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Association between Pre-intervention Physical Activity Level and Treatment Response to Exercise Therapy in Persons with Knee Osteoarthritis—An Exploratory Study

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Objective. Examine whether pre-intervention physical activity (PA) level is associated with achieving a positive treatment response of pain and/or function improvement after a 12-week exercise intervention in participants with knee osteoarthritis (OA).

Methods. We performed a secondary analysis of a randomized, single-blind comparative effectiveness trial showing similar treatment effects between Tai Chi mind-body exercise and standard physical therapy intervention for knee OA. Baseline PA was assessed by a Community Healthy Activities Model Program for Seniors (CHAMPS) questionnaire and, in a subsample, by tri-axial accelerometers. The Outcome Measures in Rheumatoid Arthritis Clinical Trials–Osteoarthritis Research Society International (OMERACT-OARSI) dichotomous responder criteria was used for clinically meaningful improvement at follow-up. Associations between baseline self-reported PA by the CHAMPS questionnaire and outcomes of responders vs. nonresponders (reference group) were assessed using logistic regressions, adjusting for demographic covariates. We compared objectively measured PA by accelerometry between responders vs. nonresponders using Wilcoxon tests.

Results. Our sample consisted of 166 participants with knee OA who completed both baseline and 12-week postintervention evaluations: mean age 60.7 year (SD 10.5), body mass index 32.4 kg/m^2 (6.9), 119 (72%) women, and 138 (83%) OMERACT-OARSI responders. Neither time spent in total PA [odds ratio (OR) 1.00; 95% confidence interval (CI) 0.96, 1.03] nor time in moderate-to-vigorous PA (OR 1.01; 95% CI 0.93, 1.09) at pre-intervention were associated with being a responder. Similar findings were observed in 42 accelerometry sub-cohort participants.

Conclusion. Pre-intervention PA levels (subjective report or objective measurement) were not associated with individuals achieving favorable treatment outcomes after a 12-week exercise intervention, which suggests that regardless of pre-intervention PA level, individuals will likely benefit from structured exercise interventions.

INTRODUCTION

Among Americans 55 years and older, 40% have frequent knee pain or radiographic knee osteoarthritis (OA) (1). Knee OA is one of the leading causes of activity limitation and disability among adults (2,3). In the elderly, knee OA is responsible for as much chronic disability as cardiovascular disease (4). There is no cure for OA; current nonsurgical management guidelines recommend exercise, weight management, and biomechanical interventions to reduce symptoms and preserve function (5). Although it is well accepted that exercise therapy leads to improvements in pain, physical function, and quality of life, the reported treatment success varies, possibly because of variances in therapy intensity or dosage (6–8) and substantial heterogeneity in disease severity, age, body mass index (BMI), and pre-intervention movement mechanics and activity levels (9–11).

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Identifying characteristics that enhance or diminish treatment response would facilitate a more tailored approach to exercise intervention and optimize efficacy and minimize adverse events.

Regular physical activity (PA) provides many general health benefits and has been shown to reduce pain and improve physical function for knee OA. Despite the well-documented benefits, adults with knee OA are largely inactive (12,13). Efforts have been directed to increase levels of PA in this population through patient education, behavioral intervention, group-based walking and/or exercise programs, and individual therapy sessions (14–17). PA monitoring is also advocated for cohort studies and clinical trials in knee OA in order to track mobility and well-being in the context of meaningful real-life behaviors outside the clinical or research settings (15,18–20).

Exercise is a planned, structured, and purposeful form of PA. PA level prior to exercise intervention may influence responses to treatment. In theory, physically inactive individuals may benefit from engaging in a regular structured exercise regime and thus achieve improvement in pain and physical function. Alternatively, baseline inactivity, which may signal poor general health and a sedentary lifestyle, could temper the benefits of exercise. It is also plausible that being more physically active at baseline may amplify or diminish the effects of exercise on pain and function. Whether pre-intervention PA level is associated with a favorable treatment response to exercise therapy in persons with knee OA is unknown. Better understanding of the effect of diverging pre-intervention activity levels on treatment response would inform future exercise trial design in participant selection and treatment stratification, and ultimately prioritize interventions in patients who will benefit most. We tested the hypothesis that pre-intervention PA level is associated with achieving a positive treatment response after a 12-week exercise intervention in participants with knee OA.

METHODS

Study Design and Participants. We conducted a secondary analysis of a randomized 52-week, single-blind, comparative effectiveness trial showing similar positive treatment effects between Tai Chi mind-body exercise and standard physical therapy interventions for knee OA (21). We enrolled participants aged 40 years or older who met all of the following three criteria. First, they met the American College of Rheumatology criteria for symptomatic knee OA (22) (pain occurring on 50% or more of the days of the past month during at least one of the activities of walking, going up/down stairs, standing upright, or lying in bed at night). Second, they had radiographic evidence of tibiofemoral and/or patellofemoral OA (Kellgren/Lawrence grade 2 or greater, ie, definite osteophyte in the tibiofemoral and/or patellofemoral compartment) in at least one knee. Third, all participants reported knee pain that was 40 or greater on at least one of the five questions in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale (each question being scored between 0 and 100, with higher scores indicating worse pain). Participants were excluded if they had prior experience either with Tai Chi and other similar types of complementary and alternative therapy or with physical therapy program for knee OA in the past year; serious medical conditions; any intra-articular steroid injections or reconstructive surgery in the past 3 months or any intra-articular hyaluronic acid injections in the past 6 months; cognitive impairment (Mini-Mental Status Exam score of less than 24); or if they were unable to walk without a cane or other assistive devices for the baseline assessment. Participants were randomized into Tai Chi (two times per week for 12 weeks) or physical therapy (two times per week for 6 weeks, followed by 6 weeks of monitored home exercise) treatment arm. At the 12-week follow-up, both groups showed similar improvements in WOMAC pain score, and the benefits maintained up to 52 weeks (22).

Pre-Intervention PA Levels. Pre-intervention PA levels were assessed using both the self-reported Community Healthy Activities Model Program for Seniors (CHAMPS) PA questionnaire and objectively measured tri-axial accelerometry. CHAMPS (23) is a 41-item questionnaire measuring weekly PA levels for older adults by computing total hours per week spent on various common activities. It includes activities of all intensity levels typically undertaken by older adults for exercise, recreation, and daily living, such as walking, swimming, attending a movie, playing cards, visiting friends, and going to church or senior centers. Higher scores reflect greater PA. The recall timeframe is "a typical week during the past 4 weeks." A reliable and valid (24–26) measure for self-reported PA, CHAMPS has been widely used in capturing activity levels for seniors in observational and interventional studies. Activities listed in the CHAMPS questionnaire were assigned a metabolic equivalent (MET) value specific for older adults. Among total activities (hr/wk), moderate-to-vigorous (MV) intensity activities (hr/wk) are activities requiring 3 or more MET values. The pre-intervention self-reported PA levels were assessed as hours per week spent in total PA and in MV intensity PA.

In a subset of participants, objectively measured PA was captured by a tri-axial accelerometer (ActiGraph GT3X), which was worn superior to the iliac crest in a custom pouch and secured to the waist belt by a Velcro fastener. Participants were instructed to wear the device for a consecutive 7-day period, except during sleep, showers, bathing, swimming, or other water activities. A participant log was recorded when the GT3X was worn. Providing activity counts as a composite vector magnitude of three orthogonal axes, the GT3X accelerometer has been shown to be a valid and reliable measure for PA when examined against a previous accelerometer model as well as whole-body indirect calorimetry (27–29). Analyses were restricted to participants with at least three valid monitoring days (ie, worn at least 10 hr/day) (30,31). Using modified Freedson (27) vector magnitude counts per minute, light intensity PA cut-points are 200-2689, and MV intensity PA cut-points are 2690 or greater. To account for variability in daily monitoring time, we standardized these PA measures to 16 hours of wear time per day. For individuals with seven valid days of monitoring, weekly activity minutes spent at each intensity level were the sum of the seven standardized daily total minutes for each intensity level; for individuals with less than seven valid days of monitoring, weekly activity minutes spent at each intensity level were estimated by multiplying seven to the average daily activity minutes over the valid days (32). To enable comparisons between self-reported PA by CHAMPS and objectively measured PA by accelerometry, we converted GT3X weekly activity minutes to hours.

Treatment Response to Exercise Therapy. We used the Outcome Measures in Rheumatoid Arthritis Clinical Trials–Osteoarthritis Research Society International (OMERACT-OARSI) responder criteria (33) to define clinically meaningful improvement after the 12-week exercise intervention. Figure 1 shows the algorithm for determining dichotomous response to exercise therapy (responders vs. nonresponders). The WOMAC is a validated, self-administered, visual analogue scale specifically designed to evaluate pain for knee and hip OA (34). The visual analogue scale version of WOMAC pain subscore has a range of 0 to 500, and the function subscore has a range of 0 to 1700, with higher scores indicating worse status. The Patient Global Assessment of disease activity is a visual analogue scale that measures the level of knee OA severity on a 10-point scale, where 0 indicates no disease activity and 10 indicates the most extreme severity. In our study, WOMAC pain and function subscores and the Patient Global Assessment score were each assessed as a person-based measure and converted to a scale of 0 to 100 at baseline and 12-week follow-up.

Statistical Analysis. We summarized pre-intervention baseline characteristics of the entire analysis sample and the responders vs. nonresponders subgroups. Two-sample Wilcoxon rank sum tests were used to compare PA measures between responders vs. nonresponders. We performed person-based multiple logistic regressions to assess the associations between baseline self-reported PA level by CHAMPS and dichotomized outcomes of treatment responders vs. nonresponders, adjusting for age, sex, and BMI (35). The assumption of linearity between predictors and logit of binary outcomes was checked before conducting logistic regressions. Results for each model were summarized as unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (CIs); results were considered to be statistically significant if the 95% CI did not include the value 1. To explore whether treatment arm impacts these relations, we carried out additional sensitivity analyses to evaluate the patterns of associations in the Tai Chi group only and in the physical therapy group only. In a subgroup of participants with accelerometry data, we compared baseline, objectively measured PA levels between treatment responders vs. nonresponders using the two-sample Wilcoxon rank sum tests. The small sample size precluded multiple logistic regression models in the accelerometry subgroup. We also evaluated whether the self-reported PA levels by the CHAMPS questionnaire are related to objectively measured levels by accelerometry using Pearson correlations. SAS Version 9.3 was used for all analyses.

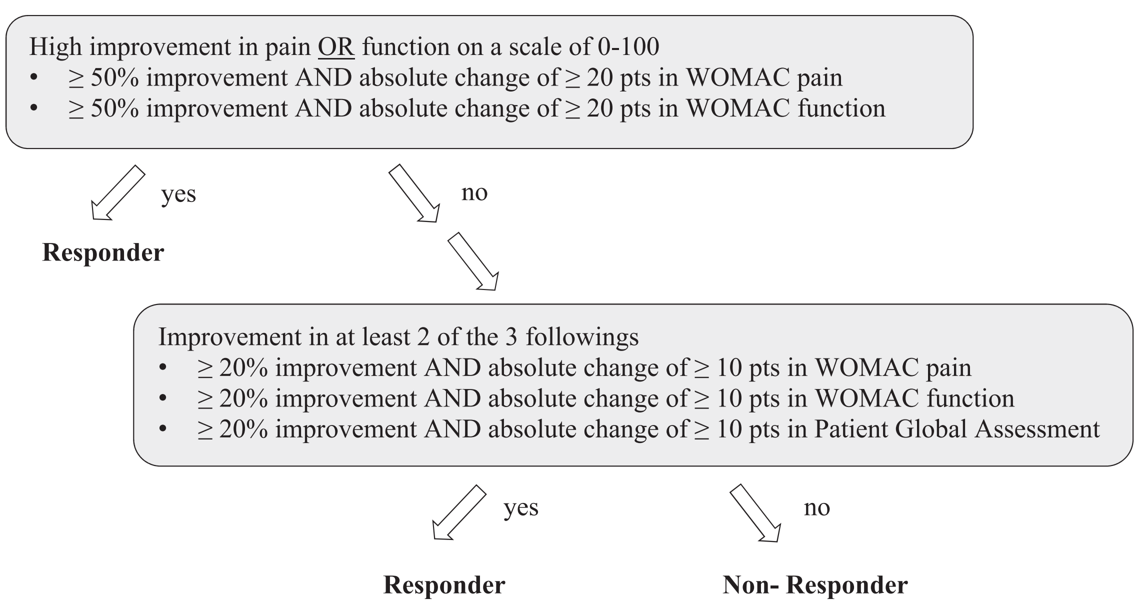

Figure 1. Outcome Measures in Rheumatoid Arthritis Clinical Trials-Osteoarthritis Research Society International (OMERACT-OARSI) responder criteria for defining clinically meaningful improvement at the end of exercise intervention (12 weeks).

RESULTS

Among 204 participants with symptomatic and radiographic tibiofemoral and/or patellofemoral OA, randomized to Tai Chi or physical therapy interventions, 167 (87 in Tai Chi and 80 in Physical Therapy group) completed both baseline and 12-week postintervention assessments. Reasons for not completing the 12-week assessments included: lost interest (n = 2); pre-existing pain in other body regions other than the knee (n = 3); time constraints (n = 4); preferred to be in the other intervention arm (n = 1); lost to follow-up (n = 24); other reasons (n = 3). One participant had missing CHAMPS data, leaving our final secondary analysis a sample of 166 persons.

Self-reported PA by CHAMPS. Table 1 summarizes pre-intervention baseline sample characteristics. Among the 166 participants, 138 (83.1%) were OMERACT-OARSI responders. The responders did not differ from nonresponders in baseline age, BMI, sex, Kellgren-Lawrence (K/L) grade (worse between two knees), WOMAC pain and function, chronic pain self-efficacy, and depression (Table 1). Table 2 shows the medians and interquartile ranges of respective time spent in total PA and in MV intensity PA, quantified by CHAMPS questionnaire, between the responders and nonresponders. In the fully adjusted regression models (Table 2), there was neither association between pre-intervention total PA and being a responder to exercise therapy (OR 1.00; 95% CI 0.96, 1.03) nor association of MV intensity PA with being a responder (OR 1.01; 95% CI 0.93, 1.09). We alternatively examined whether being in the bottom or middle tertile of PA (reference group: top tertile) was associated with treatment response and found similar null effects (ie, nonsignificant ORs). Intervention group assignment could potentially impact the PA-treatment response relationship. We repeated these analyses, separately treating PA as a continuous predictor and as a categorical predictor in the Tai Chi group only and in the physical therapy group only; we found similar null effects (ie, nonsignificant ORs) in both groups. Post hoc analyses applying an alternative definition of treatment response (separately by pain improvement only and by function improvement only) minimally changed our findings.

Objectively measured PA by accelerometry. Next, we examined PA recorded by accelerometry in a subgroup. Table 3 summarizes pre-intervention baseline sample characteristics of 42 participants in the accelerometry subgroup. The accelerometry subgroup of 42 participants did not differ from the 124 participants without accelerometry data in age, BMI, % female,

Table 1. Baseline characteristics of the analysis sample

	Entire Sample n = 166	Responders n = 138	Nonresponders n = 28
	Number (%) or mean ± SD		
Age (years)	60.7 ± 10.5	61.3 ± 10.7	57.6 ± 9.0
BMI (kg/m^2)	32.4 ± 6.9	32.1 ± 6.7	34.2 ± 7.8
Female	119 (71.7%)	102 (73.9%)	17 (60.7%)
K/L grade of the worse knee (n = 164, 136 responders)			
0[a]	3 (1.8%)	3 (2.2%)	0 (0%)
1[a]	8 (4.9%)	6 (4.4%)	2 (7.1%)
2	66 (40.2%)	55 (40.4%)	11 (39.3%)
3	57 (34.8%)	47 (34.6%)	10 (35.7%)
4	30 (18.3%)	25 (18.4%)	5 (17.9%)
WOMAC Pain (0-500), higher indicates worse pain	253.3 ± 100.7	253.0 ± 96.4	254.9 ± 121.4
WOMAC Physical Function (0-1700), higher indicates worse function	885.4 ± 367.3	888.5 ± 362.8	870.3 ± 395.4
Chronic Pain Self-Efficacy (1-10), higher indicates better status	6.3 ± 2.1	6.5 ± 2.0	5.3 ± 2.3
Beck Depression Inventory-II (0-63), higher indicates worse symptoms	7.7 ± 8.6	7.1 ± 8.3	10.6 ± 9.6
CHAMPS – Total activities (hr/wk)	17.5 ± 12.2	17.6 ± 11.6	16.9 ± 14.8
CHAMPS – MV intensity activities (hr/wk)	5.5 ± 6.0	5.7 ± 5.9	4.8 ± 6.6

Abbreviation: BMI, body mass index; CHAMPS = Community Health Activities Model Program for Seniors; K/L = Kellgren/Lawrence; MV = moderate-to-vigorous; WOMAC = Western Ontario and McMaster Universities Arthritis Index.

[a] Knees had definite osteophytes (K/L grade 2) in the patellofemoral compartment, but K/L grades 0 or 1 in the tibiofemoral compartment.

Table 2. Pre-intervention baseline self-reported physical activity level (by CHAMPS questionnaire) and treatment response to exercise therapy (by OMERACT-OARSI responder criteria) (n = 166)

	Total Activities	MV Intensity Activities
	Median (IQR), hr/wk	
Responders (n = 138, 83%)	16.0 (14.0)	4.0 (9.0)
Nonresponders (n = 28, 17%)	13.0 (19.0)	2.0 (6.5)
P value[a]	0.21	0.30
Associations of baseline physical activity (per 1 hr/wk) with responders (reference group: nonresponders)	Odds ratios[b] (95% CIs), *P* value for trend	
Unadjusted	1.01 (0.97, 1.04), *P* = 0.76	1.03 (0.96, 1.11), *P* = 0.46
Adjusted for age, sex, and BMI	1.00 (0.96, 1.03), *P* = 0.82	1.01 (0.93, 1.09), *P* = 0.83

Abbreviations: CHAMPS, Community Health Activities Model Program for Seniors; CI, confidence interval; IQR, interquartile range; MV, moderate-to-vigorous; OMERACT-OARSI, Clinical Trials Response Criteria and the Outcome Measures in Rheumatology – Osteoarthritis Research Society International.
[a] Two-sample Wilcoxon rank sum test comparing responders with nonresponders.
[b] Odds ratio with 95% CI excluding 1 indicates statistical significance.

K/L grade distribution, WOMAC pain and function scores, self-efficacy, and depression. The small sample size limited our ability to perform logistic regressions and adjust for covariates. Similar to the results characterizing PA by CHAMPS, which were based on two-sample Wilcoxon rank sum tests, there were no significant differences in the time spent in total, light, and MV-intensity activity between responders and nonresponders (Table 4). In a sensitivity analysis of the accelerometry data using a widely established cut point, we dichotomized MV intensity activity into meeting (at least 150 unbouted min/wk in MV intensity activity) (n = 25) versus not meeting (n = 17) the recently published PA guideline (36) and found that meeting the guideline was not related to treatment response. Post hoc analyses applying an alternative definition of treatment response (separately by pain improvement only and by function improvement only) minimally changed our findings.

Among 42 participants with both CHAMPS and accelerometry data, there was no significant correlation in total PA between these two measures ($r = 0.06$, $p = 0.70$). Participants markedly underestimated their total activity level [median (interquartile range (IQR)): 13.5 (13.0) hr/wk by CHAMPS vs. 41.3 (15.0) hr/wk by accelerometry]. There was no significant correlation in MV intensity activity ($r = 0.16$, $p = 0.29$). Nonetheless, the average MV intensity activity level was fairly comparable between CHAMPS and accelerometry [median (IQR): 3.5 (7.0) hr/wk by CHAMPS vs. 3.8 (5.1) hr/wk by accelerometry].

DISCUSSION

Pre-intervention PA level, quantified by either subjective report by CHAMPS questionnaire or objective measurement by accelerometry, was not significantly associated with whether an individual will achieve favorable treatment outcomes after a 12-week exercise intervention. To our knowledge, this is the first study exploring the relationship between baseline PA and treatment response to exercise interventions delivered in a randomized controlled trial for persons with symptomatic, radiographic knee OA. These findings suggest that regardless of pre-intervention PA level, individuals with knee OA will likely benefit from structured exercise interventions.

In our study, the average self-reported total activities and MV intensity activities by CHAMPS were 17.5 (SD, 12.2) and 5.5 (SD, 6.0) hr/wk, respectively, which are comparable to what have been reported in the literature (37–39). Among 150 community-dwelling older adults (65 years or older), the total PA by CHAMPS was 19.9 (SD, 10.1) hr/wk and the MV intensity PA was 5.7 (SD, 5.5) hr/wk (37). Another study of seniors (71-86 years old) showed 13.7 (SD, 9.0) hr/wk of total PA and 3.0 (SD, 4.0) hr/wk of MV intensity PA by CHAMPS (38). After participating in a PA promotion program, 575 previously underactive individuals (50 years or older) achieved a CHAMPS total PA of 12.1 (SD, 19.7) hr/wk and MV intensity PA of 5.1 (SD, 10.1) hr/wk (39).

The overwhelming benefits of exercise on physical and mental health have been well documented. Our findings support the universal positive impact of exercise therapy for individuals with knee OA, regardless of pre-participation PA levels. Similarly, a recent report of patients with systolic heart failure found comparable benefits of exercise training on exercise capacity, mortality, and hospitalization across all baseline self-reported PA tertiles (40). These observations reinforce that exercise training should be an integral part of therapeutic strategies for all older adults with chronic health conditions, even in those who are already physi-

Table 3. Baseline characteristics of the accelerometry subgroup

	Entire Sample n = 42	Responders n = 37	Nonresponders n = 5
	Number (%) or median ± IQR		
Age (years)	60.5 ± 15.0	61.0 ± 9.0	55.0 ± 18.0
BMI (kg/m^2)	30.1 ± 11.1	30.0 ± 11.1	30.3 ± 2.4
Female	30 (71.4%)	28 (75.7%)	2 (40%)
K/L grade of the worse knee			
0[a]	1 (2.4%)	1 (2.7%)	0
1[a]	2 (4.8%)	2 (5.4%)	0
2	19 (45.2%)	17 (46.0%)	2 (40.0%)
3	11 (26.2%)	10 (27.0%)	1 (20.0%)
4	9 (21.4%)	7 (18.9%)	2 (40.0%)
WOMAC Pain (0-500), higher indicates worse pain	243.1 ± 141.4	246.0 ± 138.3	240.1 ± 128.6
WOMAC Physical Function (0-1700), higher indicates worse function	880.8 ± 607.5	843.0 ± 592.5	1069.3 ± 741.2
Chronic Pain Self-Efficacy (1-10), higher indicates better status	6.8 ± 3.9	7.1 ± 3.5	4.1 ± 2.8
Beck Depression Inventory-II (0-63), higher indicates worse symptoms (n = 40)	6.0 ± 10.5	5.0 ± 9.0	13.0 ± 9.0
CHAMPS – Total activities (hr/wk)	13.5 ± 13.0	13.0 ± 12.0	18.0 ± 17.0
CHAMPS – MV intensity activities (hr/wk)	3.5 ± 7.0	4.0 ± 5.0	0.0 ± 3.0
Accelerometry – Total activities (hr/wk)	41.3 ± 15.0	41.8 ± 12.1	32.6 ± 21.5
Accelerometry – MV intensity activities (hr/wk)	3.8 ± 5.1	3.9 ± 5.2	2.2 ± 0.6
Accelerometry – Light intensity activities (hr/wk)	36.5 ± 13.6	36.5 ± 9.9	30.4 ± 20.8

Abbreviation: BMI, body mass index; CHAMPS = Community Health Activities Model Program for Seniors; IQR = interquartile range; K/L = Kellen/Lawrence; MV = moderate-to-vigorous; WOMAC = Western Ontario and McMaster Universities Arthritis Index.
[a] Knees had definite osteophytes (K/L grade 2) in the patellofemoral compartment, but K/L grades 0 or 1 in the tibiofemoral compartment.

cally active prior to participation. It is unknown whether each participant increased, maintained, or decreased their PA levels after exercise intervention. Additional information on posttherapy PA may shed light on plausible mechanisms of why exercise intervention worked for both inactive and active individuals.

Although self-reported PA provides nuanced information regarding the type of activities one is engaged in, it is subject to reporting biases, such as imprecise recall and influence of social desirability (41,42). In agreement with previous studies (43,44), we found weak correlations between self-reported and objectively measured PA in both total and MV intensity activities. Comparing CHAMPS with accelerometry among seniors (mean age = 75 years), Hekler and colleagues observed a trend of overreporting in both total and MV intensity PA (26). Interestingly, in our younger cohort (mean age = 62 years), we observed underreporting of total PA (median of 13.5 hr/wk by CHAMPS vs. 41.3 hr/wk by

Table 4. Pre-intervention baseline objectively measured physical activity level (by accelerometry) and treatment response to exercise therapy (by OMERACT-OARSI responder criteria) (n = 42)

	Total Activities (Light + MV Intensity)	Light-Intensity Activities	MV-Intensity Activities
	Median (IQR), hr/wk		
Responders (n = 37, 86%)	41.8 (12.1)	36.5 (9.9)	3.9 (5.2)
Nonresponders (n = 5, 14%)	32.6 (21.5)	30.4 (20.8)	2.2 (0.6)
P value[a]	0.32	0.36	0.27

Abbreviation: IQR, interquartile range; MV, moderate-to-vigorous; OMERACT-OARSI, Clinical Trials Response Criteria and the Outcome Measures in Rheumatology – Osteoarthritis Research Society International.
[a] Two-sample Wilcoxon rank sum test comparing responders with nonresponders.

accelerometry) and comparable self-estimation of MV intensity PA (median of 3.5 hr/wk by CHAMPS vs. 3.8 hr/wk by accelerometry).

MV-intensity PA is quantified by activities requiring 3 or more MET values in both CHAMPS and accelerometry measures. Sharing an established threshold for MV intensity, PA may have contributed to the comparable weekly hours between these two measures. The discrepancy in total PA (sum of time spent in light and MV-intensity PA) likely resulted from lower CHAMPS-recorded time in light-intensity PA. Items in the CHAMPS questionnaire were developed to specifically focus on various types of purposeful activities, such as walking briskly, cycling, swimming, gardening, and heavy or light household chores, rather than assessing all physical movements. It is plausible that numerous nonpurposeful light-intensity physical movements, such as walking to the kitchen or to the bedroom located on the second floor, were not reflected in the CHAMPS report but recorded by accelerometry. These findings potentially question the common belief that people tend to overestimate their PA when queried by a questionnaire. The relationship between self-reported versus objectively measured PA may be more nuanced. Future larger-scale studies may further elucidate these relations.

One of the strengths of our study is applying the OMERACT-OARSI responder criteria to define a favorable response to 12-week exercise interventions. Based on multiple domains that represent clinically meaningful improvements after treatment, OMERACT-OARSI responder criteria were developed and recommended as an optimal, simplified set of responder criteria for OA clinical trials (33). This approach classifies patients as responders vs. nonresponders using a combination of absolute and relative changes in WOMAC pain, WOMAC function, and Patient Global Assessment. Considering the combined effects of three primary patient-reported outcomes and accounting for the pre-intervention status by assessing changes, OMERACT-OARSI responder criteria provides a more comprehensive and meaningful assessment of treatment outcomes than a single outcome alone (45).

Recognizing the potential limitation of relying on self-reported PA as a predictor in our analysis, we performed secondary analysis using objectively measured accelerometry data available in a subset of participants. The results were similar. It should be acknowledged that the small sample size of the accelerometry sub-cohort is not optimal for adjusting for covariates and may limit the power of detecting significances. The current study has other limitations. Our study sample consisted of individuals with symptomatic, radiographic knee OA, so the findings may not be generalizable to the general population. Aligning with the overwhelming evidence that exercise intervention improves outcomes in the setting of knee OA (46,47), more than 80% of our study participants had a favorable outcome. Increasing the number of nonresponders may potentially alter the results. However, our findings are consistent with those of a recent noncontrolled exercise intervention study for persons with knee pain, suggesting that similar pain relief was observed regardless of the initial self-reported PA levels (48). It is important to note that, following the recently published 2018 PA guideline (36), the MV activity minutes we reported here are total MV time, not “bouted” (MV intensity PA accumulated in bouts lasting 10 minutes or more). Several factors could have contributed to the higher weekly MV-intensity PA hours reported in our study. First, we calculated total “unbouted” MV-intensity PA minutes, rather than the legacy “bouted” minutes; they are not directly comparable. Second, the composite vector magnitude (tri-axial) method used in our study could potentially yield higher MV intensity PA than vertical axis data alone (49). Third, our study sample was younger (mean age = 62) than the Women’s Health study (49) (mean age = 71) or the Osteoarthritis Initiative study (50) (mean age = 65). Future clinical trials with a larger sample of accelerometry data will further elucidate these relationships. Finally, waist-mounted tri-axial accelerometers do not capture water activities and may underestimate vertical acceleration/deceleration activities, such as cycling or weightlifting; however, these particular activities are queried in the CHAMPS questionnaire.

In summary, pre-intervention PA level, quantified by either subjective report by CHAMPS questionnaire or objective measurement by accelerometry, did not predict whether an individual will achieve favorable treatment outcomes after a 12-week exercise intervention for persons with knee OA. Our findings suggest that, in the setting of knee OA, structured exercise interventions can be beneficial even for physically active individuals.

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AUTHOR CONTRIBUTIONS

Each author participated in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. All authors have access to the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Chang, J. Lee, and Wang
Acquisition of data. Reid, Fielding, Driban, Harvey, and Wang
Analysis and interpretation of data. Chang, J. Lee, Song, Price, A. Lee, Reid, Fielding, Driban, Harvey, and Wang

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