# Reduced Cancer-Related Fatigue after Tablet-Based Exercise Education for Patients

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Diana J. Wilkie, PhD, RN, FAAN<sup>1</sup>, Anna L. Schwartz, PhD, FNP-BC, FAAN<sup>2</sup>, Wen-Chun Liao, PhD, RN<sup>3</sup>, Dottington Fullwood, EdD, CHES<sup>4</sup>, Yu Wu, DNP, ACNP-BC<sup>5</sup>, Tanya Wallace Farquharson, MSN, RN, PhD<sup>1</sup>, Yingwei Yao, PhD<sup>1</sup>, and Julie R. Gralow, MD<sup>6</sup>

## Abstract

**Aim:** Exercise can be an effective treatment for cancer-related fatigue, but exercise is not prescribed for many cancer patients. Our specific aim was to compare usual care and a tablet-based fatigue education and prescription program for effects on level of fatigue (primary outcome) and satisfaction with fatigue and amount of exercise (secondary outcomes).

**Methods:** In a four-week pretest/posttest randomized study, 279 patients with cancer completed a touch screen fatigue assessment and daily paper-based activity logs. The experimental group also had access to FatigueUCope, a tablet-based multimedia education intervention focused on exercise as therapy for fatigue.

**Results:** In total, 94% of intervention group accessed FatigueUCope. Controlling for baseline fatigue, compared to the usualcare group, the experimental group reported lower fatigue scores (P = .02). Neither satisfaction with fatigue nor exercise level was significantly different between groups, but not all activity logs were returned. None of the patients reported adverse effects.

**Conclusion:** Objective indicators of exercise are warranted in future studies to examine whether exercise is indeed the mechanism of the FatigueUCope effect and determine the clinical utility of this intervention. This brief, engaging tablet-based multimedia education and prescription program has promise to help patients recognize the benefits of exercise to manage cancer-related fatigue.

# Introduction

Fatigue is a significant problem for the vast majority<sup>1</sup> of the 1.9 million Americans diagnosed with cancer annually.<sup>2</sup> Interest in fatigue has grown as its incidence (90%-100% of cancer patients), and intensity has been recognized.<sup>3</sup> Patients report fatigue during and after radiation therapy; some cite it as a reason for prematurely ending treatment.<sup>4</sup> Fatigue occurs across all types of treatments, stages, and types of cancer and is experienced by persons of all ages.<sup>5-7</sup> Many interventions have been suggested to alleviate cancer related fatigue, including varied education programs,<sup>8,9</sup> exercise,<sup>10</sup> and erythropoietin agents (recombinant human erythropoietin and darbepoetin alfa).<sup>11</sup> Results have been inconsistent across studies including educational programs, especially for fatigue reduction.<sup>8,9,12,13</sup> Only one prior study,<sup>14</sup> however, focused on the effects of computer/tablet-based education to lower cancer related fatigue and none specifically focused on exercise to do

so. As a treatment for cancer-related fatigue, the purpose was to test the Fatigue*U*Cope intervention, a tablet-based

#### **Corresponding Author:**

Diana J. Wilkie, PhD, RN, FAAN, Department of Biobehavioral Nursing Science, College of Nursing, University of Florida, 1225 Center Drive, Room 2203, Gainesville, FL 32610, USA. Email: diwilkie@ufl.edu



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<sup>&</sup>lt;sup>1</sup>Department of Biobehavioral Nursing Science, College of Nursing, University of Florida, Gainesville, FL, USA

<sup>&</sup>lt;sup>2</sup>School of Nursing, Northern Arizona University, Flagstaff, AZ, USA<sup>3</sup>School and Graduate Institute of Nursing, China Medical University,

Taichung, China

<sup>&</sup>lt;sup>4</sup>Department of Aging and Geriatric Research, Institute on Aging, University of Florida, Gainesville, FL, USA

<sup>&</sup>lt;sup>5</sup>Department of Advanced Heart Failure and Heart Transplant, University of Florida Health, Gainesville, FL, USA

<sup>&</sup>lt;sup>6</sup>Department of Medicine/Oncology, University of Washington, Seattle, WA, USA



Figure 1. CONSORT flow diagram: Cancer FatigueUCope study.

innovation with a fatigue assessment scale and a tailored multimedia education program focused on exercise.

Exercise is a neglected area of the survivorship plan for cancer patients. Many healthcare providers fail to advise patients about exercise and its benefits.<sup>15,16</sup> Inactivity may in fact be a trigger for the marked fatigue and weakness experienced by cancer patients.<sup>17</sup> The benefits of both aerobic and resistance types of exercise are well-documented in the general population, and a solid body of evidence suggests that aerobic exercise may prevent reduced functional capacity, nausea, fatigue, decreased self-esteem, and other quality-of-life issues that confront patients with cancer.<sup>16-18</sup> Tests of structured aerobic exercise programs for previously sedentary cancer patients demonstrate that exercise is safe, that patients who are receiving chemotherapy exhibit a beneficial training effect, and that exercise produces positive psychosocial effects.<sup>16,17</sup> Unfortunately, exercise is still not routinely prescribed for many cancer patients, especially patients with advanced-stage cancers.<sup>19-21</sup> Managing cancer fatigue more effectively requires a new paradigm, such as using advances in computer/tablet technology to provide innovative tailored interventions based on systematic fatigue assessment.

Our specific aim was to compare the usual cancer care group and the FatigueUCope group for effects on level of fatigue, satisfaction with fatigue, and amount of exercise. Compared to the usual-care group, we hypothesized that the FatigueUCope group would report *decreased scores* for fatigue (primary outcome), *increased* satisfaction with fatigue level, and *increased* exercise (secondary outcomes).

## Methods

### Design

We conducted a four-week, randomized study in patients receiving radiation or chemotherapy for cancer with pretest/ posttest measures to determine the effect of the Fatigue*U*Cope education intervention. We used a permutated block design with 1:1 random assignment to groups stratified by fatigue intensity. Using a novel randomization program, at random, the blocks were programmed to balance groups every 18 to 24 patients. The randomization table was hidden and available only to the lead programmer via the Fatigue*U*Cope program, thereby concealing the randomization until after baseline data were collected.

## Setting

Subjects were recruited from a university-affiliated cancer center and completed study procedures during regularly scheduled clinical appointments. The Human Subjects Division at the University of Washington approved the study procedures (#99-2294-E).

#### Sample

Study inclusion criteria required that the patient: (a) had a diagnosis of cancer, any stage; (b) was receiving cancer therapy at the study site; (c) spoke and read English; and (d) was 18 years or older. Patients were excluded if they were: (a) legally blind; (b) physically unable to complete study

	Usual care	Fatigue <i>U</i> Cope	
	Mean (SD)	Mean (SD)	Þ
Age	52.3 (13.2)	52.3 (11.9)	.98 <sup>1</sup>
	n <b>(%)</b>	n <b>(%)</b>	þ
Gender			.98 <sup>2</sup>
Female	89 (65%)	91 (64%)	
Male	48 (35%)	51 (36%)	
Marital status*			.27 <mark>2</mark>
Single	35 (30%)	38 (32%)	
Married/Partnered	79 (68%)	73 (61%)	
Widowed	3 (3%)	8 (7%)	
Education**			.36 <sup>2</sup>
High school or less	33 (26%)	29 (22%)	
Some college	44 (35%)	39 (30%)	
College or higher	49 (39%)	62 (48%)	
Annual family income***			.57 <mark>2</mark>
<\$10,000	12 (12%)	8 (7%)	
\$II-20,000	9 (9%)	12 (10%)	
\$21-30,000	(  %)	II ( <b>9</b> %)	
\$3I-40,000	9 (9%)	8 (7%)	
\$4I-50,000	(  %)	21 (18%)	
>\$50,000	50 (49%)	60 (50%)	
Race/ethnicity			.55 <sup>3</sup>
Caucasian	127 (93%)	124 (87%)	
African American	4 (3%)	5 (4%)	
Hispanic/Latino	0 (0%)	I (I%)	
Asian	5 (4%)	10 (7%)	
Native American	I (I%)	2 (1%)	

**Table I.** Descriptive Statistics for Demographic Data by Usual-Care and FatigueUCope groups (N = 279).

\*Missing (20 UC; 23 FUC).

\*\*Missing (11 UC; 12 FUC).

\*\*\*\*Missing (35 UC; 22 FUC). Independent t test.

<sup>2</sup>Chi square test.

<sup>3</sup>Fisher's exact test.

Fisher's exact test.

questionnaires; or (c) participating in other fatigue studies conducted at the study site. As displayed in Figure 1, oncology physicians or nurses referred 810 patients. Nurses made initial introductions to the study research nurses who determined that 350 patients did not meet eligibility criteria or that they could not establish eligibility for 82 patients (usually seen in the clinic for second consult). All 378 eligible patients were told that the investigators were testing a new tool for cancer-related symptoms. Of the eligible patients, 286 consented, but seven decided not to participate before randomization. Therefore, 279 patients were randomized to groups, which was slightly more than the planned sample of 276 with power of .80 to detect an effect size of .30.

A total of 279 patients completed the baseline and participated in the four-week study. The mean age of the sample was  $52.3 \pm 12.5$  years. The 137 usual-care group patients and the 142 FatigueUCope group patients did not differ significantly on any demographic variable (Table 1). The FatigueUCope group included slightly more patients from minority groups than the usual-care group, but the difference was not statically significant (Table 1). Table 2 presents the types of cancer, stage, and treatments for the sample, none of which differed significantly between usual-care and FatigueUCope groups. Approximately 40% of the sample in each group had metastatic cancer.

#### Procedures

After informed consent and before a patient's scheduled appointment with the radiation or medical oncologist, a research nurse obtained baseline measures by introducing all enrolled patients to the Windows-based pen-tablet (Fujitsu 1600) with the Schwartz Cancer Fatigue Scale and Fatigue*U*Cope programs. The research nurse instructed patients to read and touch the tablet screen as indicated to start the fatigue assessment tool. If asked, the research nurse provided assistance in completing the program. Upon completion, the research nurse escorted the patient to the clinic examination room and returned to the tablet to open the intervention program and generate the customized Fatigue*U*Cope educational materials for the patients assigned to the usual-care group, a computer game list was opened from Fatigue*U*Cope.

For the Fatigue*U*Cope education group, after the visit with the oncologist or at a convenient time on the next day, the research nurse introduced the patient to the Fatigue*U*Cope education program and told the patient that the program would be available for his/her use until the end of the study. When the patient's name and code number was typed on the introduction screen, customized sets of educational materials on managing fatigue were presented on-screen in an interactive format. The patient was able to read or listen to the information on the tablet and print any of the information, which was modified from printed material tested in previous research.<sup>22-24</sup>

For the usual-care group, after the visit with the oncologist or at a convenient time the next day, the research nurse introduced the patient to the computer game portion of FatigueUCope. These patients were invited to play games on the tablet until the end of the study, at any time that the tablet was not being used by another patient. Allowing all patients access to one of the 4 study tablets was intended to decrease the chance that clinicians would guess patient group assignment when they saw a patient with a study tablet. Code numberprotected access prevented usual-care patients from gaining access to the FatigueUCope intervention until after they completed the study.

Four weeks after the baseline procedures, at another scheduled clinic appointment, the research nurse obtained the posttest measures. After the outcome assessments were completed, usual-care patients were given the opportunity to access the Fatigue *U*Cope intervention.

 Table 2. Cancer Characteristics by Usual-Care and FatigueUCope groups (N = 279).

	Usual care	FatigueUCope	Þ
Variable	Frequency (%)	Frequency (%)	
Cancer type			.40 <sup>3</sup>
Breast	48 (35%)	61 (43%)	
Head or neck	26 (19%)	23 (16%)	
Sarcoma	9 (7%)	11 (8%)	
Lung cancer	7 (5%)	8 (6%)	
Prostate cancer	5 (4%)	7 (5%)	
Cervical cancer	10 (7%)	4 (3%)	
Colon or rectal cancer	4 (3%)	6 (4%)	
Lymphoma	7 (5%)	2 (1%)	
Brain cancer	5 (4%)	2 (1%)	
Other	16 (12%)	18 (13%)	
Cancer stage*			.67
Stage 0	0 (0%)	2 (1%)	
Stage I	23 (18%)	27 (19%)	
Stage 2	29 (23%)	32 (23%)	
Stage 3	22 (17%)	20 (14%)	
Stage 4	54 (42%)	60 (43%)	
Cancer treatment history			
Had chemotherapy**	72 (53%)	83 (59%)	.35 <sup>2</sup>
Had radiotherapy***	65 (48%)	69 (49%)	.95 <sup>2</sup>
Had surgery	11 (8%)	8 (6%)	.58 <sup>2</sup>

\*Missing (9 UC; 1 FUC).

\*\*Missing (I UC; 2 FUC).

\*\*\*Missing (2 UC; 2 FUC).

<sup>1</sup>Independent t test. <sup>2</sup>Chi square test.

<sup>3</sup>Fisher's exact test.

#### Instruments

An electronic version of the 6-item Schwartz Cancer Fatigue Scale  $(SCFS-6)^{25}$  was designed as an interactive touch screen method for assessing cancer-related fatigue (Figure 2). We modified directions from the paper-and-pencil tool to address the touch screen method of recording patient responses. The SCFS-6 responses range from 1 to 5 indicating how much fatigue was experienced in the past 2 to 3 days,<sup>25</sup> a time frame that is easily and reliably recalled by cancer patient with cancerrelated fatigue. The total score is derived by summing the six items, ranges from a minimum of 6 to a maximum of 30, has excellent internal consistency reliability ( $\alpha$ >.90), and is not significantly different in groups of patients receiving radiation or chemotherapy.<sup>25</sup> The SCFS-6 is a reliable, valid, and parsimonious instrument that measures cancer-related fatigue on physical (e.g., tired and worn out) and perceptual (e.g., helpless and difficulty thinking) dimensions.<sup>25-27</sup> SCFS-6 scores show strong correlations (r = .63-.79, P<.001 for all measures) with a variety of fatigue measures.<sup>28</sup> The stability coefficient is r = .69for the total scale).<sup>29</sup> The SCFS-6 is highly sensitive to change in cancer-related fatigue over time (P<.001). The minimally

important clinical difference in fatigue for the SCFS is 1.0 (effect size .71).<sup>26</sup>

Screens were used to measure satisfaction with fatigue (yes/no/not sure) and demographic questions. As the patient touches the appropriate response on the screen, data are automatically stored in an Access database file, which can be imported into statistical programs for analysis. The study patients completed the on-screen SCFS-6 and the satisfaction with fatigue item in an average of  $2.5 \pm 1.9$  minutes.

Patients in both usual-care control and Fatigue UCope groups were asked to self-report their exercise in a paper-based daily log for the entire four-week study. The daily log allowed them to record the type of exercise (e.g., none, walking, bicycling, jogging, rowing, aerobics, skiing, cross-country skiing, and other), number of minutes exercised, and the intensity of the exercise, using a scale 0 = not at all hard to 10 = extremely hard. Analysis of the logs followed a previously developed scoring protocol.

#### Exercise Intervention

FatigueUCope provides multimedia <u>patient</u> education about cancer-related fatigue and use of aerobic exercise as

SYMPTOMReport - Fatigue	×	SYMPTOMReport - Faligue	
Touch the word(s) to indicate how much fatigue h tired in the past 2-3 days.	as made you feel	For program operator's use only Touch the word(s) to indicate how muc difficulty thinking in the past 2-3 days.	ch fatigue has made you have
Tired	Extremely	Difficulty Thinking	Estemate
Quite a	bit		Quite a bit
Moderately		Moderate	v
A little Not at all		A little	
Back	Next	Back	Next
SYMPTOMReport - Faligue     For program operator's use only	X	SYMPTOMReport - Felişue For program operator's use only	X
Touch the word(s) to indicate how much fatigue helpless in the past 2-3 days.	has made you feel	Touch the word(s) to indicate how much worn out in the past 2-3 days.	h fatigue has made you feel
Helpless	Extremely	Worn Out	Extremely
Quite	a bit		Quite a bit
A little		Moderately	
Not at all		Not at all	
Bee	Next	Back	Next
	SymptomConsult - frmEndFatigue		
	Manage vour fatigu	e with exercise.	
	5, 5		
	Would you like a handout of thi	s information? Yes No	
	Symptom Menu	Continue to Next Topic	

Figure 2. Fatigue assessment screens and screen to request handouts.

a self-care activity to reduce fatigue. All the educational materials are written at a  $6^{th}$ -grade reading level. Fati-gue*U*Cope provided two different exercise intervention doses tailored to the patient's reported fatigue level: high

(SCFS score  $\geq 15$ ) or low (SCFS score  $\leq 14$ ). Specifically, the software allows the patient to report his/her fatigue data and then reads the database for fatigue level. Then the software displays either 17 education screens (low dose)



Figure 3. Examples of screens from exercise intervention in FatigueUCope.

tailored for patients with low fatigue levels or 36 education screens (high dose) tailored for patients with high fatigue levels. The 17 screens require 3 minutes to complete and focus on the general benefits of exercise and strategies for engaging in exercise, specifically to walk at an easy pace for 10 to 20 minutes every day or every other day and if unable to do so to perform shorter bouts of exercise of 3 to 5 minutes several times a day. The 36 screens require 5.5 minutes to complete and include the 17 general exercise screens plus 19 other screens focused on the specific exercise prescription (walk at an easy pace every day or every other day for 15 minutes and slowly increasing to 30 minutes at least 4 days per week) and specific ways to implement the prescription (e.g., reduce prescription time by one-half if cannot do full prescription). The information on these screens is a modified version of previously tested printed materials.<sup>22-24,30</sup> In contrast to the exercise programs tested by others,<sup>31</sup> the Fatigue*U*Cope exercise prescription focused on walking four days per week with increased duration over the four-week study period (Figure 3).

The instruction screen for the Fatigue UCope intervention is personalized (e.g., "Betty Green, based on your Fatigue U-Cope answers, we want to share some exciting, new information that you may find helpful. Click or press here to learn about new ways to cope with or manage your fatigue"). The patient has the option of reading and listening to the information on-screen, printing it, or both viewing on-screen and printing. The on-screen option provides text, photographs, audio clips, graphics, and animations to present the exercise intervention to the patient. Figure 3 shows six of the exercise intervention screens; however, due to the interactive design of the program, only a few functional components of the program are illustrated.

#### Statistical Analysis

We performed intention-to-treat analysis including in our analysis all 279 participants that were randomized. Descriptive statistics, including mean, standard deviation (reported as ±), frequency, and percentage were obtained for baseline characteristics of patients by group. Independent t test, chi-square test, and Fisher's test were used for comparison of baseline characteristics between groups. Analyses at the end of the study focused on comparison of usual-care and the FatigueUCope groups for effects on level of fatigue, satisfaction with fatigue, and amount of exercise. We used linear regression to examine the group (usual-care vs. FatigueUCope) effect on level of fatigue, controlling for the fatigue at baseline. Satisfaction with fatigue (satisfaction) was categorized as a dichotomous variable (yes vs. no or not sure). We used logistic regression to examine the group effect on satisfaction at study end, controlling for satisfaction at baseline. Amount of exercise was represented by three variables: number of logged exercise days, total number of logged exercise minutes, and mean exercise intensity. Independent t tests examined the group effect on these three exercise variables. Statistical significance for all analyses was set at P < .05.

## Results

## Implementation

The fidelity of the FatigueUCope intervention was high, but not as complete as might be expected with tablet-based interventions. Specifically, 40 (30%) patients both viewed the intervention via the tablet screen and requested handout materials; 38 (29%) patients only viewed the intervention via the tablet screen; 46 (35%) patients received only the handout materials; and 8 (6%) patients did not receive any of the intervention according to the records (for unknown reasons). In total, 94% of patients received at least one form of the intervention.

Consistent with the length of the brief intervention, patients who viewed the intervention via the tablet screen spent an average of  $5.4 \pm 5.0$  min (median 3.7 min; maximum 28.6 min) doing so. Patients usually opened the FatigueUCope intervention only once and commonly viewed the intervention while receiving their chemotherapy or during wait-times between clinical procedures. Occasionally, special appointments were needed for patients to view the intervention. If time was an issue, patients typically requested the handout option; however, it is unknown if they read the handout materials.

## Primary Outcome: Fatigue Intensity

At baseline, only 4% of the sample reported no fatigue (score = 6), 51% reported mild fatigue (scores 7–14), and 45% reported severe fatigue (scores  $\geq$ 15); the distribution to these three

Table 3. Intervention Effect Estimates (N = 279).

Predictor	Estimate	Std error	Þ
Baseline fatigue	.463	.060	<.001
Group (Ref = UC)	-1.418	.584	.016
Baseline satisfaction	1.920	.309	<.001
Group (Ref = UC)	.535	.292	.068
	Predictor Baseline fatigue Group (Ref = UC) Baseline satisfaction Group (Ref = UC)	PredictorEstimateBaseline fatigue.463Group (Ref = UC)-1.418Baseline satisfaction1.920Group (Ref = UC).535	PredictorEstimateStd errorBaseline fatigue.463.060Group (Ref = UC)-1.418.584Baseline satisfaction1.920.309Group (Ref = UC).535.292

fatigue levels did not differ for the usual-care and Fatigue *U*-Cope groups (P = .50). The mean <u>baseline</u> fatigue intensity scores did not differ for the usual-care  $(13.9 \pm 5.0)$  and Fatigue *U*Cope  $(14.3 \pm 5.1)$  (P = .47) groups. The mean fatigue intensity scores at the end of the study were higher for the usual-care group  $(15.0 \pm 5.2)$  and lower for the Fatigue *U*Cope group  $(13.8 \pm 5.0)$ . Adjusting for baseline fatigue intensity scores, the Fatigue *U*Cope group reported significantly lower fatigue intensity scores at study end than did the usual-care group (P = .02) (Table 3).

# Secondary Outcomes: Fatigue Satisfaction and Exercise Level

At baseline, only 32% of the usual-care group and 35% of the Fatigue *U*Cope group were satisfied with their fatigue levels (P = .80). Adjusting for baseline satisfaction, the group difference in satisfaction at study end was not statistically significant (P = .07) (Table 3).

A disappointingly low number of patients in both groups returned their exercise logs, despite extensive efforts by the research nurses to obtain the logs. There was no difference in level of fatigue between patients who did or did not return their logs:  $13.8 \pm 5.1$  vs.  $14.4 \pm 5.1$ , P = .27. Based on the 61 (45%) usual-care group and 70 (49%) Fatigue UCope group patients who returned their exercise logs, there were no significant (P>.05) differences between groups in logged exercise days ( $13.4 \pm 7.2$  vs  $12 \pm 7.9$ ), logged exercise minutes ( $407 \pm 431$  vs  $358 \pm 509$ ) or logged average exercise intensity ( $4.1 \pm 1.8$  vs  $3.6 \pm 1.7$ ), respectively, for the usual-care and Fatigue UCope groups.

### Subgroup Analysis: Cancer Stage

Although the study was not powered for subgroup analyses, we conducted exploratory analyses by stage of disease given the large number of participants with stage 4 cancers. The baseline fatigue intensity did not differ significantly between patients with stage 4 cancer and others:  $14.3 \pm 5.2$  vs  $14.0 \pm 5.0$ , P = .67. The percentages satisfied with fatigue at baseline were 32% for patients with stage 4 and 35% otherwise (P = .69). Having stage 4 cancer did not have a significant effect on the intervention effect on either fatigue intensity (P = .73) or satisfaction with fatigue (P = .39). None of the patients reported adverse events.

## **Discussion and Conclusions**

This novel study is noteworthy for showing the Fatigue UCope intervention group reported significantly lower fatigue levels at study end than did the usual-care group. This finding indicates that a brief, simple table-based intervention that is easy to deliver in a clinic setting reduces fatigue. The finding that it did not reduce satisfaction with fatigue is not entirely surprising given that patients were actively receiving treatment. A factor that may have directly impacted the lack of effect in fatigue satisfaction may be that the study period was limited to four weeks a duration of time that was undoubtedly too brief a time for FatiguUCope patients to receive a sufficient dose of exercise to improve fatigue satisfaction.

The mechanism by which the Fatigue UCope intervention affected the level of fatigue and satisfaction is uncertain because those who returned their exercise logs in the usualcare group did not differ significantly from the intervention group. Additionally, lack of baseline information about participants exercise behaviors made it difficult to judge if patients in the Fatigue UCope education group initiated the exercise program after the intervention or simply maintained their previous exercise pattern. Furthermore, since we did not measure the amount of inactivity, which many patients think is an effective treatment for fatigue, it is possible that the significant difference in fatigue levels between groups could be related to increased physical activity in the experimental group.

The FatigueUCope intervention, which takes 3 minutes (low fatigue) to 5.5 minutes (high fatigue) to complete, was completed in 5.5 minutes by the average patient. This brief intervention is reasonable given typical waiting periods in many clinical settings. Although the intervention tablets were available to participants during the four-week study, the patients typically completed the tailored, tablet-based intervention the first time it was introduced to them and did not access the materials a second time. This single use is likely due to the availability of a print copy of the on-screen materials, which 65% of the intervention group requested. Previous formative research on this innovative tool, which included some of the patients in the outcome analysis, documented positive comments from patients about completing both the assessment and intervention parts of the FatigueUCope program.<sup>32</sup> Additional enhancements in the program to improve documentation of the fidelity of intervention delivery and documentation of time on educational tasks would be helpful in future studies. This brief intervention contrasts the educational programs tested by others,9 some of which required 1 hour over 3 days,<sup>33</sup> up to 12 weeks,<sup>14</sup> or 30 weeks<sup>31</sup> for complete intervention delivery.

Randomization procedures produced balanced study groups. At baseline, the fatigue intensity scores and fatigue levels were balanced between usual-care and FatigueUCope groups. These findings support use of the real-time computerized random assignment of patients to study groups for future clinical-outcome research conducted as part of routine cancer care.

Level of fatigue was moderately high in this sample that was heterogeneous in terms of education, cancer type, stage of disease, and cancer therapy. Furthermore, most of the patients were not satisfied with their fatigue level. Other investigators have reported similar fatigue levels using a variety of fatigue scales.<sup>26,28,34-37</sup> FatigueUCope was an effective means by which to assess patients' fatigue levels and to generate fatigue interventions tailored to the patients' fatigue levels. Such tablet-based symptom assessments have important implications for improving symptom assessment in routine care of cancer patients<sup>32</sup> and could provide health professionals better understanding of the magnitude of fatigue than has been documented with current assessment methods.<sup>38,39</sup> FatigueUCope is a highly scalable, low cost, unsupervised exercise intervention for fatigue reduction that contrasts with other effective interventions that include supervised components, as noted in a recent meta-analysis.<sup>40</sup>

Although other researchers have reported feasibility and the effect of aerobic exercise in patients with advanced cancer,<sup>17,31,41,42</sup> our study is notable for the large sample of patients with stage 4 cancers who completed our study. Those with metastatic disease participated in this study with no reported adverse effects. Our findings are similar to others who studied patients with stages 1–3 and included information on physical activity.<sup>14</sup> An important strength of our study was its large sample size, but our study was not powered to detect effects based on cancer stage. Therefore, our finding of no significant difference on level of fatigue between usual-care and Fatigue*U*Cope groups by cancer stage is not surprising.

Our patients were studied for a relatively short period compared to other exercise investigations.<sup>31</sup> The study period was only four weeks. Although other investigators implemented longer treatment periods to assess adoption of exercise as an intervention for fatigue, the effects of aerobic exercise on fatigue have been shown to be fairly rapid in the chemotherapy setting<sup>22</sup> but slower in the radiation therapy setting.<sup>43</sup> In contrast investigators<sup>33</sup> who used an educational intervention focused on energy balance and conservation in patients receiving chemotherapy and radiation did not observe an intervention effect. Our study included patients receiving chemotherapy and radiation therapy, and although we found an intervention effect, it is possible that effect would have been stronger with a different study design or it is possible that the effect would diminish with time. Additional research is needed to address duration of effect.

There are several limitations of this study. The high level of exercise reported by the usual-care group suggests that there may have been diffusion of the aerobic exercise intervention to usualcare patients by virtue of asking them to record their exercise for the duration of the study. We did not account for exercise habits or access to exercise equipment prior to randomization, which could have affected adoption of the exercise intervention. Obtaining a simple pretest/posttest measure of functional ability would have provided objective details of benefits gained by exercise. In future studies, we will adopt a 6-minute walk or other clinically relevant measure for this purpose. The low percentage of exercise logs returned reflects a need for use of activity monitoring devices rather than daily logs. It was assumed that random assignment to usual-care and FatigueUCope groups would control for the effects of other treatments, but validation of this assumption with data about pharmacologic and other non-pharmacologic treatments would have strengthened interpretations of study findings. Our sample was heterogeneous regarding types of cancer, both a strength for generalizability of findings and a limitation in terms of control of cancer-specific factors that could influence fatigue. Future studies should focus on cancer types with greater homogeneity.

### Conclusions

This study provided rigorous initial testing of an innovative tablet-based tool for assessing fatigue and providing patients with a multimedia aerobic exercise prescription to manage cancer-related fatigue. Findings demonstrate that the Fati-gue*U*Cope group had reduced levels of fatigue compared to the usual-care group, and that delivering an aerobic exercise prescription to patients with all stages of disease was safe. However, our sample was younger than typical and findings may not apply to older patients who may have more difficulty in use of tablet technology. Findings also indicate that satisfaction with fatigue was not different by group at the posttest. Finally, this version of the novel tablet-based intervention provided no means of reinforcing exercise adoption and/or documenting adherence to the exercise prescription, which are aspects of this work that could be further developed in the future.

Fatigue, one of the adverse effects of cancer and its treatments, is commonly seen among cancer patients regardless of the stage of their cancer. Our findings showed that patients who received education on fatigue and exercise via the FatigueUCope program reported significantly lower fatigue scores than patients in the usualcare group. Readily available tablet technology or large interactive screens located in reception or treatment rooms give oncology providers a way to utilize the fatigue assessment tool and FatigueUCope program with cancer patients during their wait time in the clinic or office or while they receive infusions. Although the feasibility of patients using this innovation shows strong promise for its use in clinical settings, the mechanism of its effect and its utility in practice environments require additional study. Studies are needed to optimize the efficacy of exercise on cancer related fatigue for specific cancers.

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#### **Author Contributions**

All authors contributed to the reported research, assuming the following roles: Conceptualization (DJW and ALS); data curation (DJW and WCL); formal analysis (YY); funding acquisition (DJW and ALS); investigation (DJW, ALS, and JRG); methodology (DJW and ALS); project administration (DJW); writing—original draft (DJW, ALS, DF, and YW); and writing—review and editing (DJW, ALS, WCL, DF, YW, TWF, and JRG). All authors approved the final manuscript.

#### **Declaration of Conflicting Interest**

DJW: eNurisng llc, Chairman, and Founder; ALS, WCL, DF, YW, TWF, and YY: none; JRG: Roche/Genentech: Steering committee Member, Data Safety Monitoring Committee Member; Astra Zeneca: Advisory Board; Puma: Advisory Board; Pfizer: Advisory Board; Novartis: Data Safety Monitoring Committee Member; Sandoz/ Hexal AG: Consultant; Immunomedics: Data Safety Monitoring Committee Member; Genomic Health: Consultant; Radius: DSMC; Inbiomotion: consultant (All < \$5000 annual)

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#### **Ethics Approval**

The Human Subjects Division at the University of Washington approved the study procedures.

#### **ORCID** iD

Dottington Fullwood, EdD, CHES (b) https://orcid.org/0000-0001-6077-3302

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