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## Acceptance and commitment therapy for patient fatigue interference and caregiver burden in advanced gastrointestinal cancer: Results of a pilot randomized trial

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### Abstract

**Background:** Fatigue often interferes with functioning in patients with advanced cancer, resulting in increased family caregiver burden. Acceptance and commitment therapy, a promising intervention for cancer-related suffering, has rarely been applied to dyads coping with advanced cancer.

**Aim:** To examine the feasibility, acceptability, and preliminary efficacy of acceptance and commitment therapy for patient-caregiver dyads coping with advanced gastrointestinal cancer. Primary outcomes were patient fatigue interference and caregiver burden.

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#### Authorship

All authors contributed to the study conception and design, acquisition, or interpretation of data. Data analyses were performed by E.S., W.W., and D.A.K. The first draft of the article was written by C.E.M. and E.S., and all authors commented on subsequent versions of the article and approved the final article.

#### Declaration of conflicting interests

The authors declare that there is no conflict of interest.

#### Research ethics and patient consent

Ethics approval of this protocol was granted by the Indiana University Institutional Review Board (protocol#: 1904388865). The trial was conducted in compliance with the Declaration of Helsinki. Informed consent was obtained from all participants.

**Design:** In this pilot trial, dyads were randomized to six weekly sessions of telephone-delivered acceptance and commitment therapy or education/support, an attention control. Outcomes were assessed at baseline and at 2 weeks and 3 months post-intervention.

**Setting/participants:** Forty patients with stage III-IV gastrointestinal cancer and fatigue interference and family caregivers with burden or distress were recruited from two oncology clinics and randomized.

**Results:** The eligibility screening rate (54%) and retention rate (81% at 2 weeks post-intervention) demonstrated feasibility. At 2 weeks post-intervention, acceptance and commitment therapy participants reported high intervention helpfulness (mean=4.25/5.00). Group differences in outcomes were not statistically significant. However, when examining within-group change, acceptance and commitment therapy patients showed moderate decline in fatigue interference at both follow-ups, whereas education/support patients did not show improvement at either follow-up. Acceptance and commitment therapy caregivers showed medium decline in burden at 2 weeks that was not sustained at 3 months, whereas education/support caregivers showed little change in burden.

**Conclusions:** Acceptance and commitment therapy showed strong feasibility, acceptability, and promise and warrants further testing.

**Trial Registration:** [ClinicalTrials.gov NCT04010227](https://clinicaltrials.gov/NCT04010227). Registered 8 July 2019, <https://clinicaltrials.gov/ct2/show/NCT04010227?term=catherine+mosher&draw=2&rank=1>

## Keywords

Neoplasms; fatigue; quality of life; acceptance and commitment therapy; family caregivers; caregiver burden; clinical trial

## Introduction

Gastrointestinal cancers are among the most prevalent cancers affecting men and women worldwide.<sup>1</sup> The majority of patients with gastrointestinal cancer have regional or distant stage disease, resulting in disabling symptoms.<sup>2-9</sup> Fatigue is a common symptom with up to 68% of patients with metastatic colorectal cancer experiencing significant fatigue.<sup>7, 9</sup> In patients with advanced cancer, fatigue and related symptoms have been associated with increased healthcare use.<sup>10</sup> Among patients with gastrointestinal cancer, fatigue has been related to other symptoms such as sleep disturbance and impaired daily activities.<sup>7, 11-13</sup> Thus, reducing fatigue interference with functioning is critical for improving their quality of life.

Family caregivers' quality of life is also affected.<sup>14-17</sup> Among caregivers of colorectal cancer patients, greater caregiving burden, or the negative impact of caregiving on daily living, has been correlated with impaired quality of life.<sup>18</sup> Caregivers with greater burden assume caregiving demands to the detriment of other important activities.<sup>18-21</sup>

Evidence-based interventions are needed to address patient fatigue and caregiver burden in advanced gastrointestinal and other cancers. According to Cochrane meta-analyses, trials have not yielded conclusive evidence regarding effects of pharmacologic and behavioral

interventions on fatigue in patients with advanced cancer.<sup>22, 23</sup> Additionally, trials have shown small to medium effects of behavioral interventions on burden and quality of life in caregivers of adults with cancer.<sup>24–26</sup> Most trials focused on patient-caregiver dyads coping with early-stage cancer and did not have a distress or symptom criterion for eligibility.

One behavioral intervention that shows promise for improving functional outcomes in advanced cancer is acceptance and commitment therapy.<sup>27–29</sup> Acceptance and commitment therapy aims to increase psychological flexibility, or mindful awareness of present experiences (e.g., symptoms, thoughts, feelings) while pursuing activities consistent with personal values. A pilot RCT in metastatic breast cancer found that telephone-based acceptance and commitment therapy showed feasibility and promise for reducing fatigue interference relative to education/support.<sup>30</sup> Other pilot trials have found effects of acceptance and commitment therapy on distress and quality of life in patients with cancer.<sup>28, 31–34</sup> One dyadic pilot of acceptance and commitment therapy in advanced lung cancer did not find substantial improvement in patient or caregiver symptom outcomes.<sup>35</sup> However, most outcomes had only moderate room for improvement at baseline.

This pilot RCT used *a priori* benchmarks to examine the feasibility and acceptability of delivering telephone-based acceptance and commitment therapy to patients with advanced gastrointestinal cancer and caregivers. We also examined the impact of acceptance and commitment therapy on patient fatigue interference and caregiver burden (primary outcomes) as well as patient sleep interference and patient and caregiver engagement in daily activities, values progress, psychological inflexibility, and quality of life (secondary outcomes) compared to education/support. Finally, we explored acceptance and commitment therapy's effects on patient and caregiver healthcare and medication use.

## Methods

### Research questions/hypotheses

We examined whether acceptance and commitment therapy showed evidence of feasibility, acceptability, and promise for patients with advanced gastrointestinal cancer and caregivers. *A priori* benchmarks for feasibility were: 1) enrolling at least 60% of screened eligible dyads in the trial;<sup>36</sup> and 2) 70% retention, defined as the percentage of randomized dyads completing 5–6 intervention sessions and the 2-week follow-up (primary end point). The acceptability benchmark was high helpfulness ratings (i.e., mean 4 on 1–5 scale across five items)<sup>37</sup> for 70% of acceptance and commitment therapy participants. We also hypothesized that acceptance and commitment therapy would improve outcomes relative to education/support.

### Study design

Methods for this pilot RCT were published.<sup>38</sup> The Indiana University institutional review board approved study procedures (IRB#: 1904388865, approved 29 April 2019). Patient-caregiver dyads were randomized to six weekly phone sessions of acceptance and commitment therapy or education/support. Outcomes were assessed at baseline and at 2 weeks and 3 months post-intervention.

## Study population

Patient inclusion criteria were as follows: 1) diagnosed with unresectable stage III or IV gastrointestinal cancer at least three weeks before enrollment; 2) moderate-to-severe fatigue interference (mean score  $\geq 2.5$  on the Fatigue Interference subscale of the Fatigue Symptom Inventory [FSI]);<sup>39, 40</sup> and 3) a consenting family caregiver. Patients were excluded if they 1) had severe cognitive impairment based on a chart review and cognitive screening ( $\geq 3$  errors);<sup>41</sup> 2) had a self-reported Eastern Cooperative Oncology Group [ECOG] score  $\geq 2$ ;<sup>42</sup> or 3) were receiving hospice care. Eligible family caregivers lived with the patient or had visited them at least twice a week for the past month. Additionally, eligible caregivers showed significant caregiving burden (score  $\geq 6$  on the 6-item Zarit Burden Interview)<sup>43</sup> or distress on the 4-item Patient-Reported Outcomes Measurement Information System (PROMIS) anxiety or depression measures (T-score  $\geq 60$  for anxiety or depression).<sup>44</sup> Both patients and caregivers had to be adults with English fluency and phone service.

## Sample

Clinic lists were consecutively screened for potentially eligible patients. Our target sample size was 40 dyads, and we calculated power for 34 dyads at 2 weeks post-intervention (assuming 15% attrition). For each primary outcome, we had 80% power ( $p=.05$ , two-tailed) to detect a large intervention effect ( $d=.99$ ) in a linear mixed model.<sup>45</sup>

## Recruitment and randomization

Participants were recruited between September 2019 and January 2021 from two medical centers in Indianapolis, IN. Initial patient eligibility was assessed via medical record review and consultation with the oncologist. Research assistants approached patients and caregivers during oncology clinic visits, enrolling 13 dyads before COVID-19 restrictions in March 2020. The remaining dyads were recruited via mailings and phone calls. Interested patients identified their family caregivers and were screened for eligibility. If patients consented to participate, caregivers were approached for eligibility screening and consent. Patients and caregivers could provide written or verbal consent.

Following baseline assessments, dyads were assigned in equal numbers to either acceptance and commitment therapy or education/support using stratified block randomization to balance the groups by patient performance status (ECOG scores 0 or 1 vs. 2).<sup>42</sup> The statistician used `blockrand` in R<sup>46, 47</sup> to produce randomly varying block sizes of 2, 4, 6, and 8 in a spreadsheet. A therapist supervisor checked the spreadsheet for the dyad's assigned condition and notified their therapist.

## Measures

Research assistants blind to group assignment administered phone assessments at baseline and at 2 weeks and 3 months post-intervention. Patients completed a 30-minute baseline and 25-minute follow-ups, whereas caregivers completed a 25-minute baseline and 20-minute follow-ups. Each person received a \$40 gift card per assessment.

**Feasibility and acceptability.**—At the 2-week follow-up, acceptability of interventions was assessed through ratings of the number and length of sessions, topics, therapist, and

telephone format on a scale from 1 (did not help at all) to 5 (extremely helpful).<sup>37</sup> Participants in both conditions also rated whether sessions met their expectations on a scale from 1 (not at all) to 5 (extremely).

**Primary outcomes.**—All outcome measures have shown strong evidence of reliability and validity.<sup>38</sup> Patient fatigue interference was assessed with the 7-item Fatigue Interference subscale of the FSI.<sup>39, 40</sup> Caregiver burden was assessed with the 12-item short form of the Zarit Burden Interview.<sup>43, 48</sup>

**Secondary outcomes.**—Patient sleep interference was assessed with the 8-item PROMIS sleep-related impairment measure.<sup>49, 50</sup> Patient and caregiver engagement in daily activities was assessed with the 6-item PROMIS measure of participation in social roles and activities,<sup>51</sup> and their progress in value-based living was evaluated with the 5-item Progress subscale of the Valuing Questionnaire.<sup>52</sup> Patient and caregiver psychological inflexibility was assessed with the 7-item Acceptance and Action Questionnaire-II.<sup>53</sup> Patient quality of life was assessed with the 15-item McGill Quality of Life Questionnaire–Revised, including physical, psychological, existential, and social quality-of-life subscales.<sup>54</sup> Caregiver quality of life was assessed with the 10-item PROMIS measure of global health.<sup>55</sup> Analyses focused on 4-item physical and mental health subscales.

**Tertiary outcomes.**—Patients and caregivers reported their healthcare use in five domains (e.g., outpatient visits, overnight hospitalizations) in the past 3 months at baseline and over the study period.<sup>56, 57</sup> At all time points, participants also reported whether healthcare professionals had referred them to mental health services and whether they were received.<sup>58, 59</sup> Additionally, participants reported current medications at each time point.<sup>60, 61</sup>

**Demographic and medical factors.**—Patient and caregiver demographics were self-reported. Patients and caregivers also completed a checklist of eight or nine chronic health conditions, respectively.<sup>57</sup> A patient-reported ECOG score<sup>42</sup> was used to assess functional status. Patient cancer information was obtained via chart review.

### Intervention conditions

Both intervention conditions involved six weekly 50-minute telephone sessions. In both conditions, patients and caregivers completed sessions 1 and 4–6 together via speakerphone, whereas sessions 2 and 3 were conducted separately. All sessions were audio recorded. Acceptance and commitment therapy was delivered by a master's level mental health clinician (18 dyads) and a doctoral level psychologist (2 dyads) with experience in acceptance and commitment therapy, whereas education/support was delivered by a master's level oncology social worker with experience in supportive counseling. The therapists were trained and supervised on a weekly basis by two psychologists. Two psychologists, a master's level clinician, and two doctoral students in clinical psychology randomly reviewed 40% of recordings for adherence to the manuals using checklists (Supplemental Tables 1 and 2). Across intervention conditions, the average fidelity rating was 98% (number of required topics and exercises covered in each session/total number of fidelity criteria). Psychologists

provided feedback on treatment fidelity and quality, and role-plays were conducted to improve fidelity.

### **Acceptance and commitment therapy**

We developed an intervention targeting all processes of the acceptance and commitment therapy model of behavior change (i.e., mindfulness, perspective taking, cognitive defusion, acceptance, values clarification, and committed action).<sup>62</sup> The intervention emphasized present-moment awareness training and setting goals to engage in actions based on personal values. For instance, patients' attempts to avoid symptoms such as fatigue may result in disengagement from valued activities. Caregivers may also neglect valued activities such as self-care as they focus on the patient's needs. Acceptance and commitment therapy supports feasible engagement in values-based activities. Each participant received handouts on session topics. Table 1 summarizes the six sessions.

During the initial session, the therapist asked about the participants' background and explored the effectiveness of the patient's strategies for coping with fatigue and the caregiver's strategies for coping with difficult thoughts and feelings. The therapist also introduced the practice of mindfulness. During the six sessions, patients and caregivers practiced mindfulness, learned adaptive coping skills (e.g., perspective taking), clarified their values, and set SMART goals (Specific, Measurable, Achievable, Relevant, and Time-Bound) based on their values. Acceptance and commitment therapy was adapted to the dyad by including joint mindfulness practices and leveraging the relationship during discussions. Participants' weekly home practice included daily 6–10 minute mindfulness practices using recordings that we developed, periodic worksheet completion on session topics, and values-based action.

### **Education/support**

Consistent with other dyadic psychosocial intervention trials in cancer,<sup>35, 63, 64</sup> the comparator was education/support. The intervention involved supportive listening and providing resources for practical and health information and contact information for support services. Table 1 summarizes the six sessions. Each participant received handouts on session topics and was asked to review them between sessions as homework. Tailoring involved skipping topics that were not applicable, and acceptance and commitment therapy concepts were not introduced.

### **Statistical analyses**

To determine acceptance and commitment therapy's feasibility, percentages were computed for each benchmark (e.g., percentage of eligible dyads that enrolled). To determine acceptance and commitment therapy's acceptability, the percentage of acceptance and commitment therapy participants meeting the benchmark (mean 4 across five helpfulness ratings) was computed. Using *t*-tests or Fisher's exact tests, baseline comparisons of study groups were conducted for patients and caregivers separately.

Data analyses were conducted following an intent-to-treat framework. Missing data were handled by multiple imputation (50 imputed data sets with 15.5% imputed data were

obtained).<sup>65</sup> Multilevel models (MLMs) were used to examine the preliminary efficacy of acceptance and commitment therapy, accounting for repeated measures. For outcomes applying to only patients or caregivers, the MLMs included main and interaction effects of study group and time (baseline, 2 weeks and 3 months post-intervention; treated as categorical). For outcomes applying to both patients and caregivers, MLMs for dyadic data were adopted.<sup>66, 67</sup> In dyadic models, fixed-effects parameters included all main effects and two- and three-way interaction effects among study group, time, and role (patient vs. caregiver). Intervention effects are evidenced by a significant group-by-time interaction. The three-way interaction among group, time, and role reflected the degree to which intervention effects differed between patients and caregivers. Random-effects parameters included separate residual variances for patients and caregivers and the covariance between the residuals which reflects similarity in the two partners' scores at a particular time point after accounting for the fixed effects. Random intercepts for dyads were also included to model variance in the average outcome across dyads. Two-tailed  $ps < .05$  were considered statistically significant. For each fixed effect, a partial correlation coefficient ( $pr$ ) was calculated as the effect size measure.<sup>68</sup>

As a supplemental analysis, among survey completers, a Cohen's  $d$  was calculated for each effect for primary and secondary outcomes. Specifically, the  $d$  for a within-group effect was calculated as the mean difference between baseline and each follow-up divided by the standard deviation (SD) of the change. The  $d$  for a between-group effect was calculated as the difference between mean changes for each condition divided by the pooled SD of the change. Due to their restricted variances, only descriptive statistics were examined for most health service use variables. Separate Poisson regression models for patients and caregivers were used to explore intervention effects on number of outpatient medical visits and number of prescribed medications over the study period, controlling for baseline values of the outcomes.

## Results

### Feasibility and acceptability

Of the 348 patients with advanced gastrointestinal cancer who were approached, 93 were ineligible, 141 declined to participate, 44 could not be reached via phone, and 70 consented (Figure 1). Thus, 54% of reached patients were screened for eligibility. Patients agreeing to the eligibility screening did not differ from those who declined with respect to gender or race/ethnicity ( $ps > .05$ ). However, patients agreeing to screening were, on average, younger (Means [ $M$ s]=59.2 vs. 62.6 years,  $p=0.02$ ). Most ineligible patients did not meet the fatigue interference criterion. Primary reasons for refusal were lack of interest and time constraints. Multiple caregivers of the same patient could be consecutively approached. Of the 77 caregivers who were approached, 29 were ineligible, 3 declined participation, and 3 could not be reached. Thus, 42 dyads were eligible, and all eligible dyads consented to participate, exceeding our benchmark of 60%. Prior to randomization, two dyads withdrew due to patient death or non-response to phone calls. Twenty of the remaining 40 dyads were randomized to acceptance and commitment therapy, and 20 were randomized to education/support. Most participants (64/80, 80%) completed all six sessions, and 81% (65/80) were

retained at 2-week follow-up, exceeding our benchmark of 70% retention. Additionally, 73% (58/80) of participants were retained at 3 months. Participants rated both interventions favorably (Table 2). Helpfulness ratings for acceptance and commitment therapy were high ( $M_{\text{patient}}=4.17/5.00$ ,  $SD_{\text{patient}}=.87$ ;  $M_{\text{caregiver}}=4.41/5.00$ ,  $SD_{\text{caregiver}}=.59$ ). Overall, 72.4% (21/29) of acceptance and commitment therapy participants reported an average helpfulness score 4.00, exceeding our benchmark of 70%.

### Participant characteristics

Participant characteristics by study group comparisons at baseline are presented in Table 3. Demographics, medical factors, and outcomes did not vary by study group at baseline.

### Preliminary efficacy: Multilevel model results

**Primary outcomes.**—Results of MLM analyses showed no group-by-time interaction effects on patient fatigue interference or caregiver burden (Table 4). Effect sizes for the interaction effects were small ( $ps=.08, .02$ ).

**Secondary outcomes.**—MLM analyses showed no group-by-time interaction effects on patient sleep interference and quality-of-life outcomes as well as caregiver quality-of-life outcomes. Additionally, results from the dyadic analyses revealed no two-way or three-way interaction effects among group, time, and role for activity engagement, values progress, and psychological inflexibility. Effect sizes for group-by-time interaction effects were small ( $ps=.02-.14$ ).

### Preliminary efficacy: Supplemental analyses of survey completers

**Primary and secondary outcomes.**—Among survey completers, patient fatigue interference showed moderate decline in the acceptance and commitment therapy condition at both follow-ups ( $ds=-.46, -.31$ ) but no improvement in the education/support condition ( $ds=-.05, .30$ ; Supplemental Table 3). Acceptance and commitment therapy caregivers showed a medium decrease in burden at 2 weeks ( $d=-.74$ ) that was not sustained at 3 months ( $d=-.26$ ), whereas education/support caregivers showed little change in burden ( $ds=-.24, -.03$ ; Supplemental Table 4). Effect sizes for secondary outcomes are shown in Supplemental Tables 3 and 4. Most quality-of-life outcomes only showed improvement among acceptance and commitment therapy participants.

**Tertiary outcomes.**—Patients and caregivers in both conditions reported little change in their physical and mental healthcare use during the study (Supplemental Table 5). Poisson regression analyses suggested no group difference in the number of outpatient medical visits or prescribed medications during the study for both patients and caregivers, controlling for the outcomes at baseline (Supplemental Table 6).

## Discussion

### Main findings

Telephone-based acceptance and commitment therapy exceeded a priori benchmarks for feasibility and acceptability among patients with advanced gastrointestinal cancer and



caregivers. In prior dyadic psychosocial intervention trials in cancer ( $N=55$  studies), on average, 33% of eligible dyads consented and 69% were retained at the final follow-up ( 3 months for 63% of studies).<sup>69</sup> In our trial, 100% of eligible dyads consented, and 73% were retained at the final 3-month follow-up. Additionally, helpfulness ratings for acceptance and commitment therapy were high. Most patient ineligibility was due to the fatigue interference criterion, which may have been affected by decreased demands during the pandemic. Differences in outcomes between intervention conditions were not statistically significant. In the acceptance and commitment therapy condition, however, patients showed moderate decline in fatigue interference across follow-ups, and caregivers showed moderate decline in caregiver burden at the first follow-up, although the decline was not sustained at 3 months. Acceptance and commitment therapy patients and caregivers also showed improvement in most quality-of-life outcomes across follow-ups. In contrast, education/support participants showed little to no change in these outcomes, similar to prior research.<sup>35</sup>

### Strengths/limitations

This trial is one of the first to test acceptance and commitment therapy for dyads coping with serious illness.<sup>35</sup> We targeted common concerns of patients with advanced cancer<sup>70</sup> and caregivers<sup>18, 19</sup> for which evidence-based interventions are lacking. Our rigorous, randomized approach employed an attention control arm, clinical criteria for study entry, blind administration of valid assessments, and quality control procedures.

Study limitations include the primarily white sample recruited from medical centers in Indiana. It is unclear whether younger patients' higher rates of eligibility screening relative to older patients affected study results. Although participants were not paid to participate in intervention sessions, they received gift cards for participating in assessments. This may have improved retention; however, the use of monetary incentives to improve retention in RCTs is not currently supported by high-quality evidence.<sup>71</sup> Finally, the small sample size reduced statistical power; however, our primary goal was to assess acceptance and commitment therapy's feasibility before conducting a fully powered trial.

### What this study adds

This trial contributes to limited evidence suggesting that acceptance and commitment therapy is feasible and acceptable for dyads coping with advanced cancer.<sup>35</sup> We also found that phone-based recruitment yielded a nearly 20% lower rate of patient agreement to eligibility screening compared to in-clinic recruitment with the same population.<sup>37</sup> Our results suggest that acceptance and commitment therapy warrants further testing in a large-scale trial. A booster session may reinforce skill practice. After demonstrating acceptance and commitment therapy's efficacy, it has high potential for integration into comprehensive cancer care.

### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Data management and sharing

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request. Intervention materials may also be requested from the corresponding author.

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**What is already known about the topic?**

- Fatigue interference with functioning is a major concern of patients with advanced cancer.
- Family caregivers of cancer patients often experience increased burden as they face demanding role changes.
- Preliminary evidence suggests that acceptance and commitment therapy may improve functional outcomes in patients with cancer; however, this therapy has rarely been tested in patient-caregiver dyads coping with advanced cancer.

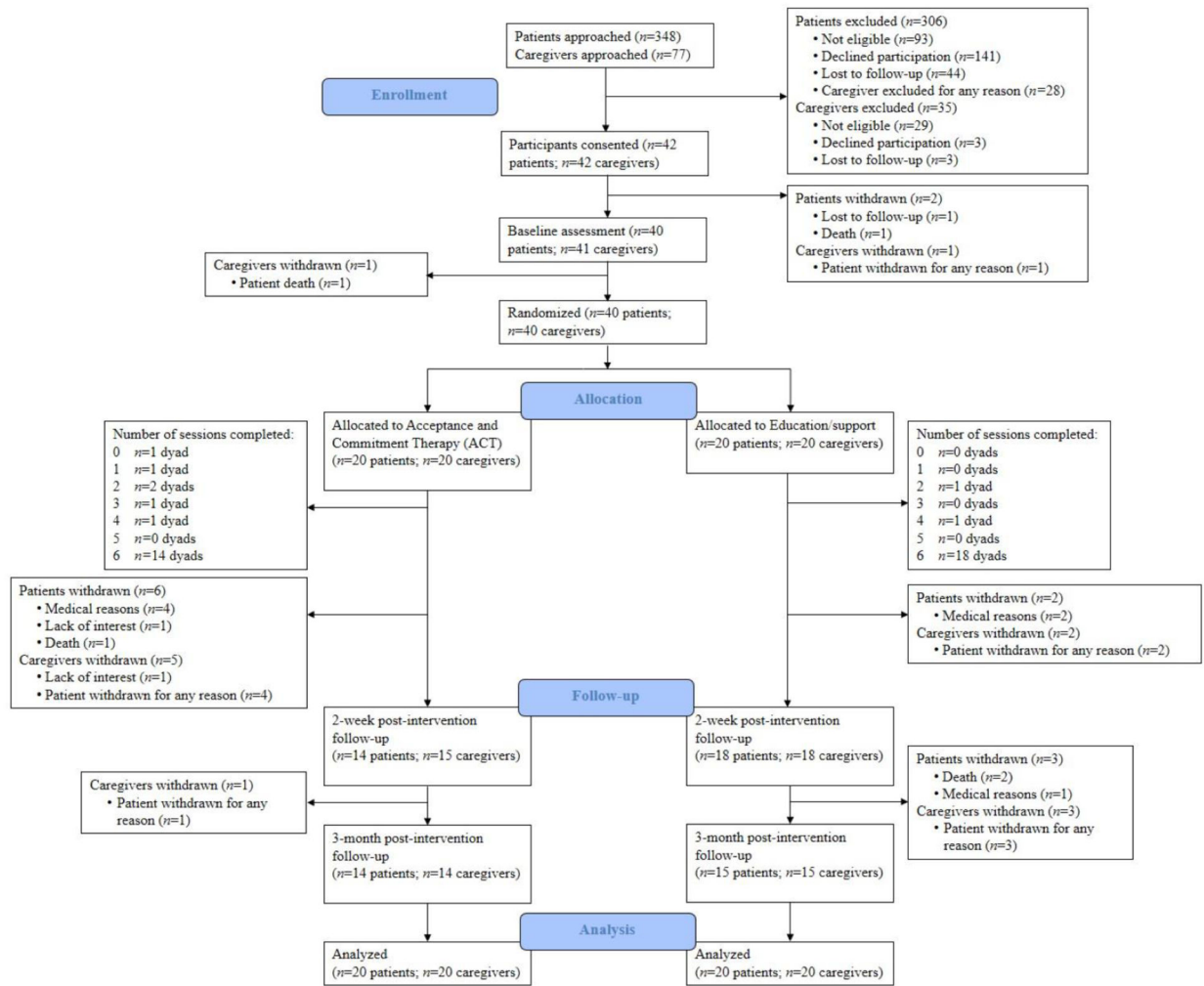
**What this paper adds**

- Acceptance and commitment therapy (e.g., present-moment awareness training and engaging in actions consistent with personal values) showed strong evidence of feasibility and acceptability for patients with advanced gastrointestinal cancer and family caregivers based on study accrual, retention, and ratings of intervention helpfulness.
- Acceptance and commitment therapy also showed promise in reducing patient fatigue interference and caregiver burden.

**Implications for practice, theory, or policy**

- Acceptance and commitment therapy shows feasibility, acceptability, and promise in improving functional outcomes of patients and caregivers coping with advanced gastrointestinal cancer and warrants further testing in large-scale trials.





**Figure 1.**  
Study flow chart.

*Note:* Multiple caregivers of one patient could be consecutively approached.

**Table 1.**

Summary of acceptance and commitment therapy and education/support sessions.

| Acceptance and Commitment Therapy                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Education/Support                                                                                                                                                                                                                                                                                                                                          |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p><u>Session 1 (Dyadic)</u></p> <ul style="list-style-type: none"> <li>• Introductions and overview of the intervention</li> <li>• Discuss control- vs. acceptance-based strategies for patient fatigue management and caregiver coping with emotions about responsibilities</li> <li>• Introduce and practice mindfulness (body scan) with therapist</li> </ul>                                                                                                                                      | <p><u>Session 1 (Dyadic)</u></p> <ul style="list-style-type: none"> <li>• Overview of sessions &amp; orientation to the medical center</li> <li>• Overview of quality of life and discussion of physical quality of life</li> <li>• Discussion of educational materials received from the healthcare team</li> <li>• Overview of treatment team</li> </ul> |
| <p><u>Session 2 (Individual)</u></p> <ul style="list-style-type: none"> <li>• Practice mindfulness (awareness of the breath) with therapist</li> <li>• Clarify personal values with birthday exercise and explore how person might choose to respond to fatigue (if patient) or thoughts/emotions about tasks (if caregiver) in an adaptive and values-consistent manner</li> </ul>                                                                                                                    | <p><u>Session 2 (Individual)</u></p> <ul style="list-style-type: none"> <li>• Review common challenges in social functioning such as talking with children and employment issues</li> <li>• Contact info for resources to address social challenges</li> </ul>                                                                                             |
| <p><u>Session 3 (Individual)</u></p> <ul style="list-style-type: none"> <li>• Practice mindfulness (“leaves on the stream”) with therapist</li> <li>• Explore workability of patient/caregiver attempts to avoid or suppress unwanted internal experiences (e.g., fatigue, thoughts/emotions about caregiving) and how these attempts lead to actions not aligned with values and reduced quality of life</li> <li>• Practice mindfulness (awareness of body and breath) with therapist</li> </ul>     | <p><u>Session 3 (Individual)</u></p> <ul style="list-style-type: none"> <li>• Review common changes in activities</li> <li>• General tips on managing the household</li> <li>• Review common emotional responses to cancer and cognitive changes following cancer treatment</li> <li>• Contact information for mental health services</li> </ul>           |
| <p><u>Session 4 (Dyadic)</u></p> <ul style="list-style-type: none"> <li>• Practice mindfulness (mindful eating of raisin) with therapist</li> <li>• Experiential exercise to support patients and caregivers in flexibly choosing their focus in the present moment and debriefing with reference to fatigue and cancer caregiving</li> <li>• Introduce concept of willingness (i.e., flexibly making contact with the present moment, including fatigue and thoughts/feelings about tasks)</li> </ul> | <p><u>Session 4 (Dyadic)</u></p> <ul style="list-style-type: none"> <li>• Review common financial concerns related to cancer and its treatment</li> <li>• Contact information for resources to address concerns</li> </ul>                                                                                                                                 |
| <p><u>Session 5 (Dyadic)</u></p> <ul style="list-style-type: none"> <li>• Practice mindfulness (3-step self-compassion practice) with therapist</li> <li>• Recap of key concepts with reference to a recent challenge faced by the patient and caregiver</li> <li>• Exercise to promote observing and detaching from fatigue and emotions about cancer or caregiving to cultivate a transcendent sense of self from which to observe and accept changing experience</li> </ul>                         | <p><u>Session 5 (Dyadic)</u></p> <ul style="list-style-type: none"> <li>• Review methods of evaluating health information on the Internet and other modalities</li> <li>• Discuss resources for evaluating health information</li> </ul>                                                                                                                   |
| <p><u>Session 6 (Dyadic)</u></p> <ul style="list-style-type: none"> <li>• Practice mindfulness (brief body scan exercise) with therapist</li> <li>• Recap of skills and what patient and caregiver learned</li> <li>• Goal setting around expanding values-consistent behavior into future</li> <li>• Practice mindfulness (compassion practice) with therapist</li> </ul>                                                                                                                             | <p><u>Session 6 (Dyadic)</u></p> <ul style="list-style-type: none"> <li>• Review all topics discussed in prior sessions and available resources for addressing each topic area</li> <li>• Discuss websites for accessing cancer-related info</li> </ul>                                                                                                    |

**Table 2.**

Patient and caregiver intervention satisfaction.

| Intervention Satisfaction <sup>a</sup>           | Acceptance and Commitment Therapy |      |      |    | Education/Support |      |   |      |    |
|--------------------------------------------------|-----------------------------------|------|------|----|-------------------|------|---|------|----|
|                                                  | N                                 | Mean | SD   | N  | Mean              | SD   | N | Mean | SD |
| <b>Patients:</b>                                 |                                   |      |      |    |                   |      |   |      |    |
| Telephone sessions met expectations <sup>b</sup> | 14                                | 4.21 | 0.80 | 18 | 4.11              | 0.83 |   |      |    |
| Number of sessions was helpful <sup>c</sup>      | 14                                | 4.00 | 1.04 | 18 | 3.61              | 0.78 |   |      |    |
| Length of sessions was helpful <sup>c</sup>      | 14                                | 4.07 | 1.07 | 18 | 3.44              | 0.86 |   |      |    |
| Topics of sessions were helpful <sup>c</sup>     | 14                                | 4.00 | 1.11 | 18 | 4.06              | 0.80 |   |      |    |
| Therapist was helpful <sup>c</sup>               | 14                                | 4.43 | 1.02 | 18 | 4.83              | 0.38 |   |      |    |
| Use of the telephone was helpful <sup>c</sup>    | 14                                | 4.36 | 0.74 | 18 | 4.56              | 0.78 |   |      |    |
| <b>Caregivers:</b>                               |                                   |      |      |    |                   |      |   |      |    |
| Telephone sessions met expectations <sup>b</sup> | 15                                | 4.53 | 0.83 | 18 | 3.94              | 1.00 |   |      |    |
| Number of sessions was helpful <sup>c</sup>      | 15                                | 4.13 | 0.83 | 18 | 3.72              | 1.18 |   |      |    |
| Length of sessions was helpful <sup>c</sup>      | 15                                | 4.07 | 0.96 | 18 | 3.78              | 1.22 |   |      |    |
| Topics of sessions were helpful <sup>c</sup>     | 15                                | 4.40 | 0.83 | 18 | 3.94              | 1.00 |   |      |    |
| Therapist was helpful <sup>c</sup>               | 15                                | 4.67 | 0.62 | 18 | 4.61              | 0.61 |   |      |    |
| Use of the telephone was helpful <sup>c</sup>    | 15                                | 4.80 | 0.41 | 18 | 4.67              | 0.59 |   |      |    |

<sup>a</sup> Intervention satisfaction was assessed at 2 weeks post-intervention.

<sup>b</sup> Rated on a 5-point Likert scale (1 = Not at all, 5 = Extremely).

<sup>c</sup> Rated on a 5-point Likert scale (1 = Did not help at all, 5 = Extremely helpful).

**Table 3.**

Patient and caregiver characteristics and group comparisons at baseline.

| Characteristics                              | Patients (n = 40) |                            |      | Caregivers (n = 40) |                            |  | t-test/Fisher's Exact Test p | t-test/Fisher's Exact Test p |
|----------------------------------------------|-------------------|----------------------------|------|---------------------|----------------------------|--|------------------------------|------------------------------|
|                                              | ACT (n = 20)      | Education/Support (n = 20) |      | ACT (n = 20)        | Education/Support (n = 20) |  |                              |                              |
| Gender, n (%)                                |                   |                            | 0.75 |                     |                            |  | 0.27                         |                              |
| Male                                         | 10 (50)           | 8 (40)                     |      | 3 (15)              | 7 (35)                     |  |                              |                              |
| Female                                       | 10 (50)           | 12 (60)                    |      | 17 (85)             | 13 (65)                    |  |                              |                              |
| Age                                          |                   |                            | 0.74 |                     |                            |  | 0.16                         |                              |
| Mean                                         | 59.25             | 57.85                      |      | 55.55               | 48.60                      |  |                              |                              |
| SD                                           | 9.96              | 15.71                      |      | 14.87               | 15.80                      |  |                              |                              |
| Range                                        | 42 – 75           | 25 – 75                    |      | 27 – 83             | 25 – 76                    |  |                              |                              |
| Race and ethnicity, n (%)                    |                   |                            | 1.00 |                     |                            |  | 1.00                         |                              |
| Non-Hispanic white                           | 19 (95)           | 19 (95)                    |      | 18 (90)             | 19 (95)                    |  |                              |                              |
| Employment status, n (%)                     |                   |                            | 0.53 |                     |                            |  | 0.11                         |                              |
| Employed full or part-time                   | 6 (30)            | 6 (30)                     |      | 9 (45)              | 14 (70)                    |  |                              |                              |
| Retired                                      | 6 (30)            | 9 (45)                     |      | 8 (40)              | 5 (25)                     |  |                              |                              |
| Unemployed                                   | 7 (35)            | 3 (15)                     |      | 0 (0)               | 1 (5)                      |  |                              |                              |
| Other                                        | 1 (5)             | 2 (10)                     |      | 3 (15)              | 0 (0)                      |  |                              |                              |
| Household income US\$, n (%) <sup>a</sup>    |                   |                            | 0.71 |                     |                            |  | 0.45                         |                              |
| \$0 – \$50,999                               | 5 (25)            | 7 (35)                     |      | 5 (25)              | 6 (30)                     |  |                              |                              |
| \$51,000 – \$99,999                          | 5 (25)            | 3 (15)                     |      | 9 (45)              | 5 (25)                     |  |                              |                              |
| \$100,000 or more                            | 10 (50)           | 9 (45)                     |      | 6 (30)              | 9 (45)                     |  |                              |                              |
| Missing                                      | 0 (0)             | 1 (5)                      |      | ---                 | ---                        |  |                              |                              |
| Years of education                           |                   |                            | 0.34 |                     |                            |  | 0.79                         |                              |
| Mean                                         | 15.48             | 14.70                      |      | 15.23               | 15.45                      |  |                              |                              |
| SD                                           | 2.66              | 2.45                       |      | 2.67                | 2.61                       |  |                              |                              |
| Range                                        | 12 – 23           | 12 – 20                    |      | 11 – 20             | 12 – 20                    |  |                              |                              |
| Caregiver relationship to the patient, n (%) |                   |                            |      |                     |                            |  | 1.00                         |                              |
| Spouse/partner                               | ---               | ---                        |      | 12 (60)             | 13 (65)                    |  |                              |                              |
| Other family member                          | ---               | ---                        |      | 8 (40)              | 7 (35)                     |  |                              |                              |
| Married/living with a partner, n (%)         | 15 (75)           | 15 (75)                    | 1.00 | 15 (75)             | 17 (85)                    |  | 0.70                         |                              |

| Characteristics                         | Patients (n = 40) |                            |                              | Caregivers (n = 40) |                            |                              |
|-----------------------------------------|-------------------|----------------------------|------------------------------|---------------------|----------------------------|------------------------------|
|                                         | ACT (n = 20)      | Education/Support (n = 20) | t-test/Fisher's Exact Test p | ACT (n = 20)        | Education/Support (n = 20) | t-test/Fisher's Exact Test p |
| Caregiver lives with the patient, n (%) | ---               | ---                        |                              | 15 (75)             | 15 (75)                    | 1.00                         |
| Type of gastrointestinal cancer, n (%)  |                   |                            | 0.29                         |                     |                            |                              |
| Colorectal                              | 10 (50)           | 6 (30)                     |                              | ---                 | ---                        |                              |
| Pancreatic                              | 3 (15)            | 7 (35)                     |                              | ---                 | ---                        |                              |
| Other (e.g., stomach, liver, anal)      | 7 (35)            | 7 (35)                     |                              | ---                 | ---                        |                              |
| Time since diagnosis in years           |                   |                            | 0.43                         |                     |                            |                              |
| Mean                                    | 2.40              | 1.67                       |                              | ---                 | ---                        |                              |
| SD                                      | 2.36              | 3.30                       |                              | ---                 | ---                        |                              |
| Range                                   | 0.13 – 9.48       | 0.12 – 15.04               |                              | ---                 | ---                        |                              |
| Treatments received, n (%)              |                   |                            |                              |                     |                            |                              |
| Chemotherapy                            | 15 (75)           | 17 (85)                    |                              | ---                 | ---                        |                              |
| Radiation                               | 2 (10)            | 6 (30)                     |                              | ---                 | ---                        |                              |
| Chemoradiation                          | 5 (25)            | 4 (20)                     |                              | ---                 | ---                        |                              |
| Surgery to remove primary tumor         | 12 (60)           | 11 (55)                    |                              | ---                 | ---                        |                              |
| Surgery to remove metastases            | 7 (35)            | 4 (20)                     |                              | ---                 | ---                        |                              |
| Targeted therapy                        | 9 (45)            | 5 (25)                     |                              | ---                 | ---                        |                              |
| Patient ECOG score                      |                   |                            | 0.85                         |                     |                            |                              |
| Mean                                    | 1.40              | 1.45                       |                              | ---                 | ---                        |                              |
| SD                                      | 0.82              | 0.89                       |                              | ---                 | ---                        |                              |
| Range                                   | 0 – 3             | 0 – 3                      |                              | ---                 | ---                        |                              |
| Number of comorbidities                 |                   |                            | 0.81                         |                     |                            | 0.53                         |
| Mean                                    | 1.35              | 1.45                       |                              | 1.05                | 0.80                       |                              |
| SD                                      | 0.93              | 1.61                       |                              | 1.47                | 1.01                       |                              |
| Range                                   | 0 – 3             | 0 – 5                      |                              | 0 – 5               | 0 – 3                      |                              |

ACT = Acceptance and Commitment Therapy; ECOG = Eastern Cooperative Oncology Group.

<sup>4</sup>The median US household income in 2020 was \$67,521.<sup>72</sup>

**Table 4.**

Results from multiply imputed multilevel linear models ( $N = 40$  dyads).

| Outcome Fixed Effect <sup>d</sup> | ACT          |              |                           |              |                            |              | df | F    | p    | Pr   | 95% CI Pr |                   |           |
|-----------------------------------|--------------|--------------|---------------------------|--------------|----------------------------|--------------|----|------|------|------|-----------|-------------------|-----------|
|                                   | Baseline     |              | 2 Weeks Post-intervention |              | 3 Months Post-intervention |              |    |      |      |      |           | Education/Support |           |
|                                   | Mean (SD)    | Mean (SD)    | Mean (SD)                 | Mean (SD)    | Mean (SD)                  | Mean (SD)    |    |      |      |      |           | Mean (SD)         | Mean (SD) |
| <b>Primary Outcomes:</b>          |              |              |                           |              |                            |              |    |      |      |      |           |                   |           |
| PT fatigue interference           | 4.25 (1.86)  | 3.93 (2.17)  | 4.27 (1.66)               | 3.58 (1.92)  | 3.47 (2.54)                | 4.26 (2.12)  | 38 | 0.47 | 0.50 | 0.11 | -0.20     | 0.42              |           |
| Group                             |              |              |                           |              |                            |              |    |      |      |      |           |                   |           |
| Time                              |              |              |                           |              |                            |              | 76 | 1.15 | 0.32 | 0.12 | -0.19     | 0.44              |           |
| Group × time                      |              |              |                           |              |                            |              | 76 | 0.52 | 0.60 | 0.08 | -0.23     | 0.40              |           |
| CG burden                         | 15.85 (3.82) | 13.92 (3.86) | 15.32 (4.59)              | 18.45 (8.52) | 16.37 (7.10)               | 18.17 (8.36) | 38 | 2.22 | 0.14 | 0.24 | -0.07     | 0.54              |           |
| Group                             |              |              |                           |              |                            |              |    |      |      |      |           |                   |           |
| Time                              |              |              |                           |              |                            |              | 76 | 2.93 | 0.05 | 0.19 | -0.11     | 0.50              |           |
| Group × time                      |              |              |                           |              |                            |              | 76 | 0.04 | 0.96 | 0.02 | -0.29     | 0.34              |           |
| <b>Secondary Outcomes:</b>        |              |              |                           |              |                            |              |    |      |      |      |           |                   |           |
| PT sleep interference             | 58.30 (7.08) | 57.37 (4.03) | 56.91 (5.22)              | 53.60 (6.33) | 52.99 (8.38)               | 53.86 (7.41) | 38 | 6.00 | 0.01 | 0.37 | 0.09      | 0.64              |           |
| Group                             |              |              |                           |              |                            |              |    |      |      |      |           |                   |           |
| Time                              |              |              |                           |              |                            |              | 76 | 0.27 | 0.76 | 0.06 | -0.26     | 0.38              |           |
| Group × time                      |              |              |                           |              |                            |              | 76 | 0.29 | 0.75 | 0.06 | -0.25     | 0.38              |           |
| PT physical QoL                   | 14.85 (5.37) | 17.30 (6.34) | 13.48 (5.40)              | 15.60 (6.31) | 16.89 (6.20)               | 14.80 (6.33) | 38 | 0.13 | 0.72 | 0.06 | -0.26     | 0.38              |           |
| Group                             |              |              |                           |              |                            |              |    |      |      |      |           |                   |           |
| Time                              |              |              |                           |              |                            |              | 76 | 3.97 | 0.02 | 0.22 | -0.08     | 0.52              |           |
| Group × time                      |              |              |                           |              |                            |              | 76 | 0.30 | 0.74 | 0.06 | -0.25     | 0.38              |           |
| PT psychological QoL              | 26.65 (9.40) | 28.58 (8.31) | 28.66 (8.36)              | 27.60 (7.29) | 29.98 (5.99)               | 26.09 (8.27) | 38 | 0.01 | 0.94 | 0.01 | -0.30     | 0.33              |           |
| Group                             |              |              |                           |              |                            |              |    |      |      |      |           |                   |           |
| Time                              |              |              |                           |              |                            |              | 76 | 1.86 | 0.16 | 0.15 | -0.16     | 0.46              |           |
| Group × time                      |              |              |                           |              |                            |              | 76 | 1.44 | 0.24 | 0.14 | -0.18     | 0.45              |           |
| PT existential QoL                | 26.55 (5.88) | 28.18 (5.35) | 28.25 (4.57)              | 26.70 (4.35) | 28.15 (5.06)               | 27.15 (4.83) | 38 | 0.07 | 0.79 | 0.04 | -0.27     | 0.36              |           |
| Group                             |              |              |                           |              |                            |              |    |      |      |      |           |                   |           |
| Time                              |              |              |                           |              |                            |              | 76 | 1.53 | 0.22 | 0.14 | -0.17     | 0.45              |           |

| Outcome Fixed Effect <sup>d</sup> | ACT               |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
|-----------------------------------|-------------------|---------------------------|----------------------------|--------------|---------------------------|----------------------------|----------|---------------------------|----------------------------|----------|---------------------------|----------------------------|--|--|--|--|--|--|--|--|--|--|
|                                   | Education/Support |                           |                            |              |                           |                            | ACT      |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
|                                   | Baseline          | 2 Weeks Post-intervention | 3 Months Post-intervention | Baseline     | 2 Weeks Post-intervention | 3 Months Post-intervention | Baseline | 2 Weeks Post-intervention | 3 Months Post-intervention | Baseline | 2 Weeks Post-intervention | 3 Months Post-intervention |  |  |  |  |  |  |  |  |  |  |
| Group × time                      |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| PT social QoL                     | 23.45 (5.66)      | 24.59 (5.18)              | 25.28 (4.30)               | 25.45 (3.85) | 24.80 (5.32)              | 25.64 (3.51)               |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Group                             |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Time                              |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Group × time                      |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| CG physical QoL                   | 44.68 (6.28)      | 46.11 (6.02)              | 45.58 (4.42)               | 44.33 (4.70) | 45.34 (5.24)              | 44.68 (3.33)               |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Group                             |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Time                              |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Group × time                      |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| CG psychological QoL              | 41.91 (6.11)      | 45.01 (5.11)              | 43.99 (4.50)               | 41.38 (8.05) | 43.48 (7.48)              | 43.30 (5.90)               |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Group                             |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Time                              |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Group × time                      |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| PT activity engagement            | 44.66 (7.04)      | 45.02 (6.60)              | 45.58 (6.92)               | 45.43 (6.07) | 42.42 (7.26)              | 46.14 (5.01)               |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| CG activity engagement            | 43.85 (3.91)      | 42.56 (4.66)              | 40.34 (2.62)               | 43.91 (8.32) | 40.40 (7.05)              | 41.04 (8.11)               |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Group                             |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Time                              |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Role                              |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Time × role                       |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Group × time                      |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Group × role                      |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Group × time × role               |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| PT values progress                | 21.90 (5.23)      | 21.71 (3.49)              | 22.71 (3.26)               | 21.75 (4.33) | 21.30 (5.29)              | 21.66 (5.09)               |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| CG values progress                | 22.10 (4.58)      | 23.05 (5.39)              | 22.97 (2.62)               | 19.75 (5.18) | 21.14 (4.33)              | 22.44 (3.05)               |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Group                             |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Time                              |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Role                              |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Time × role                       |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |
| Group × time                      |                   |                           |                            |              |                           |                            |          |                           |                            |          |                           |                            |  |  |  |  |  |  |  |  |  |  |

