

Contains Video <sup>1</sup>

## Improving Psychological Adjustment Among Late-Stage Ovarian Cancer Patients: Examining the Role of Avoidance in Treatment

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*Data suggest that individuals dealing with a cancer diagnosis are less likely to suffer from depression, anxiety, and psychological distress when they cope with their condition from a stance of emotional and cognitive acceptance (e.g. Dunkel, et al., 1992; Stanton, et al., 2000). Although traditional CBT often includes some acceptance-oriented elements, recent variants of CBT, such as Acceptance and Commitment Therapy (ACT), have acceptance as a central focus. ACT targets emotional distress directly through acceptance of difficult thoughts and emotions. The current study is a preliminary comparison of ACT and treatment as usual (TAU) in the treatment of emotional distress among women with late-stage ovarian cancer. Forty-seven women diagnosed with Stage III or IV ovarian cancer were randomly assigned to one of two treatment conditions. Treatment consisted of 12 face-to-face meetings with a therapist, each following a TAU or ACT protocol. Results indicate that both groups showed improved mood and quality of life following the intervention. The ACT group showed significantly greater improvements compared to the TAU group. Furthermore, mediation analyses indicate that the effects of treatment were mediated by cognitive avoidance. Although the study is limited by the implementation of treatment in both conditions by a single therapist, the TAU group showed improvements that were consistent with effect sizes available in the literature, suggesting that the intervention was a credible and effective control treatment. These findings provide preliminary support for the use of ACT in ovarian cancer populations. Further work is needed to investigate the effectiveness in other oncology populations as well as investigate potential patient characteristics which may interact with these interventions.*

A substantial body of evidence suggests that psychological interventions have at least some positive impact on quality of life and experience of emotional distress among individuals diagnosed with cancer (Helgeson, 2005). However, work remains to be done. For example, few studies of the efficacy of psychological interventions have included participants who have late-stage cancers (Helgeson). In addition, few trials examine direct comparisons of mainstream treatment approaches. Finally, analysis of the moderators and mediators of treatment effects remain unclear in this area.

There are, however, a few consistent findings in the existing psycho-oncology literature. First, research indicates

that individuals with cancer who engage in avoidance-based coping are more likely to experience psychological distress as compared to those who do not actively engage in psychological and behavioral avoidance of cancer-related content (e.g., Dunkel-Schetter, Feinstein, Taylor, & Falke, 1992; Stanton et al., 2000).

Second, it has been consistently reported that individuals who score higher on measures of emotional acceptance have less psychological distress throughout the cancer experience. For example, among individuals with early-stage breast cancer, those who report greater acceptance of their diagnosis and treatment tend to report less distress prior to surgical treatment, after surgery, and at 3, 6, and 12 months following the initial treatment (Carver et al., 1993). Also, those who cope with their diagnosis through cognitive and emotional acceptance have been shown to have a higher reported quality of life following completion of treatment for early-stage breast cancer and continuing through follow-up data collections as compared to women who utilize other forms of coping reactions (Stanton et al., 2000). Similar findings have also been

<sup>1</sup> Video patients/clients are portrayed by actors.

*Keywords:* ACT; cancer; distress; avoidance

1077-7229/11/xxx-xxx\$1.00/0

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reported among gynecological cancer patient populations (Costanzo, Bradley, & Rose, 2005).

Despite research suggesting that acceptance is important for cancer patients, few psychological interventions for individuals with cancer purposefully target avoidance/acceptance processes directly. Reviews of treatments indicate that the majority of interventions focus on relaxation/anxiety reduction techniques, problem solving, psychoeducation, and some cognitive-behavioral strategies (Helgeson, 2005; Newell, Sanson-Fisher, & Savolainen, 2002; Sheard & Maguire, 1999). One potential treatment approach that does explicitly target avoidance by increasing experiential acceptance is Acceptance and Commitment Therapy (ACT; Hayes, Strosahl, & Wilson, 1999).

The current study, conducted among women with late-stage ovarian cancer, was designed to gather preliminary data on the efficacy of ACT and to compare its effects to that of a treatment as usual condition (TAU), which consisted of commonly used cognitive and behavioral components. This particular cancer patient population was chosen due to the high level of psychological distress reported by women during their experience of the diagnosis (e.g., Hipkins, Tarrier, & Jayson, 2004; Zabora, Brintzenhofesoc, Curbow, Hooker, & Piantadosi, 2001). In addition, few psychosocial interventions of any sort have been investigated among individuals with this form of cancer (Manne et al., 2007). Finally, because of the poor prognosis, the potential for increasing levels of experiential avoidance seems likely as illness, disability, and mortality become more prominent.

Ovarian cancer is often a deadly diagnosis. Due to a lack of clear symptoms and screening, most women (70% to 80%) do not receive an early diagnosis and thus have a poor prognosis, with estimated chance of 5-year survival at 30% (National Ovarian Cancer Coalition, 2010). Treatment typically involves debulking surgery, followed by platinum-based chemotherapy. Though initial remission may occur in response to treatment, recurrence rates are quite high (85% to 90%; Johns Hopkins Pathology, 2010). Multiple rounds of chemotherapies follow, along with unpleasant side-effects, including hair loss, pain, intestinal blockages, ascites, neuropathy, and cognitive decline. Because there is no cure for recurrences, treatment eventually becomes ineffective, and/or patients decide they no longer want to endure the effects of treatment and choose to stop chemotherapy. On average, women survive 12 to 18 months following a recurrence, with fewer than 1 in 10 surviving more than 5 years (Cancer Connect, 2010). Given this situation, it is not surprising that over 50% of women with ovarian cancer have significant levels of depression, anxiety, and general psychological distress (Zabora, et al., 2001).

Patients with ovarian cancer are similar to other patients in that they often engage in avoidance coping methods (Power, Brown, & Ritzo, 2008), which are traditionally associated with psychological distress. Although a few

studies have examined psychosocial interventions to treat distress in this population (see Manne et al., 2007, for review), none have specifically aimed to reduce the impact of experiential avoidance upon overall psychological functioning in the manner typically delivered in ACT interventions.

Manne et al. (2007) compared a “communication-enhancing intervention (CCI)” to “supportive counseling” in treating depressive symptoms among women with gynecological cancers. The CCI condition included many common techniques, including distraction, problem solving and cognitive restructuring. Both interventions offered empathic emotional support and both were found to be superior to usual care in terms of psychological outcomes. However, neither targeted the role of experiential avoidance in distress. To date, no studies have evaluated the utility of ACT in treating distress in individuals with ovarian cancer, and none have directly compared ACT to a TAU condition in this population.

For this study, we developed a TAU protocol, incorporating common techniques such as relaxation training, problem solving, and the five-column approach to cognitive restructuring. We also developed an ACT protocol, incorporating the key psychological processes typically targeted by ACT interventions, such as mindfulness, acceptance, and values. Metaphors and therapeutic strategies, such as creative hopelessness and control as the problem, were included to set up the treatment rationale (see Hayes et al., 1999). Both protocols consisted of 12 face-to-face therapy sessions. Outcome variables of psychological distress and quality of life, as well as psychological process measures of coping and emotional control, were obtained at four time points.

We hypothesized that the two approaches to treatment would result in significant differences in avoidance, emotional control, and acceptance, given these are the processes explicitly targeted by an ACT intervention. Specifically, we expected to find that when compared to TAU, the ACT group would show greater increases in acceptance, along with greater decreases in avoidance and emotional control over time.

In terms of outcomes, we predicted that both interventions would be beneficial and associated with decreased psychological distress over time. However, because the ACT intervention directly targeted avoidance and acceptance, it was hypothesized that this group would show improved quality of life as compared to the TAU group and equivalent improvement in secondary outcomes of depression and anxiety. The later prediction is consistent with recent findings with anxious and depressed populations testing ACT and cognitive-behavioral interventions (Foreman, Herbert, Moitra, Yeomans, & Geller, 2007). Overall, such findings would be consistent with literature indicating that greater acceptance is associated with less psychological distress in various cancer populations. Our final hypothesis

concerned the mechanisms of change. We hypothesized that avoidance (mental disengagement) would serve to mediate differences in psychological distress between the TAU and ACT interventions. This would be similar to results reported by Zettle and Hayes (1986) in which similar outcomes were reported for cognitive therapy and ACT, while mechanisms of change differed.

## Methods

### Participants

Fifty-seven women with Stage III or IV ovarian cancer were invited to participate in the study. Ten declined to participate, either citing travel as an issue, as they were receiving their primary medical treatment elsewhere ( $n=6$ ), or a lack of interest ( $n=4$ ). Of the 47 participants, 31 completed the full treatment protocol and data collection. Twelve participants passed away during the course of the intervention protocol, and 4 transferred to home-based hospice care and were unable to continue. The study schema is detailed in Figure 1.

The majority of participants self-identified as Caucasian (92%), with the remainder either African American (7%) or unreported (1%). Most were married at the time of the study (68%), with 13% self-describing as a widow and 19% as divorced or single. Participants ranged in age from 32 to 74, with an average age of 56 years. The time since first diagnosis varied across patients, but all were actively undergoing treatment at the time of initial recruitment.

### Measures

The following measures were administered to the participants. With the exception of the demographic questionnaire, which was administered only at the pre-intervention time point, all measures were completed prior

to intervention, and repeated at the end of the 4th, 8th, and final (12th) session.

### Demographics

A brief questionnaire was completed to obtain demographic information, including age, race, educational level, and employment status.

### Depression

The Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996) was completed by participants at all assessment points. The BDI-II is a 21-item response inventory on which the responder is asked to rate the presence/severity of depressive symptoms on a 0–3 scale. This measure is widely used across various populations and is sensitive to change over time. Scores from 0–13 represent minimal depression; 14–19 mild depression; 20–28 moderate depression; and 29–63 severe depression.

### Anxiety

The Beck Anxiety Inventory (BAI; Beck & Steer, 1993) is a 21-item questionnaire in which symptoms of anxiety are listed and rated for severity on a 4-point scale. Scores range from 0–63, with higher scores indicating greater severity. Scores from 0–7 represent minimal anxiety; 8–15 mild anxiety; 16–25 moderate anxiety; and 26–63 severe anxiety.

### Distress

The Profile of Mood States (POMS; McNair, Lorr, & Droppleman, 1971) is a 65-item measure of mood states. Results yield scores on 5 subscales, including anxiety, depression, hostility, confusion, vigor, and fatigue. In addition, a total calculated score of total mood disturbance may be obtained. This measure has been widely used in oncology populations. According to the POMS manual, the mean mood disturbance score for women involved in outpatient treatment is 23 (McNair et al., 1971). Increasing scores are associated with increased mood disturbance.

### Emotional Control

The Courtland Emotional Control Scale (CECS; Watson & Greer, 1983) is a 21-item questionnaire designed to provide a direct measure of emotional control among patients with physical disorders. Three subscales scores (anger, anxiety, and depression) may be combined to yield a composite score of overall emotional control. This scale was included in an attempt to measure the degree to which respondents control their expression of negative emotion. Total scores range from 21–84, with higher scores indicating greater emotional control.

### Thought Suppression

The White Bear Thought Suppression Inventory (WBSI; Wegner & Zanakos, 1994) is designed to measure thought suppression. It consists of 15 items, scored on a 5-point scale from *strongly disagree* (1) to *strongly agree* (5), with higher scores indicating greater thought suppression. The WBSI

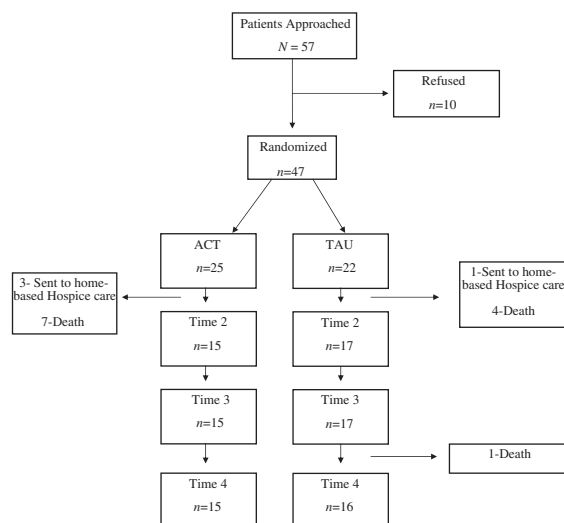


Figure 1. Study schema.

has been shown to have good internal consistency, with reported alphas of .87 to .89.

#### *Coping*

The COPE (Carver, Scheier, & Weintraub, 1989) assesses general strategies of coping, yielding scores across 15 coping strategies. From the COPE, the subscale of mental disengagement provided a measure of cognitive avoidance consistent with that conceptualized in the ACT model. The mental disengagement subscale includes items such as, "I turn to work or other activities to take my mind off things," and exemplifies the functional cognitive, emotional, and behavioral aspects of experiential avoidance. Also from the COPE, we utilized the acceptance subscale. This scale contains items such as, "I accept that this has happened and can't be changed," and "I get used to the idea that it happened." Internal consistency for the scale has been previously reported at .65 (Carver et al., 1989). Other scales include positive reinterpretation, venting, social support, active coping, denial, planning, religion, humor, behavioral disengagement, restraint, substance abuse, and suppression of competing activities.

#### *Quality of Life*

The Functional Assessment of Cancer Therapy (FACT-G; Cella et al., 1993; Cella, 1997) is a widely accepted measure of quality of life in cancer patient populations. It is designed to address the concerns and issues relevant to quality of life in this population, and has repeatedly demonstrated high reliability and validity, as well as sensitivity to changes over time. The questionnaire consists of 27 items, and produces scores of four subscales (physical well-being, social/family well-being, emotional well-being, and functional well-being), as well as an overall score of well-being.

#### **Procedures**

Women were identified as eligible based upon diagnosis through review of patient charts prior to scheduled outpatient oncology clinic visits at Washington University School of Medicine in St. Louis, MO. Those labeled as having Stage III or IV ovarian cancer were approached by an experimenter when they checked into the clinic or were waiting to see their oncologist while in the waiting room or exam room. The experimenter informed the patient that we were conducting a study designed to assess methods of interventions designed to help women cope with ovarian cancer and the emotional distress. They were informed that participation would involve meeting with a therapist on 12 occasions for 1 hour, over the course of a 4-month period. We attempted to minimize travel and time requirements by scheduling appointments in conjunction with clinic visits and/or chemotherapy treatments. Those who agreed to participate and provided informed consent

were given baseline questionnaires. Questionnaires were often completed at that time, while the patient waited for their appointment. Those who did not complete their forms immediately returned the completed forms at the first scheduled therapy meeting. Questionnaires were repeated following the fourth, eighth, and final session.

After enrollment in the study, participants were assigned to a therapy condition (ACT or TAU) using a computer-generated random number table. Each participant was then contacted by the experimenter to schedule the first therapy session. Sessions were conducted in the experimenter's clinical office, chemotherapy treatment room, inpatient hospital rooms, and physician exam rooms. Although this flexibility impaired our ability to record sessions, it decreased the responsibility, time commitment, and travel requirements for our participants—many of whom found it difficult to walk, experienced chronic pain and nausea, or faced intense fatigue. For some, end of life was imminent. Many of these individuals would not have been able to receive services were it not for this flexibility. In addition, it increased the external validity of our intervention, as this is typical for psycho-oncology services within a medical setting.

Both protocols were partially scripted, and included a specific intervention and topic to be covered at each session. A checklist for each session was completed by the therapist in attempt to ensure compliance with the protocols. Any deviation from the protocol was noted, and was revisited at the next session with the patient. The therapist was a Ph.D.-level clinical psychologist. Additional supervision was provided by the second author. Details of the protocols may be obtained by contacting the first author. Examples from a mock therapy session may be viewed in Video 1.



**Video 1.** Mock example of use of ACT intervention with cancer patient.



## Results

### Outcome Analytic Strategy

Hierarchical linear modeling (HLM) was the primary analytic method used to investigate outcomes and changes in processes using an intent-to-treat sample (Raudenbush & Bryk, 2001a,b). The HLM analyses were conducted assuming a random intercept and slope, and allowing them to be correlated. Simpler models with uncorrelated slopes and intercepts and then a random intercept only model were tested and used if they were not significantly different from the more complex model as determined by the restricted log likelihood. If the HLM analyses did not converge or the Hessian matrix was not positive definite, that is, if outcomes were not linear, a mixed model repeated measures analysis (MMRM) was conducted in which time was treated as a categorical variable rather than a linear covariate (Raudenbush & Bryk, 2001a). In all cases of MMRM analyses an unstructured covariance model performed significantly better than simpler covariance models (compound symmetry, Toeplitz, and compound symmetry heterogeneous) and thus was used. All analyses, both HLM and MMRM, were conducted with participants nested within the two treatment conditions and four assessment occasions.

Both forms of these mixed regression models use all available data from all subjects and, thus, are well suited for intent-to-treat analyses. They adjust for the obtained outcome and missingness for participants with missing data, thus reducing somewhat the analytic problem presented by missing data. For example, conditions with dropouts among participants doing poorly will have lower estimates of ultimate treatment impact. Mediation was examined using the methods suggested by Baron and Kenny (1986), as supplemented by those suggested by Preacher and Hayes (2004, 2008).

Denominator degrees of freedom for the fixed effects test statistics were based on the Satterthwaite approximation. The time value for initial assessments in all HLM analyses was set to zero and time was modeled by the sequential assessment occasion. Effects sizes (Cohen's *d*) for *F* values were based on the method suggested for repeated measures and multilevel designs by Rosenthal and Rosnow (1991; see also Verbeke and Molenbergh, 2000); for slopes as suggested by Raudenbush and Xio-Feng (2001); for MMRM contrasts as specified by Wackerly, Mendenhall, and Schaeffer (2008). The specific effect size metrics reported in a given analysis were selected so as to characterize effects adequately while avoiding redundancy. Effect sizes were discussed using the cutoffs suggested by Cohen (1988). Significance was always tested with a two-tailed distribution; values beyond  $p < .001$  were reported using that figure as a limit; values between  $p = .10$  and  $p = .05$  were termed "marginally significant," with exact *p*-values reported.

There were no significant differences in pretreatment values between conditions in any measure; thus, in all cases the key focus was the Time  $\times$  Treatment Condition interaction. For that reason only significance values will be provided for tests of time and condition, while more complete values will be provided for the Time  $\times$  Treatment interactions.

### Effects of Treatment

Table 1 shows the adjusted means for key measures for the two conditions for each measurement occasion, as taken from an MMRM analysis with unstructured covariance. The primary outcomes were distress, quality of life, acceptance, mental disengagement, emotional control, and avoidance. Secondary outcomes were depression (for those at least mildly depressed at baseline on the BDI) and anxiety (for those at least mildly depressed at baseline on the BAI).

#### Primary Outcomes: Distress

An HLM analysis showed no effect for treatment condition ( $p = .068$ ), a significant effect for time ( $p < .001$ ), and a significant effect for the interaction of condition and time,  $F(1, 42.73) = 6.23$ ,  $p = .001$ , on the POMS Distress measure. Analysis of the significance of slopes within each condition showed no significant improvement in the TAU condition [slope estimate =  $-2.31$ ,  $SE = 1.98$ ,  $t(40.82) = 1.17$ ,  $p = .25$ , effect size = .30]; a significant and large improvement for participants in the ACT condition [slope estimate =  $-9.27$ ,  $SE = 1.96$ ,  $t(44.65) = 4.74$ ,  $p < .001$ , effect size = 1.06]; and a large and significantly greater rate of improvement in the ACT condition as compared to the TAU condition [slope estimate =  $-6.95$ ,  $SE = 2.79$ ,  $t(42.73) = 2.49$ ,  $p = .017$ , effect size = .89].

#### Primary Outcomes: Quality of Life

An HLM analysis showed no effect for treatment condition ( $p = .59$ ) a significant effect for time ( $p < .001$ ), and a significant effect for the interaction of condition and time,  $F(1, 32.85) = 11.53$ ,  $p = .002$  on the FACT Total measure. Analysis of the significance of slopes within each condition showed no improvement in the TAU condition [slope estimate = .77,  $SE = .89$ ,  $t(32.29) = .87$ ,  $p = .39$ , effect size = .24]; but yielded a significant and large improvement for participants in the ACT condition [slope estimate = 5.03,  $SE = .89$ ,  $t(32.29) = 5.66$ ,  $p < .001$ , effect size = 1.59]; and a large and significantly greater rate of improvement in the ACT condition as compared to the TAU condition [slope estimate =  $-4.27$ ,  $SE = 1.26$ ,  $t(32.85) = 3.40$ ,  $p = .002$ , effect size = 1.35].

#### Primary Outcomes: Acceptance

An HLM analysis showed significant effects for treatment condition  $F(1, 43.05) = 8.37$ ,  $p = .006$  and a Condition  $\times$  Time interaction  $F(1, 43.05) = 26.77$ ,  $p < .001$ , but no significant

Table 1  
Means and Standard Error Between Groups on Outcome and Process Variables

	Time 1		Time 2		Time 3		Time 4	
	M	SE	M	SE	M	SE	M	SE
<i>Distress</i>								
ACT	29.91	7.82	26.70	7.31	15.86	6.28	2.92	5.14
TAU	35.59	8.28	37.30	7.60	32.50	6.45	29.38	5.24
<i>Quality of Life</i>								
ACT	75.63	4.14	79.13	3.73	85.93	3.64	89.98	3.90
TAU	72.39	4.54	72.18	3.98	72.45	3.82	74.57	4.03
<i>Acceptance</i>								
ACT	12.40	0.71	13.18	0.72	14.62	0.56	16.04	0.48
TAU	11.46	0.75	11.09	0.72	11.02	0.55	10.30	0.47
<i>Mental Disengagement</i>								
ACT	8.92	0.65	7.81	0.74	6.06	0.55	4.39	0.25
TAU	9.68	0.69	10.90	0.73	12.81	0.53	13.62	0.24
<i>Emotional Control</i>								
ACT	47.24	2.51	44.22	2.52	34.94	2.18	28.72	1.74
TAU	45.75	2.69	51.09	2.49	54.38	2.12	57.75	1.74
<i>Thought Suppression</i>								
ACT	60.68	3.89	57.66	3.73	49.05	3.95	42.54	3.44
TAU	57.91	4.17	61.40	3.83	64.37	3.99	68.04	3.47
<i>Depression</i>								
ACT	23.14	3.14	19.99	2.93	13.51	3.31	8.65	2.37
TAU	22.60	2.63	17.44	2.47	15.54	2.78	15.87	2.06
<i>Anxiety</i>								
ACT	16.88	2.13	16.19	2.29	12.12	2.11	5.83	1.50
TAU	19.00	2.70	18.07	2.73	15.52	2.54	13.51	1.82

Note. ACT=Acceptance and Commitment Therapy; TAU=treatment as usual.

effect for time ( $p=.462$ ). Analysis of the significance of slopes within each condition again showed no significant improvement in the TAU condition [slope estimate= $-0.35$ ,  $SE=.22$ ,  $t(41.55)=-1.60$ ,  $p=.12$ , effect size=.45]; significant large improvements for ACT condition [slope estimate= $1.23$ ,  $SE=.21$ ,  $t(44.52)=5.77$ ,  $p<.001$ , effect size= $1.58$ ] and greater improvements for ACT participants when compared with the TAU participants [slope estimate= $-1.58$ ,  $SE=.31$ ,  $t(43.05)=-5.17$ ,  $p<.001$ , effect size= $2.02$ ].

#### Primary Outcomes: Mental Disengagement

Mental disengagement was analyzed with an HLM analysis, which did not indicate a significant effect of time ( $p=.66$ ) or condition ( $p=.54$ ). Therapy condition and time showed a similar interaction to previous outcomes,  $F(1, 46.26)=81.14$ ,  $p<.001$ . ACT participants had a significant reduction in mental disengagement scores across time

[slope estimate= $-1.54$ ,  $SE=.23$ ,  $t(47.84)=-6.81$ ,  $p<.001$ , effect size= $1.83$ ], while TAU participants showed an increase in mental disengagement scores over time [slope estimate= $1.40$ ,  $SE=.23$ ,  $t(44.76)=5.95$ ,  $p<.001$ , effect size= $1.66$ ]. When ACT is compared to TAU, a large difference in mental disengagement over time occurs because of the divergence in scores [slope estimate= $2.94$ ,  $SE=.32$ ,  $t(46.26)=9.01$ ,  $p<.001$ , effect size= $3.49$ ], such that over time, the ACT results in less mental disengagement, while the TAU intervention results in increased use of mental disengagement.

#### Primary Outcomes: Emotional Control

An HLM was analyzed on emotional control using total scores from the CECS. Scores over therapy and time conditions showed that there was a significant effect for time,  $F(1, 37.76)=6.43$ ,  $p=.015$ , and the Time  $\times$  Condition interaction,  $F(1, 37.76)=121.57$ ,  $p<.001$ , but not treatment

condition ( $p=.61$ ). Emotional control scores decreased across time in the ACT participants [slope estimate =  $-6.40$ ,  $SE=.66$ ,  $t(38.15)=-9.69$ ,  $p<.001$ , effect size =  $3.76$ ], increased over time for the TAU therapy conditions [slope estimate =  $4.01$ ,  $SE=.67$ ,  $t(37.20)=5.94$ ,  $p<.001$ , effect size =  $2.36$ ], and very large differences were found when comparing the two therapy conditions across time [slope estimate =  $10.41$ ,  $SE=.94$ ,  $t(37.76)=11.03$ ,  $p<.001$ , effect size =  $6.11$ ].

#### Primary Outcomes: Thought Suppression

When thought suppression was examined with an HLM analysis, time showed a marginally significant effect,  $F(1, 35.87)=4.06$ ,  $p=.051$ , treatment condition did not show significant effects ( $p=.53$ ), but the Time  $\times$  Treatment condition interaction was significant,  $F(1, 35.87)=44.83$ ,  $p<.001$ . Suppression scores significantly decreased over time for ACT participants [slope estimate =  $-6.25$ ,  $SE=1.02$ ,  $t(35.37)=-6.14$ ,  $p<.001$ , effect size =  $1.97$ ] and increased over time for TAU participants [slope estimate =  $3.36$ ,  $SE=1.01$ ,  $t(36.15)=3.32$ ,  $p=.002$ , effect size =  $1.06$ ]. When ACT was compared with CBT participants over time, a very large effect was seen [slope estimate =  $9.60$ ,  $SE=1.43$ ,  $t(35.87)=6.70$ ,  $p<.001$ , effect size =  $3.02$ ] because of the score divergence.

#### Secondary Outcomes: Anxiety

The present sample included 21 participants who were at least mildly anxious as indicated by the BAI. The HLM analysis did not converge and thus an MMRM analysis was used. Effects showed no effect for treatment condition ( $p=.22$ ), a significant effect for time ( $p<.001$ ), and a significant and large effect for the interaction of condition and time,  $F(1, 16.75)=4.03$ ,  $p=.025$ , effect size =  $.98$ , on the BAI. Both conditions showed large and significant improvements from pretreatment to the fourth assessment period [ACT: estimate =  $-11.04$ ,  $SE=1.23$ ,  $t(21.57)=-8.96$ ,  $p<.001$ , effect size =  $2.52$ ; TAU: estimate =  $-5.49$ ,  $SE=1.46$ ,  $t(19.83)=-3.75$ ,  $p=.001$ , effect size =  $1.25$ ] but there was a large and significantly greater rate of improvement in the ACT condition as compared to the TAU condition [estimate:  $-5.51$ ,  $SE=1.91$ ,  $t(20.63)=-2.90$ ,  $p=.009$ , effect size =  $1.26$ ]. Means are shown in Table 1.

#### Secondary Outcomes: Depression

The present sample included 30 participants who were at least mildly depressed as indicated by the BDI-II. An HLM analysis assuming only a random intercept best fit the data and showed no effect for treatment condition ( $p=.58$ ), a significant effect for time ( $p<.001$ ), and a significant effect for the interaction of condition and time,  $F(1, 34.86)=7.12$ ,  $p=.012$ , on the BDI. Analysis of the significance of slopes within each condition showed a significant and large improvement both in the TAU condition [slope estimate =  $-2.59$ ,  $SE=.69$ ,  $t(35.01)=-3.75$ ,  $p=.001$ , effect

size =  $1.59$ ] and the ACT condition [slope estimate =  $-5.37$ ,  $SE=.78$ ,  $t(34.76)=-6.87$ ,  $p<.001$ , effect size =  $3.31$ ], but there was a large and significantly greater rate of improvement in the ACT condition as compared to the TAU condition [slope estimate =  $2.78$ ,  $SE=1.04$ ,  $t(34.87)=2.67$ ,  $p=.012$ , effect size =  $1.69$ ].

#### Mediation Analysis

Mediation analyses were conducted to explore the functional relationship between process changes from pretreatment to the third assessment and outcome changes from pretreatment to the final assessment using nonparametric cross-products of the coefficients approach (Preacher & Hayes, 2004). Mediation refers to the difference between the direct path (treatment to outcome or the  $c$  path) and the indirect path (treatment to outcome accounting for the mediator or the  $c'$  path). The cross-product of the coefficients for the "a path" (treatment to the mediator) and the "b path" (the mediator to outcome, controlling for treatment) approximates the difference between the direct and indirect path (Preacher & Hayes) and thus there is general agreement (MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002) that it is among the best ways to test mediation. Because the cross-product is generally not normally distributed (Preacher & Hayes), we used a nonparametric method based on bootstrapping, in which  $k$  samples of the original size are taken from the obtained data (with replacement after each specific data point is selected—in the present case 3,000 samples were obtained) and a cross-product test is then calculated in each sample (Preacher & Hayes). Bias corrected and accelerated 95% confidence intervals are similar to the 2.5 and 97.5 percentile scores of the obtained distribution of the cross-products over the samples, but with a  $z$ -score based correction for bias due to the underlying distribution (Preacher & Hayes). If the confidence intervals do not contain zero, the point estimate is significant at the level indicated.

The mediation of pretreatment to Assessment 4 changes in quality of life and distress were tested using pretreatment to Assessment 3 and pretreatment to Assessment 2 changes in mental disengagement and planning. These two processes were selected because mental disengagement represents a form of avoidant coping and planning a form of more active engagement, dependent upon some degree of acceptance, all of which were targeted by ACT. An MMRM analysis revealed that there were no significant pretreatment to Session 3 outcome differences between conditions for distress ( $p=.12$ ) and no significant pretreatment to Session 2 outcome difference between conditions for quality of life ( $p=.18$ ). Thus, mental disengagement and planning differences at Session 3 were tested as mediators for distress and mental disengagement and planning

differences at Session 2 were tested as mediators for quality of life.

Changes in distress at the final assessment session were significantly mediated by changes in mental disengagement and planning at Session 3 (point estimate = 43.16, SE = 12.14, 95% CI: 20.44, 68.81). The significant differential treatment impact on distress,  $t(28) = 2.88$ ,  $p < .008$ , was no longer significant and was moving in the other direction between conditions after accounting for the indirect effect,  $t(28) = -1.08$ ,  $p = .29$ . Change in quality of life at the final assessment session was marginally significantly mediated ( $p = .06$ ) by change in mental disengagement and planning at Session 2 (point estimate = -5.19, SE = 3.44, 95% CI: -13.59, -.17), and the significant differential treatment impact on quality of life,  $t(29) = -3.07$ ,  $p < .005$ , was marginally significant after accounting for the indirect effect,  $t(29) = -1.71$ ,  $p = .10$ . The same mediators at Assessment 3 had a more powerful mediational effect on quality of life changes at Assessment 4 ( $p < .05$ ) and the direct path was no longer significant,  $t(29) = .70$ ,  $p = .49$ .

Thus, even before outcomes were significant, mediational results were evident on distress and marginally so with quality of life. When reversed, quality of life changes from pretreatment to Assessment 2 did not significantly mediate changes from pretreatment to Assessment 4 for either mental disengagement or planning. Distress changes from pretreatment to Assessment 3 likewise did not significantly mediate planning changes from pretreatment to Assessment 4; distress changes at assessment point three did mediate mental disengagement at assessment point four ( $p = .05$ ) but the effect of treatment, after accounting for the indirect effect, was still highly significant,  $t(28) = 7.15$ ,  $p < .001$ , indicating that the indirect path was not of much functional importance when the relationship between outcome and mediator was reversed. Thus, the overall pattern of mediation evidence suggests that the differential reduction by ACT of an avoidant coping process (mental disengagement) and the differential increase by ACT of an active and engaged coping process (planning) was a functional pathway accounting in part for the differential positive impact of ACT on both distress and quality of life.

## Discussion

This study is one of few to attempt to evaluate and compare psychological interventions in the reduction of distress among women with late-stage ovarian cancer, and the only one to use an ACT treatment model. Our hypotheses were partially supported by the data. The ACT treatment group showed greater decreases in psychological distress compared to the TAU group, as well as higher reports of quality of life at the end of treatment. This change in quality of life is particularly notable, given that these changes occurred in the face of worsening physical

conditions. We suspect that the basis of this finding is the decrease in cognitive and emotional avoidance (cognitive disengagement) such that, over the course of the treatment, patients in the ACT condition became more accepting of their situation, thus allowing them to engage in value-concordant behavior. And in fact, acceptance did increase significantly over time within the ACT condition. So, despite the fact that their health had deteriorated and activities likely became limited, these patients were engaged in behaviors that were personally relevant and valued, such as being connected with others, communicating and sharing thoughts and emotions with family and friends.

Although psychological distress often varies in intensity over the course of the disease process, both of our groups showed decreases in distress over time (see Table 1). The rate and degree of this decrease, however, was greater for those in the ACT condition. Our results show initial increases in distress in the TAU condition, followed by a slow and gradual decrease. It is unclear as to why this initial increase occurred. In the future, it may be useful to conduct a more detailed component-analysis of the intervention in this type of population. The total decrease seen in the ACT condition is also notably unusual in a sample such as this and led us to review the data. We have no clear explanation for this finding, but certainly recommend that it be examined further in future work.

We did not expect ACT to outperform our TAU condition on depression and anxiety, since the TAU protocol consisted of therapy techniques which directly target those experiences. And, in fact, our results did show that anxiety and depression decreased significantly over time in the TAU condition. These decreases were larger, however, in the ACT condition. Given that the TAU condition contained techniques that have been extensively tested among anxious and depressed populations with marked success, the finding may be unique to this group. It may be, for example, that patients facing extreme physical illness and declining health may benefit additionally from acceptance-oriented interventions. It is clear that further research must be done before definitive conclusions can be drawn.

Our analyses indicated that “mental disengagement” and “active planning” served to mediate the differences in outcome between TAU and ACT on quality of life and psychological distress. The time line of the study further allows us to garner that these mediational effects occurred prior to any significant changes in the outcome variables. Although this is a small and preliminary study, it indicates a promise in the investigation of the temporal sequence of increases in acceptance and improved outcome. Data regarding mediational effects are particularly important in psycho-oncology interventions, as others have noted that although we currently have much in terms of outcome data, little is known about what is exactly responsible for the



effects of therapy (Anderson, Shelby, & Golden-Kreutz, 2007).

The findings supported our hypotheses regarding the impact of the interventions on process variables of experiential avoidance and acceptance. Acceptance dramatically increased over time in the ACT condition, and showed little change in the TAU condition. Alternatively, our measures which tap into the construct of experiential avoidance (mental disengagement, emotional control, and thought suppression) all demonstrated a consistent effect pattern, in that each decreased over time in the ACT condition, and increased in the TAU condition. All three variables resulted in significant interaction effects. These are process variables that are directly addressed through ACT, so it is promising that the treatment group would show such effects. The changes in the TAU condition are rather interesting, in that avoidance behaviors appear to have actually increased over time. We do not believe that the treatment itself engenders avoidance. No such findings have been shown in previous studies. Rather, we suspect that the increases in avoidance are the result of increasing illness, disability, and potential mortality in the absence of specific training in acceptance. It is also possible that some interventions in the TAU condition may have led to an increase in “mental disengagement.” For example, relaxation interventions may serve to decrease distress in the moment and thus lead to some degree of improved outcomes. It may also work as a distractor, increasing the individual's tendency to avoid thought content related to their life with cancer, thus creating greater disengagement from their life and values. However, this study was not designed to specifically test such hypotheses.

Although the impact of “active planning” may not be as clear, upon reflection, it demonstrates the broadened behavioral options and valued-life engagement that becomes available when an individual finds that they do not have to avoid uncomfortable cognitive/emotional content. It is likely that as patients engage with the content (“I have end-stage cancer”), rather than working to avoid the content (“can't think about my disease”) they may then have the option of planning activities, addressing relationships, investigating and planning health-care options and end-of-life directives.

This preliminary study has shortcomings. Perhaps most notable is the use of only one therapist in conducting both interventions. One might argue that this would lead to obvious allegiance effects. In response, we compared the effect size of our TAU intervention to other interventions found in the cancer literature. A recent meta-analysis (Osborn, Demoncada & Feuerstein, 2006) generated average effect sizes and confidence intervals for cognitive-behavioral therapy for cancer patients with some of the areas considered in the present study. All of the effect sizes found for the TAU condition in the present study were

within the confidence intervals reported in the meta-analysis. As such, the strength and quality of the TAU intervention appears to have been just as strong as that shown for active conditions in previous studies.

This finding also serves to address another shortcoming—the limited quality of treatment integrity checks. Because this study was conducted in a medical center, with patients who were undergoing very serious medical procedures and suffering debilitating side effects, it was impossible to create audio/video recordings of sessions. Sessions were held in various locations, including chemotherapy infusion rooms, inpatient rooms, outpatient clinics, and exam rooms, often on an impromptu schedule, based upon the patient's medical appointments and events. The sessions, conducted just as we would for patients not enrolled in a trial, were designed to be patient-centered and unburdensome. We included a checklist with each protocol and session, and the therapist used the checklist as guide to direct content and interventions. Given the significant differences between the two interventions on process-related measures, the two interventions clearly appear to be different, and given that the effect sizes are consistent with previous reports, we believe that that the interventions were conducted competently. However, we hope that future researchers will find creative methods to maintain greater control and increase the quality of treatment integrity checks. This must occur in order to draw strong conclusions regarding the efficacy of this intervention. We also failed to include any measures of social validity and acceptability of treatment. This should also be examined in future work.

Developing and determining efficacy of psychological interventions for cancer patients has been described as a high priority (Compas, Haaga, Keefe, Leitenberg & Williams, 1998). Using the Chambless and Hollon (1998) criteria for empirically supported treatments, reviewers have reported that our current interventions are at the level of “possibly efficacious” (Compas et al., 1998). We believe that the data from this study invite consideration and future work examining the efficacy of ACT in providing psychological interventions for cancer populations.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at [doi:10.1016/j.cbpra.2012.01.003](https://doi.org/10.1016/j.cbpra.2012.01.003).

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Received: December 20, 2010

Accepted: January 6, 2012

Available online xxxxx