Published in final edited form as:

Pain. 2016 July ; 157(7): 1563–1573. doi:10.1097/j.pain.0000000000000549.

Brief Time-Based Activity Pacing Instruction as a Singular Behavioral Intervention was not Effective in Participants with Symptomatic Osteoarthritis

Susan Lynn Murphy, ScD OTR^{1,2}, Anna Louise Kratz, PhD¹, Kelley Kidwell, PhD³, Angela K. Lyden, MS⁴, Michael E. Geisser, PhD¹, and David A. Williams, PhD⁵

¹Department of Physical Medicine and Rehabilitation, University of Michigan

²VA Ann Arbor Health Care System, GRECC

³Department of Biostatistics, University of Michigan

⁴Department of Cardiology, University of Michigan

⁵Department of Anesthesiology, University of Michigan

Abstract

Osteoarthritis (OA) of the lower extremities is a prevalent cause of disability in which symptoms interfere with mobility and activity participation. Behavioral self-management for OA symptomatology is commonly recommended; but these interventions are underutilized, unstandardized in application, and at times, unavailable in the context of clinical care. For people with chronic pain, rehabilitation professionals may select to apply activity pacing instruction as one behavioral strategy to manage symptoms. Activity pacing is widely used in combination with other pharmacological and behavioral interventions but has not been studied as a singular behavioral intervention for people with OA. The purpose of this study was to evaluate the effectiveness of an occupational therapist-delivered, time-based activity pacing program for treatment of pain, fatigue, and physical function in people with symptomatic knee or hip OA. A 3-arm randomized controlled trial was conducted in which 193 people were randomized into tailored activity pacing, general activity pacing, or usual care arms. Assessments were done at 10 weeks and 6 months post baseline. Using linear mixed models, WOMAC pain scores changed over time, decreasing the most in the general and usual care groups; only the usual care group had decreased pain over 6 months. The tailored and general activity pacing groups reported higher frequency of pacing behaviors than the usual care group at 10 weeks but pacing was not sustained at 6 months. This trial does not support the use of time-based pacing as a singular behavioral strategy for people with knee or hip OA.

Keywords

Pain; Fatigue; Activity Pacing; Osteoarthritis

1. Introduction

Activity pacing, defined as “the regulation of activity level and/or rate in the service of an adaptive goal or goals”[30] is a widely-used intervention to increase function for people with chronic pain. Activity pacing interventions are often guided by operant theory and involve modifying the contingency of activity being regulated by pain to a behavioral pattern where activity is contingent upon goals or time [13; 30]. For people with osteoarthritis (OA), activity pacing interventions are typically offered as part of a behavioral or pain coping skills programs [1; 20; 21]. While these multifaceted behavioral interventions have been shown to be effective, it is not known if activity pacing by itself is effective as a singular behavioral intervention.

This three-arm randomized clinical trial was designed to investigate the efficacy of a brief, theory-driven, time-based activity pacing intervention that could be feasibly delivered within typical clinical care by occupational therapists. Standard time-based activity pacing is taught by establishing a preplanned daily time schedule to balance activity and rest[13] and relies on patient self-report of daily activities and symptoms to establish the schedule. Because self-reported recall is biased to peak and recent experiences [34], we hypothesized that a brief activity pacing intervention could be more potent if tailored to the patient by using their own “actual” daily symptom and physical activity data (i.e. objectively measured via accelerometers) from a 7-day period of monitoring. In addition, theoretical models of chronic pain and disability indicate that several patterns of activity are related to increased pain and disability, suggesting the need to tailor suggestions for activity to the individual [17; 18]. The symptom data used in this study included pain, fatigue, and stiffness ratings collected at several points within each day and enabled tailoring pacing instruction based on how symptoms were related to physical activity fluctuations for a given individual. The rationale for including symptoms beyond pain for tailoring was based on our previous findings in which within-day fatigue was more associated with physical activity compared to pain[28]. In addition, the ability to graph actual physical activity data allowed the researchers to provide individualized pacing training that addressed each person's unique activity pattern. This is in contrast to the general pacing intervention, where pacing instruction was provided based on participant *recall* of symptoms and activity patterns. In a pilot study, participants of an activity pacing intervention that was individually tailored based on in-vivo monitoring of symptoms and activity had greater improvements in fatigue compared to participants of a general activity pacing intervention that did not include this tailoring[26]. The purpose of this randomized clinical trial was to compare the efficacy of three treatment groups – usual care, tailored activity pacing, and general activity pacing - in improving symptom severity and physical function in individuals with knee or hip OA. We also examined if arthritis self-efficacy moderated improvements in symptom severity and function. Because of positive pilot study findings[26], we hypothesized that tailored activity pacing would show greater improvements in fatigue, pain and physical function compared to general activity pacing or usual care. Self-efficacy, the evaluation of ones’ ability to enact a behavior, is a common pathway to behavior change [3] and is related to treatment gains via factors such as increased treatment adherence and translation of intentions to action [7; 10;

23]. Therefore, we expected that greater baseline self-efficacy would be associated with greater treatment-related gains.

2. Methods

2.1 Participants

Adults were recruited through public advertisements (e.g., newspaper, online, radio, and flyers), and through flyers at clinics at the University hospital and Veterans Administration (VA). Participants were included if they were age 50 and older, reported pain for at least 3 months duration, reported at least mild to moderate pain severity overall [a score of 4 and at least 2 activities with at least moderate pain[14] on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale[4], and had radiographic evidence of osteoarthritis in a corresponding knee or hip joint (≥ 2 on the Kellgren Lawrence scale)[22]. Participants also needed to live in the community (in their own home, senior residence, or apartment) have adequate cognitive ability (scoring ≥ 5 on the 6-item screener to identify cognitive impairment) [9], be able to enter ratings on the Actiwatch-Score accelerometer used in the study, and have a consistent, typical sleep schedule (with usual wake-up time before 11am and bedtime before 2am). People were excluded if non-ambulatory (unable to walk with or without an assistive device), experienced a period of bed-rest for >2 days in the past month, changed any medications (for osteoarthritis or other conditions) within the past 2 weeks, had medical conditions that could interfere with symptom ratings or accelerometer data (e.g., rheumatoid arthritis, Parkinson's disease, peripheral neuropathy, multiple sclerosis, lupus, current cancer treatment, cancer diagnosis in the past year, sleep apnea), if they had limb hemiplegia or amputation, or if they had anemia or unmanaged thyroid dysfunction (abnormal thyroid stimulating hormone or low hemoglobin). People were also excluded if they had a knee joint injection within the previous 3 months, had a knee arthroscopic procedure within the previous 2 months, or had a knee replacement within the previous 6 months. Lastly, people were excluded if they currently or in the last 12 months: were in receipt of physical or occupational therapy for OA symptoms for knee or hip problems or participated in a cognitive behavioral program or other self-management program that included activity pacing instruction.

2.2 Design

This study used a 3-arm, assessor-blinded, parallel group randomized controlled trial design. Assessments were done at baseline (prior to randomization), post-treatment (approximately 10 weeks after randomization), and 6 months after randomization. The study was registered on ClinicalTrials.gov (NCT01192516), and the protocol has been published elsewhere [27]. The participants were randomized into one of three groups: tailored activity pacing, general activity pacing, or usual care groups. To balance age and gender across groups, the randomization scheme was block stratified by age group (cutoff was 62 years) and male/female sex with blocks of 3. The randomization scheme was developed by a study statistician and implemented in statistical software (SAS).

2.3 Procedures

Potential participants deemed initially eligible from a phone screening came in for a baseline clinic visit. After written informed consent was obtained, further screening was done to assess eligibility (e.g., blood work, x-ray to determine osteoarthritis, and health history) and enrolled participants completed questionnaires, physical performance testing, and instruction on how to use the Actiwatch-Score accelerometer with accompanying logbook for use in a 7-day home monitoring period. Participants wore the Actiwatch-Score on their non-dominant wrist for 7 days and were asked to input ratings of pain, fatigue, and stiffness severity into the device 5 times per day at pre-specified times following an audible prompt as well as record ratings in a logbook. They also reported wake and bed times in the logbook, to assist in accelerometry data processing. A 7 day sampling period was chosen because it has been deemed an acceptable length of time needed to obtain reliable and valid physical activity data in adult samples [16; 36]. Participants were asked to wear the device continuously for the 7 day period except for times when the device could become wet (e.g., showering or swimming). At the end of the home monitoring period, participants were asked to return the device and logbook by mail in a prepaid envelope and were compensated \$20. If participants completed at least 80% of the data collection over home monitoring period, they were randomized into one of the three groups. Twenty five people had missing data on accelerometry mainly due to attrition (48%, 12 out of 25 people), followed by being unable to follow watch instructions (16%, 4 out of 25 people), 3 had data for on only 1 or 2 days, 3 people had watch malfunctions, and 3 were missing. Of those with acceptable accelerometry data, eighty-six percent of participants had complete symptom reporting (at all 35 time points over the 7 days); the remaining 14% of people had 1-5 of the 35 symptom reports missing. After being randomized into groups, participants of the tailored and general activity pacing interventions were then scheduled for 3 in-person visits with one of the trained occupational therapists. All outcome assessments were conducted by study staff blinded to group assignment of participants. After the 10 week outcome assessment visit, participants were called monthly until the following 6 month outcome assessment to ascertain any changes in health status. All study procedures were approved by the Institutional Review Board at the University of Michigan Medical School and the Subcommittee on Human Studies in the Veteran's Affairs Ann Arbor Healthcare System. Written informed consent was obtained from all participants.

2.4 Study Flow

Figure 1 shows a CONSORT diagram of participant flow through the study. Of 868 people who were screened by phone, 61% were not eligible or interested in participating. Of those who were ineligible, 66% of the people screened were ineligible due to not having chronic knee or hip pain or enough knee or hip pain ($n = 183$) or were not aged 50 or older ($n = 138$). Of the remaining 34%, 57 people reported an exclusionary medical condition (e.g., rheumatoid arthritis, cancer, Parkinson's disease, peripheral neuropathy), 39 people were participating in therapy or other treatment (cognitive behavioral therapy, joint injections, physical therapy), 32 people had no usual sleep schedule, 15 people were on bedrest 2 or more days, 12 were not ambulatory, 4 people failed the cognitive screener, and 7 were excluded for various other reasons. There were 337 people who came to our center for baseline testing which included additional eligibility screening (x-ray and bloodwork),

questionnaires, and physical performance testing. Of the 337, (42%) were not eligible (80% of those ineligible did not have radiographic knee or hip OA, 11% had abnormal blood work, and 9% had other reasons for ineligibility). Three people declined to participate from the study prior to randomization, resulting in 193 people randomized: 64 in the tailored group, 66 in the general group, and 63 in the usual care group. Twenty-two percent of the sample dropped out or were withdrawn from the study by the 6 month outcome assessment. In the tailored and general groups, 10 people (5%) were withdrawn from the study by the study team because they started new treatment (joint injections, joint replacement, or other; $n = 6$) or were unable to follow watch instructions ($n = 4$). Seventeen percent of people were lost to follow up or withdrew for other reasons (across all groups). In the general group, 2 individuals who withdrew cited reasons of not liking pacing or feeling it was not possible with comorbid symptoms of attention deficit hyperactivity disorder. Of the people randomized, the percentage of participants who received the intended treatment of 3 in-person sessions, or 2 out of the 3 sessions) was 78% in the tailored group and 82% in the general group.

2.5 Intervention Conditions

The tailored and general activity pacing interventions were provided in the same manner. There were three individual in-person sessions with an occupational therapist. The first session lasted about one hour, the second and third sessions ranged from 30 – 45 minutes each. The time between sessions was about 7 – 10 days to allow participants to practice principles learned in the sessions, although there were some variations in that timing if participants rescheduled sessions due to conflicts. Participants of both the tailored and general activity pacing interventions were given a learning module for each session consisting of objectives for each session, and specific content, exercises, and homework activities (see Supplemental Material).

2.5.1 Tailored Activity Pacing Intervention—In addition to the learning module, participants in the tailored activity pacing intervention received an individualized summary report (see Supplemental Material). This report was generated from activity and symptom data collected during the home monitoring period and comprised a personalized pacing schedule based on the associations between symptoms and physical activity for a given individual. The report consisted of a graphic (called the “actogram”) of all activity data collected from the Actiwatch-Score; activity periods that appeared to indicate prolonged high or low activity were circled as potential periods of overactivity or sedentary behavior. In addition, daily and weekly averages of each individual's symptoms and activity counts were presented alongside comparison values from a large sample of participants with knee or hip OA from the study team's previous research studies (to indicate whether the person was generally low/average/high on symptoms and activity relative to a sample of individuals with the same condition). Several graphs were created to show associations between an individual's physical activity and symptoms, and information from participant's daily activity logs that had information about the types of activities that were engaged in were integrated into the reports to highlight particular examples where pacing could be helpful. These data were presented with the goal of discussing each individual's unique association between symptoms and activity. The end of the report had pacing recommendations based on the

aggregate activity and symptom data. Reports were created by a study team member (AL) and discussed with the study principal investigator (SM) to review and refine treatment recommendations. The treating therapist received the report at least one day before the first scheduled treatment session in order to become familiar with the participant's symptom and activity patterns. This individual report was then discussed throughout the sessions of the tailored intervention.

2.5.2 General Activity Pacing Intervention—Unlike the tailored activity pacing intervention, neither the participants nor the treating therapists in the general activity pacing intervention received information or data about the home monitoring period. Participants in the general activity pacing intervention received the same learning module and time in the session was spent communicating with the therapist about usual activity and symptoms and recalling instances in which symptoms interfered with activity. The similarities and differences in the tailored and general activity pacing interventions are outlined in Table 1.

2.5.3 Usual Care—Participants of the usual care condition were instructed to continue with their usual care for OA. These participants only came in for assessments at baseline, 10 weeks and 6 months using the same procedures as participants in the pacing interventions. They also participated in monthly health status calls similar to participants of the pacing interventions. At the end of the 6 months, participants were offered the learning module used in the pacing interventions.

2.6 Treatment Fidelity

2.6.1 Treatment Delivery—There were six occupational therapists involved in administering the interventions, a set of 3 therapists for each intervention. In brief, each set of therapists (those from the tailored and general activity pacing interventions) were trained separately by the study PI (SM) using intervention-specific, therapist versions of the learning module. The specific content being provided in the other intervention was not discussed, and the therapists administering each intervention condition were told not to talk to the therapists of the other condition regarding their intervention. Therapists logged their actual treatment time with each individual and all therapists had a checklist of items to cover in each visit to ensure consistent presentation of material. Therapist sessions were audiotaped, and a random sample of audiotapes was checked to determine if original criteria was met for intervention delivery in each intervention arm. A checklist was used for this purpose and members of the study staff were trained in rating the sessions from the audiotapes. Regular meetings were scheduled with the therapists to prevent any protocol drift. Based on the checklist ratings, criteria were met for the 10% of checked audiotapes which included a sampling of both treatments and each of the three treatment sessions.

2.6.2 Treatment Receipt, Enactment, and Perceived Usefulness—Treatment receipt was checked through the completion of homework assignments which were reviewed by the therapist at the following session. The therapist had an opportunity to assess comprehension of the use of the time-based activity pacing plan and troubleshoot any issues with participants. To assess treatment enactment and perceived usefulness, we administered a blinded survey for participants of the tailored and general activity pacing interventions.

The questions on the survey were modified depending on group assignment to be related to the intervention received. The survey included a question of whether participants changed the way they complete daily activities as a result of the program. It also included questions about their experiences with the intervention including how much they felt they benefited from the program and if the program helped them deal more effectively with their symptoms.

2.7 Primary Outcome Measures

Fatigue was measured by the Brief Fatigue Inventory (BFI), a validated measure of fatigue in cancer populations that has been increasingly used in arthritis populations [25]. Respondents rate their fatigue (defined as weariness or tiredness) on a scale of 0 = no fatigue to 10 = fatigue as bad as you can imagine related to general severity of fatigue and its interference in daily life. This scale is typically scored by averaging of 9 of the 10 items. Internal reliability of all study assessments was high (Cronbach's alpha of .95).

We also used the 8-item Patient Reported Outcome Measurement Information System (PROMIS) fatigue short form from the NIH Toolbox. Internal reliability was high at all assessment periods (alpha of .95 - .96). Pain severity was measured using the pain subscale taken from the WOMAC[4], a five item scale that measures pain severity in different activities due to knee or hip pain. Scores were summed with a higher score indicating more pain. Internal reliability was adequate at all study assessment periods (alphas of .79 - .80).

2.8 Secondary Outcomes

Physical function variables included the Six Minute Walk test[8] and WOMAC physical disability scale [39]. The Six Minute Walk test is a validated objective physical function measure in which individuals are asked to walk a standard course at their usual pace for six minutes and the distance achieved in feet is recorded. The WOMAC physical disability short form scale consists of 7 items and measures perceived difficulty with a variety of activities due to knee or hip pain; it is scored on a scale of 0 – 28; a higher score indicates more physical disability. Internal reliability was good (alphas of .86 - .89).

2.9 Moderator

Arthritis Self-Efficacy Scale is an 8-item scale in which participants rate their certainty on a 1(very uncertain) –10 (very certain) scale in being able to manage symptoms, function, and mood control interference. Scores on the 8 items are averaged, for a possible range of 1-10 with higher scores indicating higher levels of self-efficacy. The scale is a shorter version of a 20-item self-efficacy scale[24] and has been recently validated in an English-speaking cohort [40]. Internal reliability of this scale was good at all assessment periods (alphas of .88 - .91).

2.10 Demographics and Clinical Variables

Demographics included age, sex, race/ethnicity, marital status, years of education, employment status, and veteran status. Clinical variables of interest included body mass index (BMI); [calculated from measured weight (kg)/ height(m)²], illness burden measured as the total number of endorsed symptoms (e.g., headache, stomach pain) out of a list of 41

possible symptoms, and depressive symptoms measured by Center for Epidemiologic Studies-Depression Scale (CES-D) [32]. Arthritis-related variables included primary study joint with symptomatic OA (knee or hip); disease severity of that joint by Kellgren-Lawrence (KL) grade (rating of 2 indicates definitive signs of OA, stages 3 and 4 indicate more severe disease shown by joint space narrowing and osteophyte formation) [21], and months with arthritis pain. Number of body regions indicated as painful on a body map was used as a measure of widespread pain. Functional capacity was measured by comfortable gait speed in which the time to walk a course of 20 feet (6.1 meters) at a comfortable pace was timed and reported in meters per second [5].

2.11 Momentary Measures and Objective Physical Activity

Five times per day for 7 days following each assessment period, participants were asked to input symptom ratings into the Actiwatch-Score accelerometer [Philips Respironics; Mini Mitter, Bend OR]. Rating times occurred at wake-up, 11am, 3pm, 7pm, and bedtime (“lights out”). An audible alarm prompted participants to enter ratings at all time-points except at wake up and bedtimes. Pain, fatigue, and stiffness severity were each rated on a scale of 0 (“no <symptom>”) – 10 (“<symptom> as bad as you can imagine”). Fatigue was defined for participants as tiredness or weariness [41]. Momentary ratings of symptoms are commonly thought to be more reliable than one-time symptom assessments because they are not as affected by recall bias [34]. The accelerometer measures changes in acceleration in terms of physical activity “counts” and has been used to assess physical activity in studies of people who have symptoms such as chronic pain [12; 15; 37]. Although worn on the wrist, it is highly associated with whole-body movement [31; 38]. The physical activity and symptom ratings at baseline were used to create individualized reports for participants in the tailored intervention. At baseline, average physical activity over the monitoring period was aggregated from the daily daytime activity counts per minute. Activity variability over the monitoring period was calculated as the standard deviation of activity counts/min for the week.

2.12 Activity Pacing Measure

To determine the usage of activity pacing behaviors, the activity pacing subscale of the Chronic Pain Coping Inventory (CPCI) [19], which has demonstrated good reliability (test-retest, internal consistency) and validity (construct, discriminant) [29], was given at the study assessment periods. The scale consists of 6 items and assesses the extent to which participants engage in their daily activities in a steady manner not contingent upon their symptoms by taking breaks and breaking up activities into smaller pieces [29]. Participants recall how many days in the past week they used each of 6 behaviors and the items are averaged; total possible score ranges from 0-7 with higher values related to greater using of pacing. Internal reliability of this scale was good at all assessment time points (alphas at all assessment periods = .86 - .88).

2.13 Power

The sample size was established based on pilot data in which we compared the tailored activity pacing intervention with the general activity pacing intervention and detected large group differences on BFI severity and interference scales at the 10 week outcome

assessment ($d = .79$ and 1.1 respectively)[26] The estimated sample size needed to detect differences between groups in the current study was 156.

2.14 Data Analysis

Demographic and clinical variables were compared between those who were screened and eligible and those who were screened and not eligible using t-tests or Wilcoxon rank sum tests for continuous variables and chi-square or Fisher's exact tests for categorical variables. Similar analyses were performed to compare the characteristics of each treatment group. Missing information was small and excluded from this analysis.

Multilevel random effects modeling (MLM) was used to test the study hypotheses. This statistical approach was optimal to examine data over time using an intent to treat model in which all available data points are utilized. Using the SAS PROC MIXED procedure, MLM also accounts for correlation between adjacent observations. In our analyses, we specified an unstructured covariance matrix and a random intercept allowing for natural heterogeneity across individuals. The normality assumption of residuals was verified for each outcome and no normalizing transformations were needed. Prior to conducting the analyses, variables were centered based on guidelines for centering data in multilevel statistical procedures [11]. Between-person variables were sample-centered so that the values indicated an individual's deviation from the sample's mean.

To examine effects of group assignment on each outcome (fatigue, pain, physical function), separate MLMs were constructed. First, unadjusted models were run with only time (categorical), treatment group and the time by treatment interaction in the model and then adjusted models were run by adding the potential confounders of BMI, age, sex, and KL grade. Estimated means from the unadjusted models are reported along with the unadjusted p-value and adjusted p-value of the time by treatment interaction. Baseline arthritis self-efficacy was tested as a moderator in each model (unadjusted and adjusted) by adding the outcome variable and investigating the time by treatment by self-efficacy interaction. All analyses were conducted using SAS software Version 9.4 [33].

3. Results

Characteristics of the sample ($n = 193$) are shown in Table 2. The sample was 61% female, and slightly over half were married. The mean age was 64.7 years. Sixteen percent of participants were from racial or ethnic minority groups other than non-Hispanic white. The sample had a mean education level of 16 years and forty one percent of participants were employed or volunteering at least 20 hours per week. Body Mass Index values indicate that, on average, the sample was obese according the United States Centers for Disease Control standards (e.g., BMI ≥ 30.0); 50% of the sample was obese. The sample reported mild levels of pain and mild to moderate fatigue. For physical function, the sample walked an average of 1207 feet on the six minute walk test, which is slightly slower than norms from a meta-analysis of studies of community dwelling older adults ($M = 1637$ feet)[6]. Seventeen percent of the sample had functional capacity in the range associated with frailty and increased risk of mortality (< 1.0 meters/second) [35]. The sample of eligible participants were not different according to demographic characteristics compared to those who were

ineligible except that those who were ineligible were younger (61.9 years, $p = .004$). People who were ineligible also on average had more fatigue ($BFI = 3.54$, $p = .02$) and less arthritis self-efficacy ($n = 140$, 5.89 , $p = .02$). When examining characteristic differences among groups, only disease grade was significantly different. The tailored group had a higher proportion of participants with low and high disease severity (KL grade of 2 and 4) compared to the other two groups. The tailored group was also more physically active based on average weekly physical activity from the accelerometer, although this difference was of marginal significance ($p = 0.07$).

3.1 Activity Pacing Use

Table 3 shows the means of self-reported activity pacing use over the three assessment periods. At 10 weeks and 6 months, participants of the pacing interventions had significantly higher reported usage of activity pacing compared to usual care. All groups had increases in activity pacing at 10 weeks which decreased at 6 months.

3.1 Primary Analyses

Of all primary and secondary outcomes, the only significant group difference between groups was for WOMAC pain in the model adjusted for covariates. Table 4 shows the estimated means at each time point by group. Participants of the general activity pacing intervention had a significant decrease in their pain from baseline to 10 weeks; however, participants of the usual care group had decreased pain from baseline to six months.

3.2 Moderator Analysis

Baseline arthritis self-efficacy was not a significant moderator of intervention effects over time of any primary or secondary outcome. This potential moderator was tested in models that were unadjusted or adjusted for covariates in the primary linear mixed model analyses; p values ranged from .10 - .80.

3.3 Treatment Enactment and Perceived Usefulness of the Interventions

The response rate from the blinded survey was 71% of completers of the tailored ($n = 34$) or general pacing interventions ($n = 33$). Of these respondents, 85% in the tailored and general groups reported that they changed the way they complete daily activities as a result of their intervention. Seventy nine percent of participants in both groups felt that they benefited from their intervention somewhat or a great deal. Ninety one percent of participants in the general group and 88% of those in the tailored group felt the program helped them manage their symptoms.

4. Discussion

This is the first study to our knowledge that has examined effects of the solitary use of time-based activity pacing on symptoms and physical function for adults with symptomatic knee or hip OA. We tested a brief time-based activity pacing intervention delivered in two conditions, tailored or general, compared to a usual care group. We did not find that activity pacing as a singular behavioral strategy was sufficient for improving pain, fatigue, or physical function for participants in this sample.

Given our sufficient sample size, well-characterized, symptomatic, and clinically relevant sample, use of multiple objective and subjective measures of outcomes, examination of moderation effects, and assessment immediately post-treatment and at 6 months follow-up, we expect that we would have detected a statistically significant difference in the outcomes if the pacing interventions had been efficacious as a single behavioral intervention. There may be several reasons for our negative findings which we believe may relate to intervention potency, differences in behaviors across study arms, or a potential mismatch between our participants and the intervention provided.

The pacing interventions, which were designed to facilitate potential uptake into standard rehabilitation care, may not have been potent enough to facilitate adoption of pacing behavior. The total pacing instruction was about 2.5 hours over three sessions. Although participants reported an increase in the use of pacing on the activity pacing subscale of the CPCI, immediately following the intervention at 10 weeks, the frequency of use of pacing dissipated by 6 months (Table 4). Additionally, a few participants commented on the post-intervention survey that they would have liked more face-to-face sessions with the therapist. It also may be that activity pacing instruction would have been more potent for people with OA if delivered in conjunction with other behavioral skills as it has been done in more traditional multi-component treatment studies [1; 20; 21]. However, it may also be possible that previous studies of such combination therapies might have obscured the lack of efficacy of activity pacing for symptom management for people with OA. Some participants commented that they would have liked to receive activity pacing instruction in combination with exercise or strength training. Our protocol focused on balancing activity and rest to keep a steady pace throughout the day. A previous multi-component intervention by Keefe and colleagues that involved activity pacing did not have a structured exercise component as part of their pain coping skills training intervention [20; 21]; however, their time-based activity pacing instruction involved enhancing physical activity by increasing set time quotas for more active periods throughout the day. Judicious inclusion of physical activity, as done in the study by Keefe and colleagues, may be an important element of effective activity pacing for this population.

Another potential explanation for the negative findings is differences in participant behavior across study arms. The usual care group had the biggest decrease in pain over time (a finding of marginal significance $p = .06$) and these reductions may be due to increased exercise, other health behavior, or a natural decline in pain among persons seeking out medical care for knee or hip OA. A higher percentage of participants in the usual care group reported starting an exercise program during the study period compared to participants in the intervention groups (48% versus 32% respectively, Chi-Square = 4.25, $p = .04$). The positive changes in pain for the usual care group might also be attributable to individuals in this group actively pursuing OA treatments whereas the intervention groups were deemed ineligible and dismissed from the study if undertaking these treatments in the active treatment period (0 – 10 weeks). Of note, a greater percentage of the usual care group increased their usage of pain medications compared to those in the interventions groups, although this difference was not statistically significant (24% versus 14%, Chi-Square = 2.97, $p = .09$).

It is also possible that the OA study sample may not have been the optimal target group for the intervention. In general, our sample reported having mild average pain and fatigue and there was not much room for improvement. Additionally, our eligibility criteria may have been too restrictive, omitting people with higher fatigue who may have benefitted from the treatment. Beyond the study-specific issues of recruitment, it appeared that time-based activity pacing interventions are appropriate only for a small subset of patients whose symptoms and functioning are highly related to activity level. This point became evident during creation of individual summary reports for participants in the tailored activity pacing intervention in which there were several instances where symptoms appeared unrelated to activity patterns and the treatment recommendations for establishing a preplanned schedule of activity and rest were difficult to generate. Furthermore, feedback from participants indicated some problems with acceptability of the treatment. For example, while some people articulated that they had less pain with attention to time-based breaks throughout the day, time-based pacing was viewed negatively by others because they did not like to stop an activity at a certain time before it was completed. In addition, time based pacing may only be appropriate for use at certain points during a disease course. In terms of the tailored pacing, the weeklong reports that were the basis for tailored pacing strategies (See Supplemental Material) were configured to simultaneously optimize the amount of relevant information and the accessibility/comprehensibility of the information. However, future studies of tailored pacing might benefit from evaluating the accessibility of this type of report across a broad range of educational and literacy levels; such work might indicate the need for changes (e.g. simplification) in how data is presented to the consumer. We have already presented the possibility that symptoms and functional limitations that are too mild might present limited potential for improvement. In contrast, those with very advanced OA might not benefit from an activity-based intervention such as this due to pathological processes that override the influence of activity on experience of symptoms and functional ability. In fact, one person mentioned that her OA was “too advanced for her to benefit from this, [time-based pacing] would have been useful 5 or 6 years ago”. Notably, at the start of the study, more people with severe OA were in the intervention groups compared to usual care and those individuals may have experienced some difficulty fully participating in the intervention. It is possible that pacing interventions might be demonstrated to be more effective in a sample with less disease severity but higher symptom burden.

Although the results of this clinical trial overall were negative, this study provides important information for the development of future activity pacing interventions. It appears that future interventions need to be more potent, perhaps with more face-to-face sessions and booster sessions and may show stronger effects if there are goals to increase the active time periods as done by Keefe and colleagues [20; 21]. Although our method of tailoring activity pacing using data on symptom and activity patterns in the 7-day monitoring period to generate individualized reports did not impact study outcomes, we believe that the association between symptoms and physical activity is still relevant and worthy of study in service of helping individuals improve their functioning. In this study, there were large variations in associations between symptoms and activity by participants both in strength of the association and the type of symptoms (pain, fatigue, stiffness) that were reported to interfere with activity for participants. We also found that while prevention of overactivity (overdoing

physical activity to the point of a symptom flare) is often the focus of pacing instruction, many people in the sample tended to have low levels of activity and symptoms. The prevalence of underactivity in the OA population is important to further study as pacing interventions may need to be adapted accordingly with regard to activity level. Lastly, it may be important to consider other factors such as underlying medical conditions, symptom burdens, and physical impairments when developing activity pacing interventions. The correlations between pacing behaviors and measures of pain and functioning are largely inconsistent across studies which include a variety of study samples with different medical conditions underlying their chronic pain [2]. A future direction is to examine whether individuals with some conditions naturally respond better or are in greater need of pacing compared to those with other conditions.

Conclusion

The time-based activity pacing interventions tested in this study as singular behavioral interventions (i.e., tailored and general versions) did not improve outcomes of fatigue, pain, or physical function in a sample of people with symptomatic knee or hip OA. Future studies will need to determine how pacing should be delivered for optimal effectiveness, and to identify for whom time-based activity pacing works best.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The authors report no conflicts of interest. This project was supported by grant 1101RX000410 from the Rehabilitation and Research Branch of the Veterans Affairs Office of Research Development. Dr. Kratz was supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases under award number 1K01AR064275 while working on this manuscript. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The authors have no conflicts of interest to report. We thank Molly Santioni MOTR/L, Katie Woloszyn MOTR/L, Sharifa Bilbeisi MOT, OTR/L, Maria Clary MOTR/L, Katelin Iott, OTD/L, and Stacey Schepens PhD OTR/L for serving as interventionists for this study.

References

1. Allen KD, Oddone E, Coffman CJ, Datta SK, Juntilla KA, Lindquist JH, Walker TA, Weinberger M, Bosworth HB. Telephone-based self-management of osteoarthritis: A randomized trial. *Ann Intern Med.* 2010; 153:570–79. [PubMed: 21041576]
2. Andrews NE, Strong J, Meredith PJ. Activity pacing, avoidance, endurance, and associations with patient functioning in chronic pain: A systematic review and meta-analysis. *Arch Phys Med Rehabil.* 2012; 93:2109–21. [PubMed: 22728699]
3. Bandura A. The explanatory and predictive scope of self-efficacy theory. *J Soc Clin Psychol.* 1986; 4:359–73.
4. Bellamy N, Buchanan W, Goldsmith C, Campbell J, Stitt L. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol.* 1988; 15:1833–40. [PubMed: 3068365]
5. Bohannon RW. Comfortable and maximum walking speed of adults aged 20–79 years: reference values and determinants. *Age Ageing.* 1997; 26:15–19. [PubMed: 9143432]

6. Bohannon RW. Six-minute walk test: A meta-analysis of data from apparently healthy elders. *Top Geriatr Rehabil*. 2007; 23:155–60.
7. Burleson JA, Kaminer Y. Self-efficacy as a predictor of treatment outcome in adolescent substance use disorders. *Addict Behav*. 2005; 30:1751–1764. [PubMed: 16095844]
8. Butland RJ, Pang J, Gross ER, Woodcock AA, Geddes DM. Two-, six-, and 12-minute walking tests in respiratory disease. *Br Med J (Clin Res Ed)*. 1982; 284:1607–08.
9. Callahan C, Unverzagt F, Hui S, Perkins A, Hendrie HC. Six-item screener to identify cognitive impairment among potential subjects for clinical research. *Med Care*. 2002; 40(9):771–81. [PubMed: 12218768]
10. Diclemente, CC.; Carbonari, J.; Daniels, J.; Donovan, D.; Bellino, L.; Neavins, T. Self-efficacy as a matching hypothesis: Causal chain analysis.. In: Longabaugh, R.; Wirtz, P., editors. *Project MATCH hypotheses: Results and causal chain analyses*. National Institute on Alcohol Abuse and Alcoholism; Rockville, MD: 2001. p. 239-56.
11. Enders C, Tofighi D. Centering predictor variables in cross-sectional multilevel models: a new look at an old issue. *Psychological methods*. 2007; 12:121–38. [PubMed: 17563168]
12. Fischer JS, LaRocca NG, Miller DM, Ritvo PG, Andrews H, Paty D. Recent developments in the assessment of quality of life in multiple sclerosis (MS). *Mult Scler*. 1999; 5:251–59. [PubMed: 10467384]
13. Fordyce, W. *Behavioral methods for chronic pain and illness*. Mosby; St. Louis: 1976.
14. Goggins J, Baker K, Felson D. What WOMAC pain score should make a patient eligible for a trial in knee osteoarthritis? *J Rheumatol*. 2005; 32:540–2. [PubMed: 15742450]
15. Haerens L, Deforche B, Vandelanotte C, Maes L, De Bourdeaudhuij I. Acceptability, feasibility and effectiveness of a computer-tailored physical activity intervention in adolescents. *Patient Educ Couns*. 2007; 66:303–10. [PubMed: 17298873]
16. Hart TL, Swartz AM, Cashin SE, Strath SJ. How many days of monitoring predict physical activity and sedentary behaviour in older adults? *Int J Behav Nutr Phys Act*. 2011; 8:62. [PubMed: 21679426]
17. Hasenbring MI, Hallner D, Klasen B, Streitlein-Böhme I, Willburger R, Rusche H. Pain-related avoidance versus endurance in primary care patients with subacute back pain: Psychological characteristics and outcome at a 6-month follow-up. *PAIN*. 2012; 153:211–7. [PubMed: 22093816]
18. Hasenbring MI, Verbunt JA. Fear-avoidance and endurance-related responses to pain: New models of behavior and their consequences for clinical practice. *Clin J Pain*. 2010; 26:747–53. [PubMed: 20664333]
19. Jensen MP, Turner JA, Romano JM, Strom SE. The Chronic Pain Coping Inventory: development and preliminary validation. *PAIN*. 1995; 60:203–16. [PubMed: 7784106]
20. Keefe FJ, Caldwell DS, Williams DA, Gil KM, Mitchell D, Robertson C, Martinez S, Nunley J, Beckham JC, Crisson JE, Helms M. Pain coping skills training in the management of osteoarthritic knee pain: A comparative study. *Behav Ther*. 1990:49–62.
21. Keefe FJ, Caldwell DS, Williams DA, Gil KM, Mitchell D, Robertson C, Martinez S, Nunley J, Beckham JC, Helms M. Pain coping skills training in the management of osteoarthritic knee pain-II: Follow-up results. *Behav Ther*. 1990:435–47.
22. Kellgren J, Lawrence J. Radiological assessment of osteoarthritis. *Ann Rheum Dis*. 1957; 16:494–501. [PubMed: 13498604]
23. Lippke S, Wiedemann AU, Ziegelmann JP, Reuter T, Schwarzer R. Self-efficacy moderates the mediation of intentions into behavior via plans. *Am J Health Behav*. 2009; 33:521–9. [PubMed: 19296742]
24. Lorig K, Chastain RL, Ung E, Shoor S, Holman HR. Development and evaluation of a scale to measure perceived self-efficacy in people with arthritis. *Arthritis Rheum*. 1989; 32:37–44. [PubMed: 2912463]
25. Mendoza TR, Wang XS, Cleeland CS, Morrissey M, Johnson BA, Wendt JK, Huber SL. The rapid assessment of fatigue severity in cancer patients: use of the Brief Fatigue Inventory. *Cancer*. 1999; 85:1186–96. [PubMed: 10091805]

26. Murphy SL, Lyden AK, Smith DM, Dong Q, Koliba JF. Effects of a tailored activity pacing intervention on pain and fatigue for adults with osteoarthritis. *Am J Occup Ther.* 2010; 64:869–76. [PubMed: 21218677]
27. Murphy SL, Lyden AK, Clary M, Geisser ME, Yung RL, Clauw DJ, Williams DA. Activity pacing for osteoarthritis symptom management: study design and methodology of a randomized trial testing a tailored clinical approach using accelerometers for veterans and non-veterans. *BMC Musculoskelet Disord.* 2011; 12(177)
28. Murphy SL, Smith DM, Clauw DJ, Alexander NB. The impact of momentary pain and fatigue on physical activity in women with osteoarthritis. *Arthritis Rheum.* 2008; 59(6):849–56. [PubMed: 18512720]
29. Nielson WR. An activity pacing scale for the chronic pain coping inventory: development in a sample of patients with fibromyalgia syndrome. *Pain (Amsterdam).* 2001; 89:111–15.
30. Nielson WR, Jensen MP, Karsdorp PA, Vlaeyen JW. Activity pacing in chronic pain: Concepts, evidence, and future directions. *Clin J Pain.* 2013; 29:461–8. [PubMed: 23247005]
31. Patterson SM, Krantz DS, Montgomery LC, Deuster PA, Hedges SM, Nebel LE. Automated physical activity monitoring: validation and comparison with physiological and self-report measures. *Psychophysiology.* 1993; 30:296–305. [PubMed: 8497559]
32. Radloff L. The CES-D scale: A self-report depression scale for research in the general population. *Appl Psychol Meas.* 1977; 1:385–401.
33. SAS Institute Inc. SAS Version 9.4. SAS Institute Inc.; Cary, NC: 2008.
34. Shiffman S, Stone AA, Hufford MR. Ecological momentary assessment. *Ann Rev Clin Psychol.* 2008; 4:1–32. [PubMed: 18509902]
35. Studenski S, Perera S, Patel K, Rosano C, Faulkner K, Inzitari M, Brach J, Chandler J, Cawthon P, Connor EB, Nevitt M, Visser M, Kritchevsky S, Badinelli S, Harris T, Newman AB, Cauley J, Ferrucci L, Guralnik J. Gait speed and survival in older adults. *JAMA.* 2011; 305:50–8. [PubMed: 21205966]
36. Trost SG, McIver KL, Pate RR. Conducting accelerometer-based activity assessments in field-based research. *Med Sci Sports Exerc.* 2005; 37:S531–43. [PubMed: 16294116]
37. Vandelandotte C, De Bourdeaudhuij I. Acceptability and feasibility of a computer-tailored physical activity intervention using stages of change: project FAITH. *Health Educ Res.* 2003; 18:304–17. [PubMed: 12828232]
38. Westerterp KR. Physical activity assessment with accelerometers. *Int J Obes Relat Metab Disord.* 1999; 23:S45–9. [PubMed: 10368002]
39. Whitehouse SL, Crawford RW, Learmonth ID. Validation for the reduced Western Ontario and McMaster Universities Osteoarthritis Index function scale. *J Orthop Surg.* 2008; 16:50–4.
40. Wilcox S, Schoffman DE, Dowda M, Sharpe PA. Psychometric properties of the 8-Item english Arthritis Self-Efficacy Scale in a diverse sample. *Arthritis.* 2014:385256. [PubMed: 25215233]
41. Wolfe F, Hawley DJ, Wilson K. The prevalence and meaning of fatigue in rheumatic disease. *J Rheumatol.* 1996; 23:1407–17. [PubMed: 8856621]

Figure 1.
Study Flow Chart

Table 1

Summary of content of activity pacing interventions

	Objectives	Both Interventions		Tailored Activity Pacing		General Activity Pacing	
		Content	Exercise	Content	Exercise	Content	Content
Session 1	1. Develop awareness of behaviors that increase osteoarthritis symptoms. 2. Develop a time-based activity pacing plan of <i>on-off</i> periods for a specific type of activity. 3. Set goals based on number of successful <i>on-off</i> cycles participant expects to complete before next session.	<ul style="list-style-type: none"> Impact of OA on daily life; identify behaviors as the target of the intervention Persistence & OA symptoms – provide examples of maladaptive behaviors Identify goal of balancing activity/rest Introduction to planned breaks according to <i>time</i> Teach core pacing behaviors—attending to behaviors and activities that contribute to symptoms; prioritizing important activities; planning how to complete activities without doing too much of one thing (sitting, standing) Ask client about current pacing techniques 	<ul style="list-style-type: none"> Developing a time-based activity plan Set goal for number of times participant will use personal time-based pacing plan 	<ul style="list-style-type: none"> Refer to logbook & accelerometry report-highlight overall activity and symptom patterns Find and discuss an example of symptom- or task-based pacing from logbook and activity report 	<ul style="list-style-type: none"> Refer to logbook & accelerometry — provide an example of how activity-rest balance can be helpful Identify examples when time-based pacing might be appropriate Homework: Develop awareness between behaviors, symptoms and activities Identify activities, symptoms and changes in behavior related to them 	<ul style="list-style-type: none"> provide an example of a situation of “too much” activity contributing to a symptom flare 	
Session 2	1. Evaluate use of planned <i>on-off</i> periods. 2. Discuss barriers. 3. Develop a plan for overcoming barriers.	<ul style="list-style-type: none"> Recognition that behavior change is not easy; accept that changing how one does activities will require multiple attempts Review list of common barriers to time-based pacing Identify personal barriers Discuss plans for circumventing personal barriers 	<ul style="list-style-type: none"> Evaluation worksheet Break through barriers; identify solutions to things that interfered with attempts to use time-based pacing 				
Session 3	1. Evaluate use of planned <i>on-off</i> periods. 2. Discuss lapses, high-risk situations & flare-ups. 3. Establish long-term goals for continued use of time-based activity pacing.	<ul style="list-style-type: none"> Define different types of lapses in behavior Define flare-up and management strategies for increases in symptoms Illustrate modified <i>on-off</i> plan for a flare up period Develop long-term goals that include plans for desired and necessary activities 	<ul style="list-style-type: none"> Discuss participant's use of on-off periods Identify high-risk situations that might increase the likelihood of a relapse 	<ul style="list-style-type: none"> Identify symptom flare-ups (review logbook and accelerometry report for examples) 	<ul style="list-style-type: none"> Identify high-risk situations that might increase the likelihood of a relapse Emphasize use of logbook as a tool 	<ul style="list-style-type: none"> Emphasis on long-term management Discuss past experiences with lapses (i.e. with diet and exercise, e.g.) Define high-risk situations in which lapses are more likely to occur 	

Table 2

Baseline characteristics of sample (N = 193)

Variable	Total Sample	Tailored N = 64	General N = 66	Usual Care N = 63	P value*
Age (y)	64.7 (8.41)	64.36 (8.26)	64.05 (8.32)	65.75 (8.68)	0.48
Sex (% female)	119 (61.7)	39 (60.9)	41 (62.1)	39 (61.9)	0.99
Race (n = 192)					0.48
White	162 (83.9)	56 (87.5)	55 (83.3)	51 (81.0)	
Black	21 (10.9)	5 (7.8)	6 (9.1)	10 (15.9)	
Asian	4 (2.1)	2 (3.1)	2 (3.0)	0 (0)	
American Indian/Alaskan Native or More than one race	5 (2.1)	1 (1.6)	3 (4.5)	1 (1.6)	
Married (%)	103 (53.4)	36 (56.3)	37 (56.1)	30 (47.6)	0.50
Years of education (n = 187)	16.19 (3.07)	16.21 (3.14)	16.29 (3.35)	16.08 (2.74)	0.97
Employed or volunteering (Part Time or Full Time) (n = 184)	79 (41.8)	30 (46.9)	27 (40.9)	22 (34.9)	0.39
Veteran status (yes) (n = 188)	31 (16.5)	10 (16.1)	12 (18.8)	9 (14.5)	0.81
BMI (n = 191)	31.05(6.67)	31.70 (6.81)	30.62 (6.72)	30.86 (6.54)	0.63
Illness Burden (# of endorsed symptoms in the past year) (n = 185)	7.55 (5.89)	7.84 (5.68)	7.54 (5.86)	7.28 (6.19)	0.70
Depression (CES-D) (n = 191)	8.91 (8.10)	9.08 (8.66)	9.36 (7.92)	8.27 (7.80)	0.51
% Knee OA	139 (72.0)	44 (68.8)	54 (81.8)	41 (65.1)	0.09
Study joint disease grade (K-L grade)					0.03
2	110 (57.0)	43 (67.2)	36 (54.5)	31 (48.4)	
3	66 (34.2)	13 (20.3)	27 (40.9)	26 (40.6)	
4	14 (7.3)	7 (10.9)	2 (3.0)	5 (7.9)	
Months of arthritis pain (n = 171)	138.19 (131.43)	140.86 (122.07)	124.48 (90.64)	150.79 (174.43)	0.97
Total painful regions (out of 34) (MI bodymap) (n = 191)	5.50 (3.49)	5.95 (3.89)	5.22 (3.20)	5.33 (3.36)	0.75
Average Physical Activity (ac/min) (n = 168)	341.42 (100.68)	360.35 (113.48)	347.21 (99.67)	318.20 (89.44)	0.07
Activity Variability (SD of act counts) n = 162	188.83 (46.29)	196.95 (60.38)	189.58 (41.10)	180.60 (32.24)	0.34
Comfortable Gait Speed (% > 1.0 meters/sec)	33 (17.1)	12 (18.8)	10 (15.2)	11 (17.5)	0.86
WOMAC pain scale (n = 192)	8.23 (3.22)	8.24 (2.99)	8.19 (3.37)	8.27 (3.32)	0.99
WOMAC physical disability	10.90(4.84)	11.43 (4.45)	10.78 (5.14)	10.48 (4.92)	0.53
Brief Fatigue Inventory	2.94 (2.36)	2.93 (2.33)	3.18 (2.45)	2.70 (2.31)	0.54
PROMIS fatigue (n = 188)	51.54(9.42)	52.32 (9.53)	51.76 (9.70)	50.49 (9.06)	0.54
6 minute walk test (feet) (n=192)	1206.66 (261.52)	1202.03 (273.21)	1208.56 (255.16)	1209.40 (260.09)	0.99
Arthritis self-efficacy (n = 192)	6.33 (1.65)	6.32 (1.63)	6.24 (1.62)	6.43 (1.74)	0.82

* P-value from the t-test or Wilcoxon rank sum test for continuous variables and Chi-Square or Fisher's exact test for categorical variables excluding missing

Table 3

Average activity pacing for each treatment group over time

CPCI Pacing Score	Tailored Activity Pacing (n = 64)	General Activity Pacing (N = 66)	Usual Care (N = 63)	p-value
Baseline	3.92 (1.85)	3.81 (1.91)	3.29 (1.80)	0.14
10 Weeks	4.83 (1.60)	4.68 (1.61)	3.54 (1.90)	0.0004
6 Months	4.27 (1.60)	4.17 (1.57)	3.43 (1.87)	0.06

Table 4

Estimated means from unadjusted linear mixed models.

Outcome	Time Point/Variable	Estimated Means (SE) from Unadjusted Model			F (df,df)	Unadj P *	F (df,df)	Adj P **
		Tailored Activity Pacing (N = 64)	General Activity Pacing (N=66)	Usual Care (N=63)				
BFI Fatigue Total	Baseline	2.37 (0.31)	2.49 (0.31)	2.06 (0.29)	0.25 (4,190)	0.91	0.41 (4,181)	0.80
	10 wks	2.81 (0.33)	2.76 (0.32)	2.45 (0.29)				
	6 mos	2.94 (0.33)	2.71 (0.31)	2.30 (0.28)				
	Group				0.85 (2,190)	0.43	0.95 (2,181)	0.39
	time				3.00 (2,190)	0.05	4.07 (2,181)	0.02
WOMAC Pain Score	Baseline	8.21 (0.40)	8.19 (0.39)	8.27 (0.40)	2.33 (4,190)	0.06	2.61 (4,181)	0.04
	10 wks	8.25 (0.45)	7.25 (0.45)	7.93 (0.43)				
	6 mos	7.93 (0.45)	7.46 (0.44)	6.78 (0.43)				
	Group				0.58 (2,190)	0.56	0.31 (2,181)	0.73
	time				6.52 (2,190)	0.002	5.75 (2,181)	0.01
PROMIS Fatigue	Baseline	52.37 (1.18)	51.63 (1.17)	50.27 (1.19)	0.24 (4,189)	0.92	0.16 (4,180)	0.96
	10 wks	52.80 (1.11)	52.64 (1.10)	51.70 (1.04)				
	6 mos	53.42 (1.18)	53.27 (1.15)	51.45 (1.11)				
	Group				0.87 (2,189)	0.42	0.99 (2,180)	0.37
	time				2.18 (2,189)	0.12	2.41 (2,180)	0.09
Physical Function (six minute walk)	Baseline	1202.03 (32.53)	1208.56 (32.04)	1209.81 (32.84)	0.69 (4,190)	0.60	1.09 (4,181)	0.36
	10 wks	1204.40 (33.12)	1224.08 (32.65)	1227.27 (32.57)				
	6 mos	1223.39 (32.93)	1223.16 (32.48)	1208.63 (32.54)				
	Group				0.02 (2,190)	0.98	0.33 (2,181)	0.72
	time				0.85 (2,190)	0.43	1.34 (2,181)	0.27
WOMAC disability score (short-form)	Baseline	11.43 (0.60)	10.78 (0.59)	10.48 (0.61)	0.78 (4,190)	0.54	0.48 (4,181)	0.75
	10 wks	11.08 (0.59)	9.81 (0.59)	9.69 (0.57)				
	6 mos	10.84 (0.67)	9.93 (0.65)	8.82 (0.64)				
	Group				1.87 (2,190)	0.16	1.43 (2,181)	0.24
	time				6.25 (2,190)	0.002	7.33 (2,181)	0.01

wks = weeks; mos = months; unadj = unadjusted; adj = adjusted

* p-value of the interaction of treatment and time in unadjusted model controlling only for time, treatment and their interaction

** p-value of the interaction of treatment and time in adjusted model also controlling for BMI, age, sex, and KL grade