Although ACT has shown promise in a few pilot studies with post-treatment cancer survivors, additional research is necessary to establish links between ACT constructs and common cancer-related symptoms before investing resources in large-scale trials. To date, a few studies have associated greater psychological flexibility and mindfulness with reduced distress in post-treatment survivors [13–15], and one study linked greater mindfulness to reduced physical symptoms in breast cancer survivors [14]. Building on this limited literature, the present study examined relationships between a range of ACT constructs and subgroups of cancer survivors based on symptom levels. Latent class analysis was used to group post-treatment solid-tumor survivors by level of fatigue, sleep disturbance, pain, anxiety, and depressive symptoms. Based on the ACT model [8] and prior literature [14, 16, 17], we hypothesized that survivor subgroups with higher symptom levels would have lower mindfulness, acceptance, and values progress and higher cognitive fusion, psychological inflexibility, and values obstruction compared to those with lower symptom levels.

Methods

Participants and procedures

Study procedures were approved by the Indiana University Institutional Review Board. Recruitment took place from February to October of 2018. Survivors were recruited from a public hospital, an academic medical center, and an affiliated clinic in the midwestern United States. Potential participants were identified through the Indiana University Health and Eskenazi Health Cancer Registries, and eligibility was confirmed through medical chart review. Patients were eligible if they 1) had been diagnosed with breast, prostate, gastrointestinal (GI), or lung cancer; 2) had completed primary treatment for stage I or II cancer at least 6 months ago (ongoing endocrine therapy was allowed) or were at least 3 weeks post-diagnosis of stage IV cancer; 3) were at least 18 years of age; and 4) were fluent in English. Survivors were excluded if they made 3 or more errors on a validated 6-item cognitive screener [18] or could not provide informed consent.

Of the 701 patients who were mailed a study introductory letter and consent form, 592 (84%) were reached via phone. Of those reached, 99 (17%) refused to participate and 29 (5%) were ineligible or deceased. Common reasons for refusal included a lack of interest in the study and time constraints. Of the 464 consenting participants, 430 (93%) completed REDCap or paper surveys. Only participants who had received treatment for stage I or II cancer (n=203) were included in the current analyses, as their symptom profiles were expected to differ from those with advanced cancer [19]. Our findings on adults with advanced cancer will be published in a separate report.

Measures

Demographic and medical information—Demographic and medical information was retrieved from survivors' medical records including age, gender, cancer type and stage, date of diagnosis, and cancer treatments. Participants reported their race/ethnicity, marital status, education, income level, and employment status. Participants also indicated whether they had been diagnosed with or received treatment for 12 common medical comorbidities within the last three years, such as hypertension and diabetes [20].

Physical and psychological symptoms—Patient-Reported Outcomes Measurement Information System (PROMIS) measures were used to assess the severity of psychological and physical symptoms during the past week. These NIH-funded measures have undergone rigorous psychometric testing [21], and evidence supports their reliability and validity in cancer survivors [19, 22]. The severity of anxiety and depressive symptoms was assessed with the 4-item PROMIS short form anxiety and depression measures [23]. Short form PROMIS measures were also used to assess the severity of physical symptoms, including 4-item measures of sleep disturbance and fatigue and a 3-item measure of pain intensity [21, 24]. T-scores <50 for fatigue measures and T-scores <55 for sleep disturbance, pain, anxiety, and depression measures are considered normal based on published threshold scores [25, 26].

Cognitive fusion—The 7-item Cognitive Fusion Questionnaire (CFQ) was used to assess participants' tendency to allow their behavior to be overly influenced by their thoughts [27]. The CFQ has demonstrated strong internal consistency, test-retest reliability, and ability to predict anxiety in cancer survivors [27]. Participants rated how true each statement was for them on a 7-point scale ranging from "never true" to "always true." A sample item is "I struggle with my thoughts."

Mindfulness—Mindfulness was assessed with the Act with Awareness, Nonjudging, and Nonreactivity subscales of the Five Facet Mindfulness Questionnaire-Short Form (FFMQ-SF) [28]. In research with cancer survivors, these subscales have demonstrated strong internal consistency [29] and have been related to health outcomes [30, 31]. For the current analysis, we combined the 5-item Acting with Awareness and Nonjudging subscales to assess mindfulness, as they were highly correlated in our sample (r=.61, p<.01), whereas Nonreactivity showed small correlations with these subscales. Participants rated each statement on a 5-point scale ranging from "never or very rarely true" to "very often or always true." A sample item is "I make judgments about whether my thoughts are good or bad."

Acceptance—Acceptance of cancer was measured using the Peace, Equanimity, and Acceptance in the Cancer Experience scale (PEACE) [32]. The current analysis focused on the 5-item Peaceful Acceptance subscale. This subscale has shown good internal consistency (α=0.78) and criterion validity in adults with cancer [32]. Items are asked in question form (e.g., "To what extent are you able to accept your diagnosis of cancer?") and answered on a 4-point scale ranging from "not at all" to "to a large extent."

Psychological inflexibility—The 7-item Acceptance and Action Questionnaire-II (AAQ-II) was used to measure psychological inflexibility, or attempts to avoid unwanted thoughts and emotions even when doing so contributes to behaviors that are not in line with personal values. This measure has shown good discriminate validity and test-retest reliability [33]. Additionally, in research on the AAQ-II in adults with cancer, alphas have ranged from 0.78 to 0.87 [34]. Participants were asked to rate how true each statement was for them on a 7-point scale ranging from “never true” to “always true.” A sample item is “I worry about not being able to control my worries and feelings.”

Value-based living—Value-based living, or living in accordance with one’s personal principles, was assessed with the 10-item Valuing Questionnaire (VQ) [35]. The obstruction subscale contains five negatively worded items (e.g., “Difficult thoughts, feelings or memories got in the way of what I really wanted to do”), whereas the progress subscale contains five positively worded items (e.g., “I was proud about how I lived my life”). Both VQ subscales have shown good internal consistency (obstruction, α=0.79; progress, α=0.81) and concurrent validity with measures of ACT constructs in healthy samples [35]. Both have also been used with adults with cancer [36]. Participants rated how true each item was for them on a 7-point scale ranging from “not true at all” to “completely true.”

Analysis—Descriptive statistics were computed for demographic and medical characteristics and main study variables, and intercorrelations were computed between physical and psychological symptoms and ACT variables using the Statistical Package for the Social Sciences, Version 25.0 (SPSS). Then a latent class analysis was conducted in Mplus, Version 8 to group survivors based on fatigue, sleep disturbance, pain intensity, anxiety, and depressive symptoms. After six class solutions were tested iteratively, model fit indices (e.g., information criterion and likelihood ratio tests) and conceptually meaningful interpretability were assessed to determine the final number of survivor subgroups [37]. Lower values for information criterion [38], such as the Bayesian Information Criterion (BIC) and Akaike Information Criterion (AIC), and statistical significance (p<.05) of the Vuong-Lo-Mendell-Rubin likelihood ratio test (VLMR LRT) [39] indicate better model fit. Entropy above .80 also indicates a good-fitting model [40, 41]. Differences in demographic and medical characteristics between classes were assessed using chi- square tests, one-way ANOVAs, and Kruskal-Wallis tests. P values <.01 were considered statistically significant. Finally, multinomial logistic regressions employing Vermunt’s 3-step approach [42] were used to examine ACT variables as correlates of survivor subgroups based on symptoms. P values <.01 were considered statistically significant due to the number of regression analyses.

Results

Preliminary analyses

Sample characteristics are presented in Table 1. The majority of participants were non-Hispanic White and married or partnered with an average age of 63 years. The sample had about equal numbers of men and women and a wide range of education and income levels. Each cancer type (breast, prostate, GI, and lung) and stage was approximately evenly

represented in the sample, and the average time since diagnosis was 3.5 years at the time of survey completion.

Intercorrelations, descriptive statistics, and Cronbach's alphas for main study variables are presented in Table 2. Significant negative correlations were found between all five symptoms and the ACT variables of mindfulness, acceptance, and values progress, except for a non-significant association between pain intensity and values progress. Additionally, all symptoms showed significant positive correlations with ACT variables related to psychopathology, including cognitive fusion, psychological inflexibility, and values obstruction. All measures had good to excellent internal consistency reliability (α range = 0.82–0.95).

Primary analyses

A latent class analysis was conducted to group participants into classes based on the severity of fatigue, sleep disturbance, pain intensity, anxiety, and depressive symptoms. Anxiety and depression were allowed to covary in this analysis. Solutions ranging from one to six classes were tested iteratively. The 3-class solution fit the data significantly better than the 2-class solution (VLMR $p<.05$, entropy = 0.95), with enhanced interpretability that was conceptually meaningful. Although model fit indices (i.e., BIC and AIC) favored the 4-class solution, class sizes and interpretability were markedly reduced using this model. Model fit indices are presented in Table 3. Thus, the 3-class solution was selected due to conceptually meaningful interpretability, adequate class sizes, and good class separation. Class 1 ($n=29$) had mild to moderate levels of all symptoms except for normal pain intensity. Class 2 ($n=69$) had mild anxiety, moderate fatigue, and normal levels of all other symptoms. Class 3 ($n=105$) was characterized by normal levels of all symptoms [25]. Of the demographic and medical characteristics listed in Table 1, only being married or partnered was significantly associated with class, $\chi^2(2, N=203)=12.88$, $p=.002$. Descriptive statistics for symptoms and ACT variables by participant class are presented in Table 4.

Multinomial logistic regressions found that ACT variables were related to patient classes based on symptom severity (see Table 5). Lower mindfulness, acceptance, and values progress and higher cognitive fusion, psychological inflexibility, and values obstruction were associated with a higher likelihood of being in class 1 or 2 compared to class 3.

Discussion

This study identified subgroups of post-treatment, solid-tumor survivors based on levels of common symptoms and their associations with ACT constructs. Three subgroups of survivors were identified: those with mild to moderate levels of all symptoms except for normal pain intensity; those with mild anxiety, moderate fatigue, and normal levels of all other symptoms; and those with normal levels of all symptoms. Prior research has also found heterogeneity with respect to the clustering and severity of survivors' symptoms [2, 3]. In the current study, compared to survivors with normal levels of all symptoms, the other survivor subgroups displayed lower mindfulness, acceptance, and values progress as well as higher cognitive fusion, psychological inflexibility, and values obstruction. Findings are consistent with the ACT model [8] and suggest that post-treatment survivors with higher

symptom burden have greater difficulty accepting their cancer diagnosis and internal, present-moment experiences (e.g., thoughts, feelings, symptoms). Results also suggest that survivors with greater symptom burden may be more likely to withdraw from activities consistent with personal values.

One prior study with disease-free breast cancer survivors found that greater psychological inflexibility, or avoidance of unwanted experiences, was associated with higher levels of distress [13], and other studies have found this association in patients of mixed cancer types and stages [7, 43]. Our results extend this work by correlating this avoidance with a range of physical and psychological symptoms in post-treatment survivors. One potential explanation for these findings is that survivors may cope with long-term treatment side effects by attempting to avoid difficult thoughts, feelings, and bodily sensations. Additionally, attempts to avoid symptoms may increase their severity, as survivors may not seek appropriate care or may engage in ineffective methods of symptom control (e.g., avoiding social activities to conserve energy). It is also possible that an unmeasured third factor (e.g., emotional reactivity) may underlie symptom perceptions and psychological inflexibility.

This study also examined mindfulness and acceptance processes and commitment and behavior change processes that comprise psychological flexibility. Increased mindfulness has been associated with lower physical and psychological symptoms in breast cancer survivors [14] and less distress in survivors of various cancer types [7, 15, 44]. This study found that higher levels of mindfulness facets—acting with awareness and nonjudging—were associated with reduced physical and psychological symptoms during the post-treatment period. One explanation is that perceived symptom burden may decrease if survivors give full attention to activities in the present moment. Additionally, a non-judgmental stance may interrupt maladaptive reactions to symptoms, such as rumination and catastrophizing. Relatedly, in our study, greater cognitive fusion, or being overly entangled with one's thoughts, was correlated with higher symptom levels, whereas greater acceptance of cancer was correlated with lower symptom levels. While an accepting attitude towards cancer has been repeatedly associated with less distress [45], cognitive fusion has rarely been studied in cancer, with one survey linking it to greater distress in a heterogeneous sample of cancer survivors [27]. Commitment and behavior change processes, or value-based actions, have also received limited research attention in cancer [36, 43]. Our findings suggest that even mild to moderate symptoms in survivors are correlated with perceptions of limited progress in pursuing meaningful activities.

Limitations of this study should be noted. Although this sample was diverse in terms of gender, socioeconomic status, and cancer type, 76% of participants identified as non-Hispanic White. Future studies should examine the generalizability of these findings to racially and ethnically diverse populations. Due to the cross-sectional design, temporal relationships between ACT constructs and symptoms could not be determined. Longitudinal designs could elucidate potentially bidirectional relationships between ACT constructs and symptoms. Additionally, future studies could include other ACT processes such as self as context. Finally, because of the exploratory nature of latent class analysis, findings warrant replication.

Conclusion

Many cancer survivors experience persistent symptoms long after treatment is completed [1]. Our results suggest that symptoms may interfere with purposeful attention to the present moment, acceptance of one's experiences, and living according to personal values. Alternatively, survivors who maintain an open, accepting posture toward present-moment experiences while pursuing meaningful activities may perceive less symptom burden. This research and ACT pilot trials [11, 12] provide strong support for large-scale investigation of ACT for reducing symptom interference with functioning in post-treatment survivors. Our results also point to potential treatment targets in ACT, such as mindfulness and value-based action, that may be assessed as mediators of ACT's effect on symptom interference in future trials. Indeed, interventions emphasizing mindfulness meditation have significantly reduced fatigue in cancer survivors, although more research is needed to determine their long-term efficacy (Johns et al., under review). If found to be efficacious, ACT and other mindfulness-based interventions could be readily disseminated to clinicians and fulfill an unmet need in the comprehensive care of cancer survivors.

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Table 1.

Sample characteristics ($N = 203$)

Characteristic	
Age, years	
Mean (SD)	63.16 (10.25)
Range	33–89
Gender, *n* (%)	
Male	97 (47.78)
Female	106 (52.22)
Race/ethnicity, *n* (%)	
Non-Hispanic White	154 (75.86)
Black/African American	27 (13.30)
Hispanic or Latino/a	8 (3.94)
Other[a]	14 (6.90)
Married or partnered, *n* (%)	140 (68.97)
Employed, *n* (%)	92 (45.32)
Education, *n* (%)	
No college	52 (25.62)
Some college	65 (32.02)
Graduated College	86 (42.36)
Household income, *n* (%)	
$0–$21,000	31 (15.27)
$21,000–$39,999	32 (15.76)
$40,000–$65,999	39 (19.21)
$66,000–$105,999	45 (22.17)
$106,000 +	53 (26.11)
Missing	3 (1.48)
Cancer type, *n* (%)	
Breast	51 (25.12)
Prostate	50 (24.63)
Gastrointestinal	51 (25.12)
Lung	51 (25.12)
Cancer stage, *n* (%)	
Stage I	97 (47.78)
Stage II	106 (52.22)
Time since diagnosis, years	
Mean (SD)	3.50 (2.98)
Range	.62–18.93
Missing	1 (0.49)

[a]Asian American, Pacific Islander, Native American, and other.

Table 2.

Descriptive statistics and intercorrelations for main study variables

		1	2	3	4	5	6	7	8	9	10	11
1	Fatigue											
2	Sleep disturbance	.65**										
3	Pain	.42**	.34**									
4	Anxiety	.49**	.41**	.32**								
5	Depressive symptoms	.47**	.41**	.31**	.81**							
6	Cognitive fusion	.37**	.42**	.17*	.64**	.62**						
7	Mindfulness	−.32**	−.37**	−.16*	−.54**	−.55**	−.68**					
8	Acceptance	−.31**	−.34**	−.15*	−.49**	−.52**	−.39**	.33**				
9	Psychological inflexibility	.35**	.38**	.28**	.66**	.67**	.78**	−.60**	−.46**			
10	Value obstruction	.37**	.39**	.22**	.63**	.61**	.70**	−.69**	−.40**	.68**		
11	Value progress	−.24**	−.19**	−.12	−.36**	−.42**	−.51**	.29**	.36**	−.45**	−.44**	
	Mean	51.94	50.38	40.94	50.17	48.48	17.64	39.84	16.76	15.04	6.73	20.82
	Standard deviation	9.88	8.66	10.61	9.41	8.76	9.11	7.84	3.48	8.87	6.42	6.61
	Cronbach's α	.94	.89	.92	.91	.92	.94	.88	.85	.95	.82	.83

* $p<.05$.

** $p<.01$.

Table 3.

Latent class analysis model fit indices

Classes	LL[a]	Entropy	BIC[b]	ssBIC[c]	AIC[d]	VLMR LRT[e]
1	−3597.81	--	7254.06	7219.21	7217.62	--
2	−3511.56	0.738	7113.45	7059.59	7057.12	0.0001
3[f]	−3469.68	0.949	7061.56	6988.69	6985.36	0.0321
4	−3408.17	0.980	6970.43	6878.55	6874.35	0.0167
5	−3360.29	0.986	6906.55	6795.66	6790.59	0.0237
6	−3326.66	0.938	6871.16	6741.26	6735.32	0.0178

[a] LL = Log-likelihood

[b] BIC = Bayesian Information Criterion

[c] ssBIC = Sample size adjusted BIC

[d] AIC = Akaike's Information Criterion

[e] VLMR LRT = Vuong–Lo–Mendell–Rubin likelihood ratio test

[f] The 3 class solution was chosen for interpretability, good entropy, and class size.

Table 4.

Descriptive statistics for symptoms and ACT[a] variables by survivor class

	Class 1 (*n*=29)[b]		Class 2 (*n*=69)[c]		Class 3 (*n*=105)[d]	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Symptom						
Fatigue	61.40	5.58	54.78	8.42	47.55	9.24
Sleep disturbance	58.25	6.23	51.59	7.68	47.49	8.38
Pain	47.78	10.89	42.64	10.20	38.00	9.79
Anxiety	62.13	6.10	55.32	6.45	43.47	5.67
Depressive symptoms	63.72	3.65	53.44	3.47	41.00	0.02
ACT variable						
Cognitive fusion	27.44	10.68	20.06	8.77	13.35	5.56
Mindfulness	33.18	7.16	37.22	7.41	43.37	6.34
Acceptance	14.31	3.84	15.49	3.66	18.28	2.38
Psychological inflexibility	25.25	10.53	17.88	8.66	10.40	4.32
Values obstruction	14.41	7.18	7.93	5.19	3.83	4.75
Values progress	16.00	6.18	19.83	6.80	22.82	5.75

[a] ACT = Acceptance and Commitment Therapy.

[b] Class 1 had mild to moderate levels of all symptoms with the exception of normal pain intensity.

[c] Class 2 had mild anxiety, moderate fatigue, and normal levels of all other symptoms.

[d] Class 3 had normal levels of all symptoms.

Table 5.

Comparisons of ACT[a] variables by survivor class using class 3 as the reference

	Class 1[b] v 3[d]		Class 2[c] v 3[d]	
	B (SE)	**OR (99% CI)**	**B (SE)**	**OR (99% CI)**
Cognitive fusion	0.22*** (0.04)	1.25 (1.14, 1.36)	0.13*** (0.03)	1.14 (1.07, 1.22)
Mindfulness	−0.20*** (0.04)	0.82 (0.74, 0.90)	−0.13*** (0.03)	0.88 (0.82, 0.94)
Acceptance	−0.40*** (0.08)	0.67 (0.55, 0.81)	−0.32*** (0.06)	0.73 (0.62, 0.86)
Psychological inflexibility	0.29*** (0.04)	1.33 (1.19, 1.49)	0.21*** (0.04)	1.23 (1.12, 1.35)
Values obstruction	0.34*** (0.06)	1.40 (1.21, 1.63)	0.15*** (0.03)	1.16 (1.07, 1.26)
Values progress	−0.17*** (0.04)	0.85 (0.77, 0.93)	−0.08** (0.03)	0.92 (0.86, 0.99)

[a] ACT = Acceptance and Commitment Therapy.

[b] Class 1 (n=29) had mild to moderate levels of all symptoms with the exception of normal pain intensity.

[c] Class 2 (n=69) had mild anxiety, moderate fatigue, and normal levels of all other symptoms.

[d] Class 3 (n=105) had normal levels of all symptoms.

** p<.01.

*** p<.001.