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Original article

Effect of mHealth plus occupational therapy on cognitive function, mood and physical function in people after cancer: Secondary analysis of a randomized controlled trial

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A B S T R A C T

Background: Medical and surgical treatments for breast cancer have various adverse effects. Both mobile health and supervised intervention strategies have been implemented to overcome these effects, but some gaps remain to be addressed. Scientific evidence for the effectiveness of occupational therapy in cancer is limited.
Objective: To compare the clinical effectiveness of the BENECA mHealth app used alone or combined with an integral supervised rehabilitation strategy that focused on cognitive performance, mood state, functional capacity, and cancer-related pain and fatigue in overweight women after breast cancer.
Methods: In this secondary analysis of an assessor-blinded randomized controlled clinical trial, 80 overweight women after breast cancer (stage I-IIIA) were randomly allocated to an integral approach group (IA; *n*=40) or a control group (CG; *n*=40). All participants participated in an 8-week intervention. Assessments were performed at baseline, 8 weeks, and 6 months and included cognitive performance (Trial Making Test and Wechsler Adult Intelligence Scale), psychological state (Hospital Anxiety and Depression Scale), pain (Brief Pain Inventory), fatigue (Piper Fatigue Scale), and physical function (6 min walk test). An intention-to-treat analysis was conducted with analysis of covariance.
Results: Selective attention (TMT) was significantly higher in the IA group, with a moderate to large effect size for TMT A (T2: d=1.1; T 3: d=1.2), working memory and processing speed (WAIS), anxiety and general HADS score (*d*=1.6), and functional capacity at 8 weeks and 6 months (*d*=1.5). Fatigue perception (mean difference, -0.6; 95% CI -1.4 to 0.04; *p*=0.009) and pain (intensity level *p*<0.001; interference level *p*=0.002) were also significantly more improved in the IA group.
Conclusions: An integral strategy involving the BENECA mHealth app with a supervised, multimodal intervention improved cognitive, psychological, and functional performance in women after breast cancer more than mHealth alone. Occupational therapy has a role to play in breast cancer rehabilitation.

Introduction

Cancer-related cognitive impairment is a highly reported problem in women after breast cancer [1]. Estimates of the rates of cognitive impairment related to cancer or chemotherapy treatment are varied, but the prevalence has been established to be between 65% and 75% after chemotherapy is completed, and 60% of individuals experience

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late effects [2]. The exact causes of this phenomenon are not well known, but studies suggest it results from the cancer and its treatment and the individual's lifestyle and health [2]. Obesity can increase the risk of cancer worsening, recurrence and mortality and is also associated with neurocognitive disorders and poor mood in adults [3]. The effect on anxiety and depression is particularly relevant in women after cancer: after treatment, more than 30% of women experience anxiety and depression, which can persist for up to 10 years after diagnosis [4].

In addition to the emotional effects of cancer, cancer-related pain and fatigue form a cluster of symptoms that that lead to general deconditioning. Chronic pain is the most reported complication and usually has a neuropathic and nociceptive origin. Moderate to severe cancer-related fatigue is experienced by as many as one-third of women, even 10 years after the completion of treatment [4] and approximately 90% will have permanent treatment-related sequelae of this type [5]. These factors have a negative impact on the performance of their daily activities and on the satisfaction perceived in carrying them out [6]. New and effective intervention strategies are thus necessary.

Many women also report an inability to fully participate in social, physical, or instrumental activities of daily living after cancer treatment [7]. Occupational therapy (OT) is the most relevant rehabilitation discipline to address these difficulties. OT has been shown to improve psychological, cognitive, and functional processes in several populations including older people and those with stroke or hip fracture [8–10]. However, the scientific evidence available for its effectiveness in oncological populations is limited and inconclusive [11]. Innovative research is thus needed to fill the gap in the literature.

Our research team recently developed a randomized clinical trial that attempted to address the issues raised above. A mobile health application (app) called BENECA was designed and validated to monitor energy balance and promote a healthy lifestyle among women after cancer. We also developed an integral strategy that combined this application with a face-to-face OT rehabilitation program [12]. Our main results showed that this multimodal program is feasible and safe, and that it significantly improves quality of life, active range of motion, and upper limb function after 8 weeks of intervention [13]. The objective of this secondary analysis was to compare the clinical effectiveness of the BENECA mHealth app used alone versus the integral supervised rehabilitation strategy on cognitive performance, mood state, functional capacity, and cancer-related pain and fatigue. We hypothesized that both strategies would improve outcomes but that the integral strategy would produce larger improvements than the BENECA-alone strategy.

Methods

Study design and procedures

The rationale and study design have been previously described [12,13]. In brief, an assessor-blinded randomized controlled clinical trial compared an 8-week integral approach that combined the BENECA mHealth app and a face-to-face OT program (integral approach group: IA) with a usual care group that only received the mHealth lifestyle app (control group: CG). Both groups were followed up at 6 months. The study was approved by the Research Ethics Committee of the province of Granada (FIS PI14-01627). We reported the study according to the Consolidated Standards of Reporting Trials (**CONSORT**) statement.

Integral approach

The BENECA app is a validated mobile health application [14,15] that monitors the energy balance of individuals in terms of physical activity and diet. It provides real-time feedback about a possible energy imbalance and recommendations to improve this [14]. The program included technical-therapeutic activities based on the Occupational Therapy Practice Framework: Domain and Process developed from the American Occupational Therapy Association [16] and Cognitive Orientation to Daily Occupational Performance (CO-OP) cognitive functional training [17] (supplementary Table 1). No major changes in methodology were made after the start of the trial [12,13].

Participants

The sociodemographic and clinical characteristics of the participants can be found in a previously published study, along with the RCT flowchart [13]. Participants were recruited from two hospitals: "Virgen de las Nieves" University Hospital and "San Cecilio" University Hospital, Granada (Spain). Eligible participants 1) were aged 25-75 years, 2) were diagnosed with stage I-IIIA breast cancer, 3) were overweight or obese according to the Spanish SEEDO guideline, 4) were able to access mobile apps or living with someone who had this ability, 5) were medically cleared for participation, 6) completed adjuvant therapy, except hormonal therapy, and 7) signed informed consent. The exclusion criteria were: 1) cancer recurrence, 2) chronic disease or orthopaedic issues that would interfere with study participation, and 3) uncontrolled hypertension (diastolic pressure > 95 mmHg).

Randomization and masking

In our previous primary study, subjects were randomly assigned using 3 waves (25:30:25) (Epidat, v. 4.2, 2016. Consellería de Sanidade, Xunta de Galicia, España; Organización Panamericana de la salud; Universidad CES, Colombia). An external researcher was responsible for treatment allocation with opaque envelopes to ensure blinding of the assessor to the whole randomisation process.

Outcomes

Participants were evaluated at 3 stages: baseline (T1), postintervention (T2) and 6-month follow-up (T3). The outcomes of the current study are described below.

Cognitive performance

Trail making test (TMT). TMT part A (TMT-A) consists of randomly connecting numbers from 1 to 25 as quickly as possible in the correct way. This test portion is related to visual searching, visual scanning attention and motor speed. In TMT part B (TMT-B), both numbers (from 1 to 13) and letters (from A to L) are connected in an alternating manner (1-A-2-B-3-C, etc.). TMT-B has been reported as a valid measure of the executive function of set shifting**.** The time required is recorded for both sections (s). We also calculated the derived ratio score (TMT-B/TMT-A).

Wechsler adult intelligence scale (WAIS). The Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV) is a recognized task in neuropsychological assessments. Considering our purpose, we used only two subtests of a total of 15 (core and supplemental subtests). The Working Memory Index (WMI) measures how well the individual can remember things using two specific tasks (arithmetic and digit span), and the Processing Speed Index (PSI) evaluates how quickly the person works with the other two tasks (digit symbol coding and symbol search). We calculated WAIS-IV scores according to standardized procedures (Cronbach's alpha > 0.9).

Psychological state

Hospital anxiety and depression scale (HADS). The HADS measures symptoms of anxiety and depression in people with cancer. It contains 14 items on a four-point Likert scale (ranging from 0 to 3) to assess anxiety (odd items) and depression (even items) (Cronbach's α=0.85 and α=0.83, respectively).

Pain perception and fatigue

Brief pain inventory (BPI). The BPI short form (BPI-SF) includes 4 intensity and 7 interference pain items. All of them refer to the last 24 h. In this study, both blocks of items were averaged (Cronbach's α=0.87-0.89).

Piper fatigue scale (PFS). The revised version (R-PFS) of this scale was used to measure fatigue, with a total of 22 items divided into 4 dimensions: behavioural/severity, affective meaning, sensory, and cognitive/mood (Cronbach's α=0.97).

Functional capacity

6 min walk test (6MWT). The test was performed in a 30-m-long hallway in our research centre. Participants were asked to walk as quickly as possible for 6 min while a qualified staff member counted every lap (60-m round trip). During the task, standardized phrases of encouragement were given (intraclass correlation coefficient = 0.88<r<0.94).

Data analyses

First, descriptive analysis and normal distribution verification tests were carried out. Second, homogeneity between groups at baseline was tested using a Student *t* or Chi-squared/Fisher tests or equivalent nonparametric tests, as appropriate. The data contained few missing values (< 5% of the total number of cases), thus we considered missing values to be random and inconsequential and did not apply any imputation method. Finally, and consistent with our main analysis, we used intention-to-treat (ITT) analysis. If a significant interaction was found in the analysis of covariance (ANCOVA), we performed a *post hoc* Bonferroni test. Based on clinical and research knowledge, we analysed the following covariates: age, BMI, type of surgery, cancer treatment received, stage, time since diagnosis and surgery, and marital status. We calculated Cohen *d* effect sizes (ES) to examine clinical differences. All statistical tests were two-tailed and p< 0.05 was considered significant. To avoid repeating details that have been published elsewhere, we have provided here a summary of the statistical data. All statistical analyses were performed using Stata Statistical Software StataCorp. 2019: Release 16. College Station, TX: StataCorp LLC.

Results

The final sample included in the analysis consisted of 78 women after breast cancer: IA group (n=40) and CG (n=38). The baseline scores of each of the variables did not differ between groups (Supplementary Table 2).

Cognitive performance

For the TMT (Table 1) the main ANCOVA indicated a significant time x group interaction for both parts A (*F*=15.1; *p*<0.001) and B (*F*=4.5; *p*=0.014) as well as the ratio score (*F*=5.8; *p*=0.004), with higher scores in the IA group. Between-group analysis of change from T1 to T2 showed significantly greater change in the IA group, with a greater reduction in performance time: part A (*p*<0.001), part B (*p*=0.004) and the ratio score (*p*=0.005). At T3, although scores improved in the CG, the significantly greater improvements in the IA group were maintained on all subscales: part A (*p*<0.001), part B (*p*=0.035), and the ratio score (*p*=0.002). The results did not change when the covariates were included.

For the WAIS (Table 1), significant interactions were found for both the WMI (*F*=13.5; *p*<0.001) and the PSI (*F*=5.4; *p*<0.006), with higher scores in the IA group than in the CG. The scores for both subscales improved in both groups from T1 to T2, however, between-group analysis of change showed that the change in the IA group was significantly greater than that of the CG: WMI (*p*<0.001) and PSI (*p*=0.036). At T3, the greater improvement in the IA group were maintained, whereas the CG group score decreased slightly compared with T1: WAIS (*p*<0.001) and PSI (*p*=0.002). The results did not change when the covariates were included.

Psychological state

For the HADS (Fig. 1), the main ANCOVA indicated a significant time x group interaction on the anxiety subscale (*F*=24.7; *p*<0.001) and the global score (*F*=13.1; *p*<0,001) but not on the depression subscale (*F*=0.8; *p*=0.463). At T2, anxiety levels (*p*<0.001) and overall score (*p*<0.001) were significantly more reduced in the IA group compared than the CG. At T3, the between-group difference was maintained for both anxiety (*p*<0.001) and global score (*p*=0.001). The results did not change when the covariates were included.

Pain perception

For the BPI (Table 2), there was a significant time x group interaction for the intensity level (*F*=25.6; *p*<0.001) and the interference level (*F*=6.6; *p*=0.002). Between-group analysis of change from T1 to T2 showed a significantly higher reduction in pain intensity perception score (*p*<0.001) and pain interference (*p*=0.001) in the IA group than the CG. At T3, between-group differences were maintained on the intensity subscale (*p*<0.001), whereas the interference subscale showed a trend towards significance (*p*=0.050). The results did not change when the covariates were included.

Fatigue

For the PFS (Table 2), the main analysis showed a significant time x group interaction for the cognitive (*F*=7.9; *p*=0.001) and affective (*F*=3.5; *p*=0.036) dimensions as well as in the overall scale score (*F*=5.0; *p*=0.009) but not in the behaviour (*F*=2.1; *p*=0.125) or mood (*F*=1.3; p=0.287) dimensions. From T1 to T2 perception of fatigue reduced in the cognitive dimension for the IA group (*p*<0.001), whereas it increased in the CG for this dimension. Affective dimension (*p*=0.024) and global score (*p*=0.007) both reduced in both groups, with a significantly greater reduction in the IA group. At T3, only the between-group difference for the cognitive dimension was maintained (*p*=0.007), with a tendency towards significance on the global score (*p*=0.074), and a loss of the effect on the affective dimension (*p*=0.334). All the scores were better in the IA group for the other items, although the between-group difference was not significant. The results did not change when the covariates were included.

Functional capacity

For the 6MWT (Fig. 2), significant effects for distance were found in the main analysis (*F*=24.0; *p*<0001). Distance walked improved in both groups from T1 to T2 and T1 to T3, however between-group analysis of change from T1 to T2 showed that distance walked improved significantly more in the IA group (*p*<0.001); this effect was maintained at T3 (*p*<0.001). The results did not change when the covariates were included.

Table 1
Within-group and between-group effects for cognitive outcome measures at T1–T3.

Outcome Measures	Study Group Control Group (n = 38) mean (SD; 95% CI)	IA Group (n = 39)[a] mean (SD; 95% CI)	Between-Group Effects mean diff (95% CI)
Trail Making Test (TMT)			
TMT A			
T1	40.9 (19.0; 34.7 to 47.2)	45.4 (13.2; 41.1 to 49.7)	
T2	39.90 (18.9; 33.7 to 46.1)	35.1 (9.9; 31.9 to 38.3)	
T3	40.5 (17.8; 34.7 to 46.4)	34.9 (9.4; 31.9 to 37.9)	
Within-group effects			
T1 to T2	-1.0 (-3.8 to 1.7)	-10.3 (-12.9 to -7.8)	-9.3 (-12.9 to -5.6)[b]
T1 to T3	-0.4 (-3.0 to 2.2)	-10.5 (-13.1 to -7.9)	-10.1 (-13.8 to -6.4)[b]
TMT B			
T1	97.9 (30.4; (87.9 to 107.9)	107.3 (35.9; 95.7 to 118.9)	
T2	93.0 (27.9; 83.8 to 102.2)	92.9 (25.9; 84.5 to 101.4)	
T3	91.8 (27.3; 82.8 to 100.8)	92.5 (24.8; 84.5 to 100.5)	
Within-group effects			
T1 to T2	-4.9 (-9.4 to -0.4)	-14.4 (-18.8 to -9.9)	-9.5 (-15.8 to -3.1)[c]
T1 to T3	-6.1 (-11.9 to -0.3)	-14.8 (-20.5 to -9.1)	-8.7 (-16.8 to -0.6)[c]
TMT Ratio B:A			
T1	2.6 (0.8; 2.4 to 2.9)	2.50 (0.9; 2.1 to 2.8)	
T2	2.5 (0.7; 2.3 to 2.8)	2.8 (0.9; 2.5 to 3.1)	
T3	2.4 (0.7; 2.2 to 2.7)	2.8 (0.9; 2.5 to 3.1)	
Within-group effects			
T1 to T2	-0.1 (-0.3 to 0.1)	0.3 (0.1 to 0.4)	0.4 (0.1 to 0.6)[c]
T1 to T3	-0.2 (-0.4 to 0.03)	0.3 (0.1 to 0.5)	0.5 (0.1 to 0.7)[c]
Wechsler Adult Intelligence Scale			
WMI			
T1	76.7 (15.6; 71.6 to 81.9)	72.3 (17.9; 66.5 to 78.0)	
T2	84.9 (13.2; 80.6 to 89.3)	99.3 (15.0; 94.5 to 104.1)	
T3	80.6 (14.4; 75.8 to 85.3)	95.9 (9.9; 92.8 to; 99.1)	
Within-group effects			
T1 to T2	8.2 (2.1 to 14.2)	27.1 (21.2 to 33.0)	18.9 (10.4 to 27.3)[b]
T1 to T3	3.8 (-1.6 to 9.2)	23.7 (18.4 to 29.0)	19.9 (12.3 to 27.4)[b]
PSI			
T1	95.4 (11.0; 91.8 to 99.0)	92.9 (16.8; 87.6 to 98.3)	
T2	97.6 (12.8; 93.4 to 101.9)	102.6 (12.1; 98.7 to 106.4)	
T3	94.7 (11.9; 90.8 to 98.7)	103.1 (12.2; 99.2 to 107.0)	
Within-group effects			
T1 to T2	2.2 (-2.8 to 7.2)	9.7 (4.8 to 14.5)	7.4 (0.5 to 14.4)[c]
T1 to T3	-0.7 (-5.4 to 4.0)	10.2 (5.5 to 14.8)	10.8 (4.2 to 17.4)[c]

Abreviations: CI, Confidence Interval; PSI, Processing Speed Index; WMI, Working Memory Index. Bonferroni adjustment was used for pairwise comparisons.
[a] A withdrawal due to the impossibility of taking the test on the day of the evaluation
[b] p<0.001 (significant between-groups effect)
[c] p<0.05 (significant between-groups effect).

Clinical effect

The ES of the significant differences between groups at T2 and T3 are shown in Fig. 3. Most ES were moderate to large, with the largest ES found at T2 and T3 for TMT A time (*d*=1.1; CI 95% 0.7−1.6; *d*=1.2; CI 95% 0,7−1,7, respectively), as well as for the reduction in the anxiety level measured with the HADS (*d*=1.6; CI 95% 1.1−2.1; *d*=1.2; CI 95% 0.6−1.5, respectively), and functional capacity assessed with the 6MWT (*d*=1.5; CI 95% 1.0−2.01; *d*=1.2; CI 95% 0.6−1.6, respectively).

Discussion

The results showed improvements in most variables for both the IA group and CG, however, improvements were significantly greater in the IA group for selective attention (TMT), working memory and processing speed (WAIS), anxiety, general HADS score and functional capacity (6MWT) after the intervention. Furthermore, results were mostly maintained at 6 months. Fatigue perception and pain also improved more in the IA group, especially after intervention, with some scores maintained at 6 months.

Cognitive performance

ES for the TMT and WAIS subscales were larger in the IA group after the intervention (moderate-to-large) (*d* >1). There is a lack of studies on multimodal interventions for cognitive impairment in women with breast cancer post-chemotherapy [18], but the existing evidence indicates that multimodal approaches for the treatment of cognitive decline may be more effective than single modalities owing to the enhanced brain stimulation from different interventions [18].

Nonpharmacological cognitive treatments based on cognitive interventions, physical activity or meditation/relaxation techniques have also been shown to improve cognitive impairment in individuals after cancer [19]. However, these improvements have been mainly found in evaluations close to the end of treatment (immediately after intervention [20] and 2 months after completion [21]) in studies involving computer applications. These results corroborate the more significant improvement in scores in our CG at the end of the mHealth app intervention than at the 6-month follow-up. In contrast, improvements were greater in the IA group at all time points. A study involving a supervised cognitive-behavioural approach that comprised cognitive skills, education, self-awareness, and activity scheduling with a phone call follow-up found improvements in cognitive function and quality of life that were also maintained at 6 months (ES for TMTA = 0.9 and for TMTB = 0.6) [22]. We believe that the similar results of the present study, as well as the maintenance of the effect size in the long term, may be due to the combination of functionally based cognitive training involving on purposeful activity combined with strategies that included new technologies, as pointed out in recent systematic reviews [23]. This theory supports our hypothesis regarding the need to combine strategies to provide a comprehensive and holistic intervention for women after breast cancer.

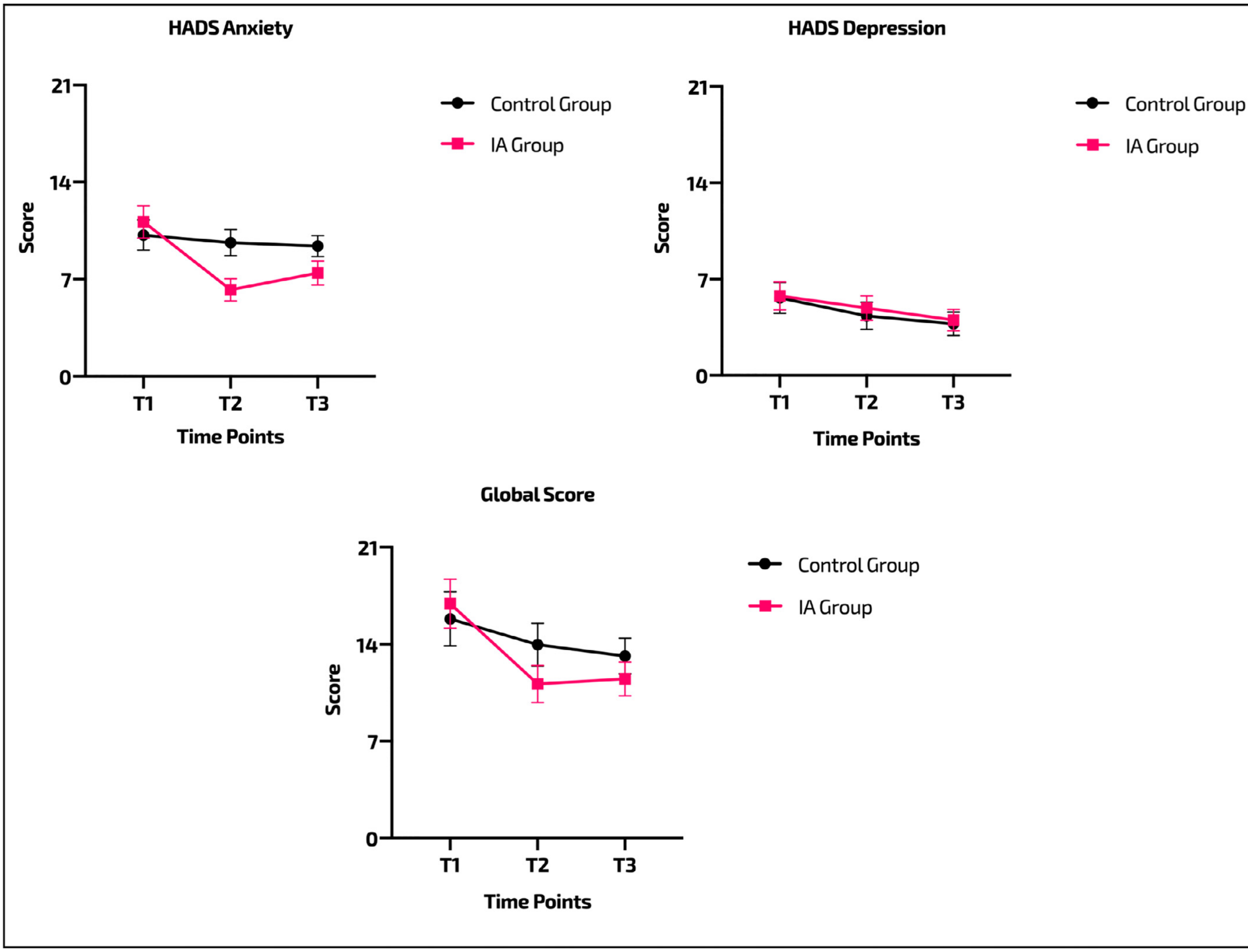

Fig. 1. Within-group and between-group effects for mean HADS outcome measures at T1, T2 and T3.Data are shown as mean and 95% CI for the mean values at baseline (T1), end of the 8-week intervention (T2) and 6-month follow-up (T3).

Psychological state

Several studies have also found that psychosocial strategies, including educational [24] and exercise interventions [25], reduce anxiety and depression post-treatment. For example, a recent study compared the effects of the use of a health and wellness coaching app versus a self-guided toolkit and one-time health education session to improve diet, physical activity rates, weight loss, depression, and fatigue in women with breast cancer (stage 0-III). In the app group, weight reduced, levels of strenuous physical activity increased, and dietary patterns improved. Fatigue and depression also improved although not significantly [26]. This matches our findings regarding depression levels, which did not improve as much as the other variables. We believe that this may relate to the duration of our study (8 weeks): it seems that interventions that last longer than 12 weeks produced larger effects on depression.

Pain

The between-group ES for pain interference was moderate however, the ES for pain intensity was large, in favour of the IA group. The evidence on the benefits of different interventions for pain in people with breast cancer mostly refers to unimodal treatments. However, the considerable heterogeneity of the available studies of this type and their methodological limitations prevent well-established conclusions from being drawn. We believe that the multimodal approach of our program accounts for the improvements in the variables evaluated and explains the significant improvements in pain levels in the IA group.

Fatigue

The between-group ES for fatigue was moderate for all the subscales. It is known that exercise interventions significantly reduce fatigue levels in people with cancer. A recent meta-analysis stated that exercise produces moderate benefits for cognitive, physical, and general cancer-related fatigue ($p<0.01$) [27], and studies of other mobile health interventions have also found that exercise contributes to reducing fatigue more than a self-guided toolkit or usual care [26]. Nevertheless, the self-management of perceived fatigue is influenced not only by treatment or physical state but also by social support [28]. The participants in the IA group were integrated into a group composed of health personnel and peers who provided social support during the intervention. This group created bonds that we think positively influenced improvements in their subjective perception of fatigue that may partly explain the significantly lower levels of fatigue in all subscales compared to the CG. Nonetheless, the type of exercise we implemented may also have influenced the results. Low- and moderate-intensity exercise seems to be more effective than high intensity exercise; it allows the individual to pace themselves

Table 2
Within-group and between-group effects for pain and fatigue measures at T1–T3.

Outcome Measures	Study Group Control Group (n = 38) mean (SD; 95% CI)	IA Group (n = 40) mean (SD; 95% CI)	Between-Group Effects mean diff (95% CI)
Brief Pain Inventory (BPI)			
BPI Intensity			
Baseline	4.3 (1.6; 3.8 to 4.9)	4.9 (1.9; 4.4 to 5.6)	
8 week Intervention	4.5 (1.9; 3.9 to 5.2)	2.4 (1.7; 1.8 to 2.9)	
6 months Follow-up	3.9 (1.7; 3.4 to 4.5)	2.3 (1.7; 1.8 to 2.9)	
Within-group effects			
Baseline to 8 weeks	0.22 (-0.33 to 0.78)	-2.56 (-3.10 to -2.02)	-2.8 (-3.6 to -2.0)[a]
Baseline to 6 months	-0.3 (-0.9 to 0.3)	-2.7 (-3.3 to -2.0)	-2.3 (-3.2 to -1.4)[a]
BPI Interference			
Baseline	4.9 (1.9; 4.3 to 5.6)	4.6 (2.1; 3.9 to 5.3)	
8 week Intervention	3.8 (1.9; 3.2 to; 4.4)	2.0 (1.9; 1.4 to; 2.7)	
6 months Follow-up	3.5 (1.9; 2.8 to; 4.1)	2.2 (2.0) (1.5; 2.8)	
Within-group effects			
Baseline to 8 weeks	-1.1 (-1.7 to -0.5)	-2.5 (-3.1 to -1.9)	-1.4 (0.6 to 2.3)[b]
Baseline to 6 months	-1.4 (-2.1 to -0.7)	-2.4 (-3.1 to -1.7)	-0.9 (-1.9 to -0.01)
Piper Fatigue Scale (PFS)			
PFS Behaviour			
Baseline	3.8 (2.5; 2.9 to 4.6)	3.1 (2.2; 2.4 to 2.9)	
8 week Intervention	3.4 (2.1; 2.7 to; 4.1)	1.9 (1.7; 1.4 to 2.5)	
6 months Follow-up	3.2 (1.9; 2.6 to; 2.9)	1.9 (1.5; 1.5 to 2.5)	
Within-group effects			
Baseline to 8 weeks	-0.4 (-0.9 to 0.1)	-1.1 (-1.6 to -0.5)	-0.7 (-1.4 to 0.0)
Baseline to 6 months	-0.5 (-1.1 to 0.1)	-1.0 (-1.6 to -0.5)	-0.5 (-1.3 to 0.3)
PFS Mood			
Baseline	3.3 (2.2; 2.6 to 4.1)	3.6 (2.6; 2.8 to; 4.4)	
8 week Intervention	2.9 (2.1; 2.2 to; 3.6)	2.5 (1.8; 1.9 to 3.0)	
6 months Follow-up	2.7 (1.7; 2.1 to 3.3)	2.5 (1.8; 1.9 to 3.1)	
Within-group effects			
Baseline to 8 weeks	-0.4 (-1.0 to 0.2)	-1.0 (-1.7 to -0.4)	-0.6 (-1.5 to 0.2)
Baseline to 6 months	-0.6 (-1.2 to 0.0)	-1.0 (-1.6 to -0.4)	-0.4 (-1.3 to 0.4)
PFS Cognitive			
Baseline	3.2 (2.1; 2.5 to 3.9)	3.6 (2.3; 2.8 to 4.3)	
8 week Intervention	3.9 (2.2; 3.2 to 4.6)	2.6 (1.6; 2.1 to 3.1)	
6 months Follow-up	3.6 (2.2; 2.9 to 4.3)	2.6 (1.9; 1.9 to 3.3)	
Within-group effects			
Baseline to 8 weeks	0.7 (0.1 to 1.3)	-0.9 (-1.5 to -0.3)	-1.6 (-2.5 to -0.7)[a]
Baseline to 6 months	0.4 (-0.2 to 1.1)	-0.9 (-1.6 to -0.2)	-1.3 (-2.2 to -0.3)[b]
PFS Affective			
Baseline	3.5 (1.9; 2.8 to 4.1)	3.7 (2.3; 2.9 to 4.4)	
8 week Intervention	3.5 (1.8; (2.9 to 4.1)	2.8 (1.8; 2.2 to 3.4)	
6 months Follow-up	2.9 (1.6; 2.5 to 3.5)	2.7 (1.7; 2.2 to 3.3)	
Within-group effects			
Baseline to 8 weeks	-0.0 (-0.5 to 0.5)	-0.8 (-1.4 to -0.3)	-0.8 (-1.6 to -0.1)[b]
Baseline to 6 months	-0.5 (-1.2 to 0.2)	-0.9 (-1.6 to -0.2)	-0.4 (-1.4 to 0.5)
PFS Global			
Baseline	3.5 (1.9; 2.8 to 4.1)	3.5 (2.1; 2.8 to 4.1)	
8 week Intervention	3.3 (1.8; 2.8 to 3.9)	2.4 (1.5; 1.9 to 2.9)	
6 months Follow-up	3.1 (1.6; 2.6 to 3.6)	2.4 (1.5; 1.9 to 2.9)	
Within-group effects			
Baseline to 8 weeks	-0.1 (-0.6 to 0.4)	-1.0 (-1.5 to -0.6)	-0.9 (-1.6 to -0.2)[b]
Baseline to 6 months	-0.3 (-0.9 to 0.2)	-1.0 (-1.5 to -0.5)	-0.6 (-1.4 to 0.1)

Abbreviations: CI, Confidence Interval. Bonferroni adjustment was used for pairwise comparisons.
[a] $p<0.001$ (significant between-groups effect)
[b] $p<0.05$ (significant between-groups effect.

and perform graded activities and thus helps fatigue management [29]. Adherence appears to be equally important: a meta-analysis showed that high adherence rates lead to better fatigue outcomes in cancer [29].

Functional capacity

The between-group ES for functional capacity was also in favour of the IA group (d>1). Another study showed that 8-week internet-based tailored exercise program significantly improved functional and cognitive performance in women with breast cancer compared with the CG [30]. Distance on the 6MWT improved significantly in the telehealth system group (d=0.9, p<0.001), and the positive effects were maintained at the 6-month follow-up. Similarly, a study of a personalized circuit training program (50-minutes of group exercise twice a week for 6 weeks) for palliative cancer care, found a significant improvement in the participants' walking distance [31].

Some factors must also be considered when analysing our results, such as the interplay between symptoms and between symptoms and cognitive function. Pain and psychological disorders are strongly related in people with cancer, and pain is a known aggravating factor for depression [32] and anxiety [33], which are common in people with chronic pain [34]. Pain intensity is higher in individuals with cancer and depression [35], and mood disorders are worse in people with cancer-related pain. Thus, we hypothesize that some cognitive improvement is partially due to improvements in these variables, as the literature suggests. However, precautions should be taken when making assumptions regarding emotional outcomes. Although depression and anxiety are frequently associated with cognitive impairment, the association between psychological variables and

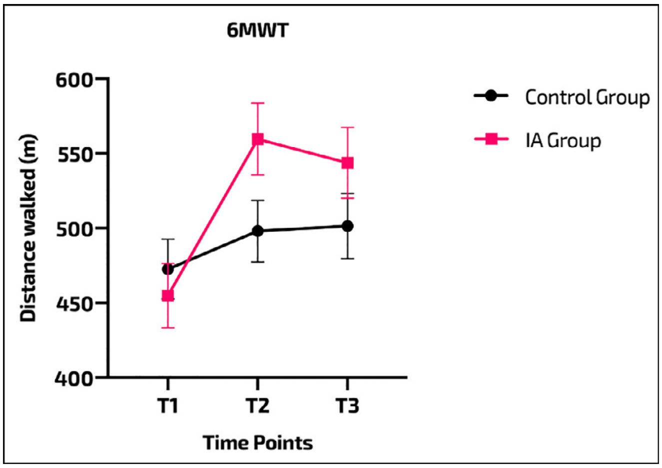

Fig. 2. Within-group and between-group effects for mean 6MWT outcome measures at T1, T2 and T3.Data are shown as mean and 95% CI for the mean values at baseline (T1), end of the 8-week intervention (T2) and 6-month follow-up (T3). 6MWT: 6-min walk test.

cognitive impairment is inconsistent among studies, especially with objectively measured cognitive impairment, as in our study [36]. Finally, concerning fatigue, several studies have also demonstrated a relationship between subjective cognitive impairment and fatigue [37,38]: processing speed is reduced when participants report high levels of fatigue [39]. However, short-term fluctuations may have little effect on perceived cognition months later [38].

When considered as a whole, the literature suggests that the cooccurrence of symptoms such as pain, fatigue or affected mood may result from shared physiological and/or behavioural mechanisms that may together contribute to cognitive impairment beyond the contribution of a single side effect. In addition, one symptom may exacerbate others, contributing to reduced cognitive function. Nevertheless, although research supports an association between these symptoms and cognitive impairment, the direction of the relationships remains unclear.

Regarding the effects of our interventions, previous studies have reported that mHealth interventions offer a promising approach to encourage health behaviour changes among cancer survivors [40], with positive effects on diet, activity participation and fatigue. Our app was designed to monitor physical activity and diet and provides recommendations to improve them when unbalanced. Our integral approach also included individualized technical-therapeutic exercises and group psychomotricity sessions. In addition, participants were guided to extrapolate the exercises to their daily activities. Other studies found that improved health behaviours, including more physical activity and changes in diet, are related to improvements in several cancer parameters, such as emotional well-being and mental health, fatigue, and pain [41]. There is also strong evidence supporting the positive impacts of physical activity on cognition across the lifespan [42], and physical activity has been shown to confer other health benefits to people with breast cancer [43]. The literature highlights exercise training as a potential method to improve varying cognitive domains after breast cancer [44], such as processing speed, spatial working memory, and self-reported cognition [45]. Even low-intensity exercises, such as those used in our study, may benefit cognitive function [46]. The mechanisms underlying the influence of physical activity on cognitive function are unknown, but research suggests that exercise may impact cellular ageing, which could reduce accelerated ageing and improve cognitive function in these populations [47].

Most of the symptoms evaluated improved in both intervention groups in the present study. However, compared with face-to-face interventions that incorporated supervision and interaction [40], fewer positive results, which were also less well maintained over time, were found in the BENECA mHealth group. Group interventions provide emotional and social support and help participants cope with symptoms and fears and, consequently, reduce symptoms of depression [48]. The IA group participated in a compensation-based program targeted at performance and participation to help participants improve and learn new skills to complete everyday life activities; this type of support is typically provided by occupational therapists [17]. This program used education in occupational performance, occupational balance, performance of activities of daily living and stress management as strategies to manage cancer related cognitive impairment. The evidence suggests that this type of program improves executive functions and activity performance [49], and other psychoeducational approaches have already been shown to be effective in people with cancer [19]. The theories that explain this effectiveness are based on experience-dependent neuroplasticity [50] and the consequent functional changes in the brain. A study of metacognitive strategy training found that a Cognitive Orientation to daily Occupational Performance program improved cognitive performance and subjective activity performance in women with chemotherapy-induced cognitive impairment [17], similarly to our study.

This study has several limitations [13]. For ethical reasons, we did not include a CG with no intervention, and our intention was to identify differences between the 2 intervention modalities. Nevertheless, our IA group intervention aligns with the recommendations in the literature. The OT intervention followed previous recommendations in cancer therapy and included exercise/physical activity and occupation-based interventions (such as energy conservation and other education techniques to address symptoms). This group received an integral strategy, and several studies have also compared combined interventions with simple interventions, reporting better results in the groups that received the combined interventions. However, the IA group received far more health-professional attention compared to the m-Health group, which may be a limitation of the work. Applications specifically designed to address all these variables would be necessary to draw firm conclusions about the comparison with the face-to-face intervention. Finally, the program in this study may not be sustainable due to the time required by staff.

A strength of this study, is that it was a comparative effectiveness study. We wanted to determine if mHealth is as good as mHealth combined plus a face-to-face intervention to determine if the face-to-face intervention is truly worthwhile. As a comparative effectiveness study, our research sought to determine whether mHealth is as effective as mHealth plus face-to-face intervention to determine whether face-to-face intervention, which is very costly, is essential. Finally, some inclusion criteria, such as overweight/obesity, may limit the generalizability of the results. However, overweight/obesity has recently become a cancer comorbidity of special research interest, requiring specific and detailed analysis due to its consequences, such as increased recurrence or mortality.

Along with the results in the literature, the results of the present study show that mHealth may be useful in many circumstances, including in people after cancer. First, its benefits seem to outweigh its costs. Second, some studies have also shown that mHealth can improve health in terms of quality of life, pain, function, fatigue and cognition [30]. Furthermore, our study also reveals the valuable role of including an individualized intervention in people with breast cancer. Equally, our results support the inclusion of OT in cancer rehabilitation: OT is underused in this field according to the literature [40]. In addition, we consider the use of multidisciplinary teams appropriate. The multidisciplinary approach plays a key role in helping clinicians engage with the growing needs of people with cancer. Likewise, our study may help to overcome the research gap concerning cancer rehabilitation, as we have tested the effects of multiple components in this population through the OT perspective. Our results showed that the inclusion of a supervised OT intervention along with an

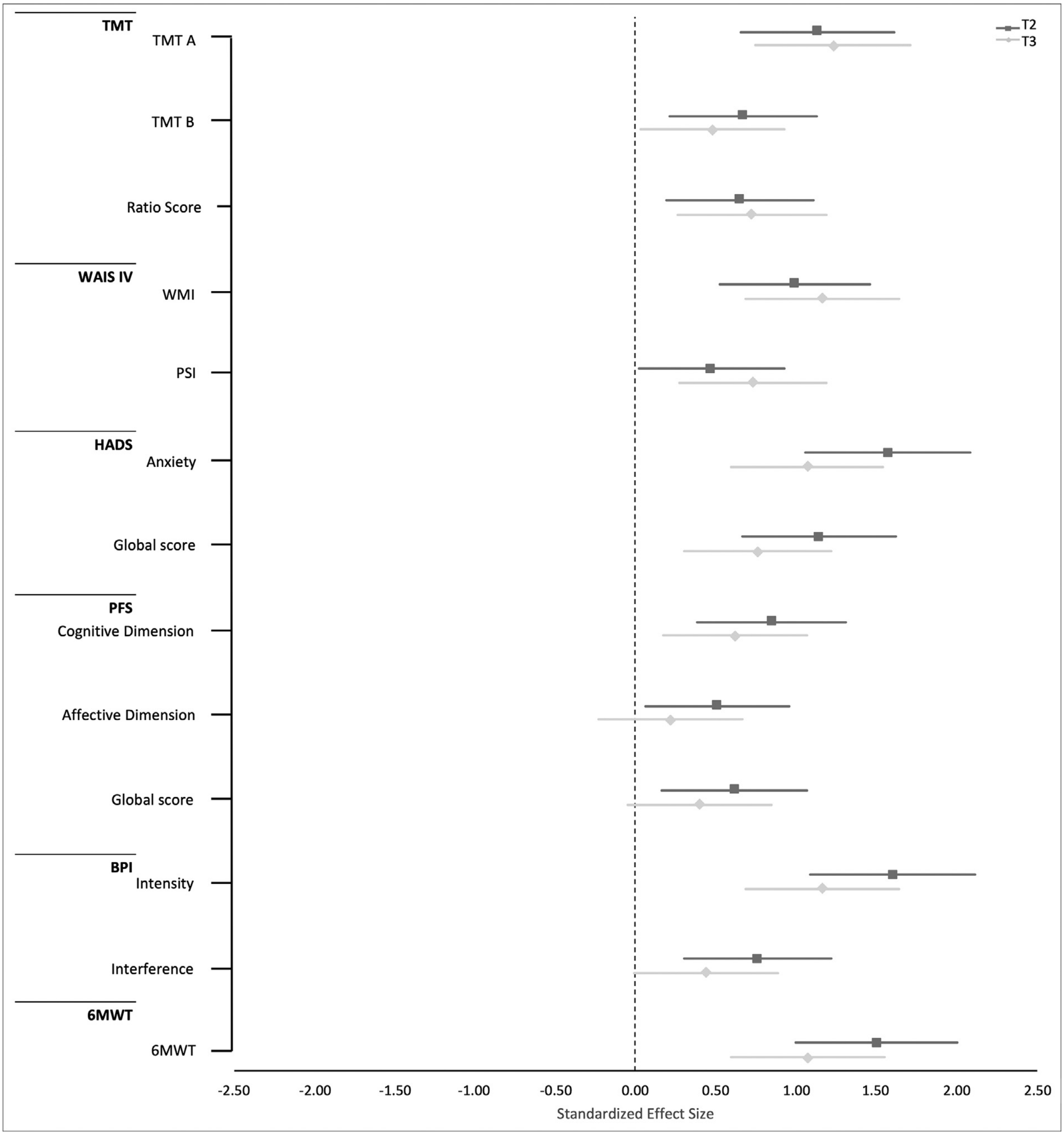

Fig. 3. Standardized effect sizes (and 95% CIs) of the difference between treatment groups for cognitive performance, psycholgical state, fatigue and pain perception and functional capacity outcomes.

mHealth app is more beneficial for people after cancer than mHealth alone. Future research should attempt to design an application that assists in the identification of individuals who benefit eligible for mHealth alone and those who need to be supported by an additional face-to-face intervention.

Declaration of Competing Interest

None.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.rehab.2022.101681.

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