

Marquette University
e-Publications@Marquette

Physical Therapy Faculty Research and Publications

Physical Therapy, Department of

4-1-2017

Physical Activity Minimum Threshold Predicting Improved Function in Adults With Lower-Extremity Symptoms

Dorothy D. Dunlop
Northwestern University

Jing Song
Northwestern University

Jungwha Lee
Northwestern University

Abigail L. Gilbert
Northwestern University

Pamela A. Semanik
Rush University

See next page for additional authors

Accepted version. *Arthritis Care & Research*, Vol. 69, No. 4 (April 2017): 475-483. DOI. © 2017 John Wiley & Sons, Inc. Used with permission.

Daniel Pinto was affiliated with Northwestern University at the time of publication.

Authors

Dorothy D. Dunlop, Jing Song, Jungwha Lee, Abigail L. Gilbert, Pamela A. Semanik, Linda S. Ehrlich-Jones, Christine A. Pellegrini, Daniel Pinto, Barbara Ainsworth, and Rowland W. Chang

Physical Therapy Faculty Research and Publications/College of Health Sciences

This paper is NOT THE PUBLISHED VERSION; but the author’s final, peer-reviewed manuscript. The published version may be accessed by following the link in the citation below.

Arthritis Care & Research, Vol. 69, No. 4 (April, 2017): 475-483. [DOI](#). This article is © Wiley and permission has been granted for this version to appear in [e-Publications@Marquette](#). Wiley does not grant permission for this article to be further copied/distributed or hosted elsewhere without the express permission from Wiley.

Contents

Abstract.....	3
Objective.....	3
Methods.....	3
Results.....	3
Conclusion.....	3
INTRODUCTION.....	3
Box 1. Significance & Innovations.....	3
MATERIALS AND METHODS.....	4
Study population.....	4
Outcomes.....	5
Physical activity assessment.....	6
Baseline covariates.....	6
Statistical analysis.....	6
RESULTS.....	7
DISCUSSION.....	11
ACKNOWLEDGMENTS.....	13
AUTHOR CONTRIBUTIONS.....	13

Study conception and design	14
Acquisition of data	14
Analysis and interpretation of data	14
REFERENCES	14

Physical Activity Minimum Threshold Predicting Improved Function in Adults With Lower-Extremity Symptoms

Dorothy D. Dunlop

Northwestern University Feinberg School of Medicine, Chicago, IL

Jing Song

Northwestern University Feinberg School of Medicine, Chicago, IL

Jungwha Lee

Northwestern University Feinberg School of Medicine, Chicago, IL

Abigail L. Gilbert

Northwestern University Feinberg School of Medicine, Chicago, IL

Pamela A. Semanik

Rush University, Chicago, IL

Linda Ehrlich-Jones

Rehabilitation Institute of Chicago, Chicago, IL

Christine A. Pellegrini

Northwestern University Feinberg School of Medicine, Chicago, IL

Daniel Pinto

Northwestern University Feinberg School of Medicine, Chicago, IL

Barbara Ainsworth

Arizona State University, Phoenix, AZ

Rowland W. Chang

Northwestern University Feinberg School of Medicine, Chicago, IL

Abstract

Objective

To identify an evidence-based minimum physical activity threshold to predict improved or sustained high function for adults with lower-extremity joint symptoms.

Methods

Prospective multisite data from 1,629 adults, age ≥ 49 years with symptomatic lower-extremity joint pain/aching/stiffness, participating in the Osteoarthritis Initiative accelerometer monitoring substudy were clinically assessed 2 years apart. Improved/high function in 2-year gait speed and patient-reported outcomes (PROs) were based on improving or remaining in the best (i.e., maintaining high) function quintile compared to baseline status. Optimal thresholds predicting improved/high function were investigated using classification trees for the legacy federal guideline metric requiring 150 minutes/week of moderate-vigorous (MV) activity in bouts lasting 10 minutes or more (MV-bout) and other metrics (total MV, sedentary, light intensity activity, nonsedentary minutes/week).

Results

Optimal thresholds based on total MV minutes/week predicted improved/high function outcomes more strongly than the legacy or other investigated metrics. Meeting the 45 total MV minutes/week threshold had increased relative risk (RR) for improved/high function (gait speed RR 1.8, 95% confidence interval [95% CI] 1.6, 2.1 and PRO physical function RR 1.4, 95% CI 1.3, 1.6) compared to less active adults. Thresholds were consistent across sex, body mass index, knee osteoarthritis status, and age.

Conclusion

These results supported a physical activity minimum threshold of 45 total MV minutes/week to promote improved or sustained high function for adults with lower-extremity joint symptoms. This evidence-based threshold is less rigorous than federal guidelines (≥ 150 MV-bout minutes/week) and provides an intermediate goal towards the federal guideline for adults with lower-extremity symptoms.

INTRODUCTION

Physical activity is endorsed as a healthy lifestyle strategy. Federal guidelines for adults stipulate a minimum threshold of 150 minutes/week of moderate intensity, or 75 minutes of vigorous-intensity physical activity or an equivalent combination.¹ These guidelines utilize a legacy metric requiring activity bouts of moderate or vigorous activity lasting at least 10 minutes, based on studies demonstrating cardiovascular benefits from aerobic activity.²⁻⁵ However, the vast majority of adults fail to meet these guidelines.^{6,7} Even more concerning is that as many as 2 in 5 adults with lower-extremity joint conditions not only fail to meet guidelines, they register zero on the legacy bout metric; over an entire week they do not have a single session of moderate physical activity lasting 10 minutes.^{8,9}

Box 1. Significance & Innovations

- These results support an intermediate threshold to spend at least 45 minutes/week in accumulated physical activity of at least moderate intensity among adults having lower-extremity joint symptoms.
- This evidence-based threshold is less rigorous than federal guidelines (150 minutes/week of moderate to vigorous activity in bouts lasting 10 minutes or more).

Maintaining function is crucial to independent community living for adults with physical impairments. For many adults living with joint conditions, improving or maintaining high function may be as great a concern as cardiovascular health. Physical function has long been recognized as a proxy for overall health. Physical function assessed by gait speed reflects functional status and health.¹⁰ Gait speed has been repeatedly associated with survival in epidemiologic studies.¹¹⁻¹³ Similarly, patient-reported functional status is related to quality of life and life expectancy.¹⁴ Lower-extremity joint conditions such as hip or knee osteoarthritis (OA) increase a person's risk for subsequent loss of function.^{12,15} While being physically active is associated with functional gains¹⁶ among adults with joint disease,¹⁷ it is not known if there is a level of physical activity that may promote better function or maintain high functional ability.¹⁸

Investigating what physical activity levels might improve low function or maintain high (improved/high) function among adults with lower-extremity symptoms motivates 2 questions: 1) Are there alternative physical activity metrics that better predict improved/high function than the legacy bout-based metric, which registers zero for a large portion of these adults? and 2) What minimum threshold of physical activity best predicts improved/high function? The objective of this study is to identify optimal physical activity metrics and dosage thresholds related to improving low function or maintaining high function among adults with lower-extremity joint symptoms.

MATERIALS AND METHODS

Study population

Participants were a subcohort of the Osteoarthritis Initiative (OAI) enrolled into an accelerometer ancillary study conducted at the OAI 2008–2010 clinic visit (OAI 4-year followup), which is baseline for this study. The OAI is a multicenter prospective study investigating risk factors and biomarkers for the progression and/or onset of knee OA (see <http://www.oai.ucsf.edu/datarelease/About.asp>). At enrollment, the OAI recruited 4,796 men and women between ages 45 and 79 years from 4 clinical sites: Baltimore, Maryland; Pittsburg, Pennsylvania; Pawtucket, Rhode Island; and Columbus, Ohio. The OAI enrolled participants with or at high risk for developing symptomatic, radiographic knee OA. High risk was defined as frequent knee symptoms without radiographic OA, or 2 or more eligibility risk factors (e.g., age, high body mass index [BMI], prior knee injury, knee surgery, family history of total knee replacement for OA, Heberden's nodes, and repetitive knee bending).¹⁹ OAI eligibility criteria have been described in detail elsewhere.²⁰ Approval was obtained from the institutional review board at each OAI site and at Northwestern University. Each participant provided written informed consent.

A subgroup of 2,127 OAI participants participated in an accelerometer study at the 48-month clinic visit, which represents our study's baseline. Eligibility for the substudy required a scheduled OAI followup visit between August 2008 and June 2010. The present study sample included 1,919 accelerometer study participants reporting ankle, foot, knee, and/or hip lower-extremity joint symptoms of pain, aching, or stiffness. Ankle, foot, and knee questions solicited symptoms over the past 30 days; hip questions solicited symptoms over the past 12 months. Of individuals reporting hip symptoms, 90% were in the analysis sample based on symptoms reported in another joint. Loss to followup was minimal; over 96% of this cohort (1,845 of 1,919) participated in a followup visit 2 years later. For analysis purposes, we restricted our sample to 1,647 individuals with baseline and 2-year followup (2010–2012) physical function measured objectively by gait speed ($n = 1,476$) and/or by patient-reported outcome (PRO)

based on the 12-item Short Form (SF-12) health survey physical component score (n = 1,629), respectively (Figure 1). Excluded were 173 persons with inadequate accelerometer monitoring to support reliable physical activity estimates [7](#) (i.e., less than 4 valid days of monitoring based on daily evidence of ≥ 10 hours of accelerometer wear), and 89 participants did not have 2-year followup outcomes (64 with no contact, 23 with only phone contact, and 2 refused).

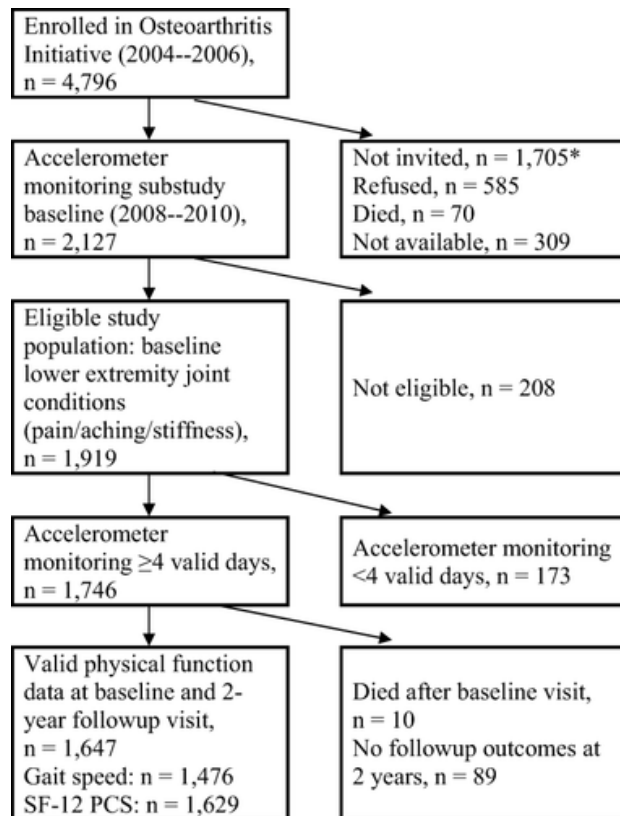


Figure 1. Flow of analytical sample. * = participants with scheduled visits outside the substudy recruitment period; SF-12 = 12-item Short Form health survey; PCS = physical component score.

Outcomes

The primary outcome was change in improved or high (improved/high) physical function status between baseline and 2-year followup, separately assessed by objective gait speed and by the PRO physical function SF-12 physical component score. Improved/high function was based on transitions across functional quintiles over time. This method captures practical, meaningful changes in function over time in OA populations.²¹⁻²³ Five quintile groups are defined from the full parent enrollment OAI knee OA cohort for objective gait speed physical function (Q1: < 3.7 , Q2: 3.7–4.0, Q3: 4.1–4.3, Q4: 4.4–4.7, and Q5: ≥ 4.8 feet per second) and PRO physical function (Q1: < 39.4 , Q2: 39.4–46.9, Q3: 47.0–52.1, Q4: 52.2–56.0, and Q5: ≥ 56.1). Baseline and 2-year function scores from accelerometer substudy participants (n = 1,647) were categorized into each of these groups. Subsequent improved/high function was defined by maintaining function in the best group (i.e., Q5 at both evaluations) or moving into a better group (i.e., moving from Q1–Q4 to a higher group) at 24 months compared to baseline. We used function transitions to identify improved/high physical function outcomes rather than an improvement exceeding a minimum clinically important difference (MCID) due to 1) the value of retaining participants who

maintain high function (e.g., participants whose high baseline function makes them unable to improve an MCID) and 2) validity concerns when applying MCIDs estimated from randomized clinical trial samples to community populations.²⁴

Physical activity assessment

Physical activity was monitored using the ActiGraph GT1M uniaxial accelerometer.²⁵ Trained research personnel gave uniform scripted in-person instructions to wear the accelerometer for 7 consecutive days on a belt at the natural waistline in line with the right axilla upon arising in the morning until retiring, except during water activities. Participants maintained a daily log to record time spent in water and cycling activities, which may not be fully captured by accelerometers. Such activity was negligible (interquartile range [IQR] 0–0 minutes/week) and not utilized in the present study.

Accelerometer data were analytically filtered using validated methodology.^{26,27} Nonwear periods were defined as ≥ 90 minutes with zero activity counts (allowing for 2 consecutive interrupted minutes with counts < 100).² We identified participants with 4–7 valid monitoring days (i.e., ≥ 10 wear hours per day) needed for reliable physical activity estimates.² Thresholds used by the National Cancer Institute on a minute-by-minute basis were applied to identify intensity levels as sedentary (counts/minute < 100), nonsedentary (counts/minute ≥ 100), light (100–2,019 counts/minute), and moderate-to-vigorous (MV; counts/minute $\geq 2,020$) (MV-total),² and MV activity accumulated in bouts lasting ≥ 10 minutes (MV-bout). Due to negligible vigorous (counts/minute $\geq 5,999$) activity (median 0, IQR 0–0 minutes/week) in this cohort, vigorous time and vigorous bouts were not separately evaluated. Weekly activity minutes spent at each intensity level are summed from the daily totals over the monitoring hours and averaged across valid monitored days; for individuals with 4, 5, or 6 valid days of monitoring, weekly activity minutes were estimated as 7 average daily activity minutes spent at each intensity level.

Baseline covariates

Demographic factors included age and sex. BMI was calculated from measured height and weight (kg/m^2) to classify individuals as normal weight (BMI 18.5–24.9), overweight (BMI 25.0–29.9), or obese (BMI ≥ 30). If baseline (i.e., OAI 4-year) BMI was missing (0.2%, $n = 4$), the most recent annual assessment was used as a proxy. Knee OA was identified by a Kellgren/Lawrence grade of ≥ 2 in 1 or both knees assessed from fixed-flexion knee radiography protocol.²⁸

Statistical analysis

Candidate metrics (sedentary, nonsedentary, light, and MV-total) were screened by comparing each to the legacy MV-bout metric, the basis for assessing current physical activity guidelines. For this purpose, we calculated the area under the receiver operating characteristic curve (AUC) to transform the predictive ability of each metric to a common 0 to 1 scale. For each legacy and candidate metric we first derived the receiver operating curve, which is graphically represented by the metric sensitivity plotted versus the fraction of false positives (i.e., 1-specificity) in relation to a physical function outcome. We then determined the AUC area.²⁹ Candidate metrics that performed at least as well (i.e., greater than the AUC) as the legacy MV-bout reference metric AUC were retained for predictive modeling. Comparison of candidate metric AUC with the legacy MV-bout AUC used a test developed by DeLong et al.³⁰

Thresholds were identified using classification and regression tree (CART) methodology. We separately predicted improved/high gait speed and improved/high PRO physical function. For both outcomes, all

candidate metrics with AUCs that exceeded the reference MV-bout metric AUC were used as classification tree predictors in addition to the reference MV-bout metric. A classification tree identifies the predictors and threshold of the selected predictor with the strongest relationship to the outcome based on the criterion of minimum classification error.³¹ To avoid overfitting, models were evaluated using cross-validation subsets and pruned to the most parsimonious model within 1 standard prediction error from the best-fit model.³² Classification tree analysis was selected over other traditional methods (e.g., stepwise logistic regression), given the goal to identify thresholds in an optimal prediction model (i.e., minimize misclassification error).^{33,34} Analyses were performed using Salford Predictive Modeler software, version 8.0.³⁵ Classification tree algorithms retain all records having outcomes; missing predictors are handled by substituting “surrogate splitters,” which are back-up rules that closely mimic the primary splitting rules. Recognizing that systematic differences between people with and without followup outcomes could influence our findings, we conducted weighted analyses recommended by Hogan et al.³⁶ For simplicity, we report unweighted analyses because weighted analyses provided identical findings. To investigate the stability of thresholds across age, sex, BMI, and radiographic knee OA presence, we performed sensitivity analyses. Each factor was separately entered into a classification tree analysis in addition to physical activity metrics to predict improved/high function to explore separate thresholds within the factor investigated. Other analyses were performed using SAS software, version 9.4. Statistical testing was conducted at a 2-sided 5% significance level.

RESULTS

Participants in the OAI accelerometer substudy with baseline lower-extremity joint symptoms and subsequent function outcomes (n = 1,647) were primarily female (56%), obese (37%), and ranged in age from 49 to 83 years. The most common lower-extremity symptoms reported were knee symptoms (93%, 61% of these had radiographic disease), followed by hip symptoms (60%), foot symptoms (12%), and ankle symptoms (11%). Both hip and knee symptoms were reported by 54% of this sample.

The baseline values of the legacy physical activity metric and candidate metrics are shown in Table 1 by subsequent improved/high function status. At the 2-year followup, 34% (500 of 1,476) had improved/high gait speed and 38% (622 of 1,629) had improved/high PRO physical function. The baseline legacy MV-bout metric and MV-total activity metric showed the greatest separation across all metrics between people who did or did not belong to improved/high function groups (25% difference or greater). It is notable that only sedentary time did not significantly differ between groups for either function measure.

Table 1. Baseline physical activity metrics of adults by physical function status at 2-year followup^a

Baseline physical activity metric, minutes/week	Improved/high objective gait speed (n = 1,476)			Improved/high PRO (n = 1,629)		
	Yes (n = 500)	No (n = 976)	Difference (95% CI)	Yes (n = 622)	No (n = 1,007)	Difference (95% CI)
Legacy metric MV-bout ^b	76 ± 111	47 ± 87	29 (19, 40)	68 ± 103	50 ± 92	17 (8, 27)

Candidate metrics

Baseline physical activity metric, minutes/week	Improved/high objective gait speed (n = 1,476)			Improved/high PRO (n = 1,629)		
	Yes (n = 500)	No (n = 976)	Difference (95% CI)	Yes (n = 622)	No (n = 1,007)	Difference (95% CI)
Sedentary	4,123 ± 647	4,118 ± 614	5 (-63, 72)	4,125 ± 629	4,122 ± 620	3 (-59, 66)
Light activity	2,058 ± 536	1,964 ± 554	94 (36, 154)	2,002 ± 524	1,964 ± 558	38 (-17, 93)
MV-total ^c	166 ± 149	108 ± 122	58 (43, 72)	146 ± 141	114 ± 129	33 (19, 46)
Nonsedentary	2,224 ± 576	2,072 ± 599	152 (89, 216)	2,149 ± 568	2,078 ± 605	71 (12, 130)

a Values are the mean ± SD unless indicated otherwise. PRO = patient-reported outcome; 95% CI = 95% confidence interval; MV = moderate to vigorous activity.

b Minutes of MV physical activity acquired in bouts lasting 10 or more minutes.

c Total accumulated minutes of MV physical activity.

The relative predictive value of each metric to distinguish improved/high function status at 2 years is visually represented by receiver operating characteristic curves shown in Figure 2A for improved/high gait speed function and Figure 2B for improved/high PRO physical function. The calculated AUC indicates all metrics performed better than a random “coin flip” (AUC 0.5) to predict improved/high function measures. However, only the MV-total activity metric had greater AUC than the legacy MV-bout reference metric to predict both improved/high gait speed (AUC 0.65 versus 0.60; difference 0.05; 95% CI 0.03, 0.07) and PRO physical function (AUC 0.59 versus 0.57; difference 0.02; 95% CI 0.001, 0.03).

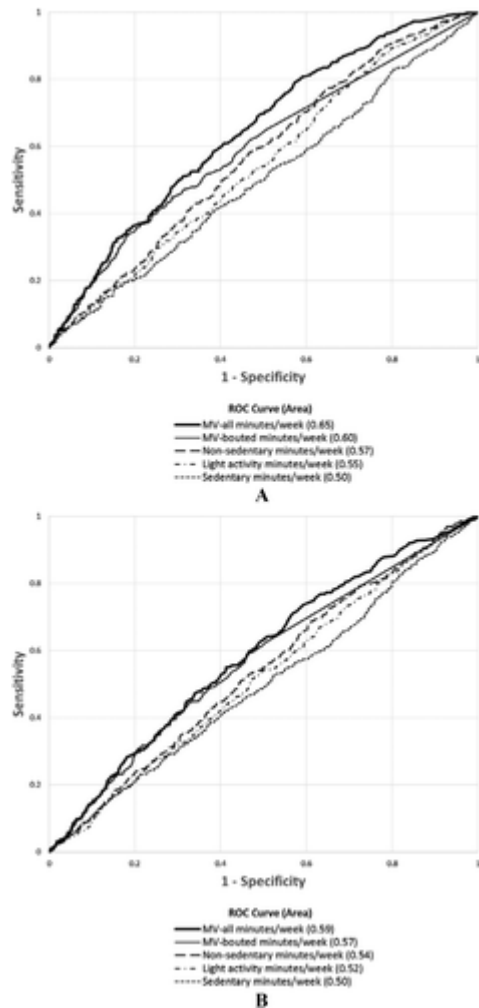


Figure 2 Receiver operating characteristic (ROC) curves for improved/high physical function outcomes for **A**, objective gait speed and **B**, patient-reported outcomes at 2 years by physical activity metrics. MV = moderate to vigorous physical activity.

Classification tree analysis was used to identify both the optimal metric and the physical activity threshold to best predict improved/high function. The MV-total candidate metric and the reference MV-bout metric were entered as classification tree predictors. Separate trees were grown to predict improved/high gait speed and improved/high PRO physical function outcomes. The optimal classification trees are shown in Figure 3. The MV-total metric was selected over MV-bout as the best predictor of both outcomes, consistent with the Figure 2 AUC analyses. The optimal threshold to predict improved/high objective gait speed physical function was 45 MV-total minutes/week. The optimal minimum threshold to predict improved/high PRO physical function was 47 MV-total minutes per week.

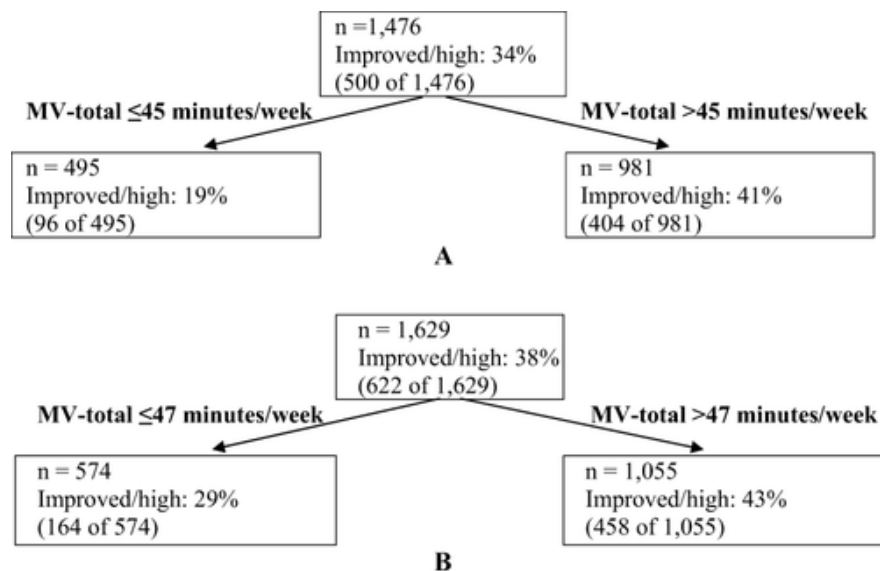


Figure 3 Classification trees selecting physical activity dosage thresholds to predict improved/high 2-year function in **A**, objective gait speed physical function and **B**, patient-reported physical function. MV = moderate to vigorous physical activity.

Sensitivity analyses investigated whether optimal physical activity thresholds were specific to age, sex, presence/absence of knee OA, or BMI. Each factor was separately entered in addition to MV-total and MV-bout into a classification tree analysis to predict improved/high function in gait speed and in PRO physical function. Seven of the 8 sensitivity classification tree analyses (i.e., 4 exposure factors × 2 outcome trees) solely selected an MV-total threshold (MV-total thresholds of 45 minutes/week for gait speed and 47 minutes/week for PRO physical function). One of the 8 sensitivity analyses to predict improved/high gait speed initially split on age (age ≤69 years MV-total threshold: 46 minutes/week, age >69 years threshold: none). Further investigation of the age >69 years subgroup identified a candidate MV-total threshold (10 minutes/week), but the improvement in prediction accuracy was insufficient for retention (i.e., below the 1 SE rule criterion). These sensitivity analyses demonstrate good stability of the MV-total thresholds.

Table 2 summarizes the ability of the thresholds to predict subsequent improved/high function based on relative risks (RRs). The optimal gait speed MV-total threshold (>45 minutes/week) better discriminated subsequent improved/high function status than the current guideline (MV-bout ≥150 minutes/week) demonstrated by the stronger RR (1.8 versus 1.4). Similarly, the optimal PRO physical function MV-total threshold (>47 minutes/week) had a higher RR (1.4 versus 1.3) to predict improved/high function than the current guideline.

Table 2. Improved/high 2-year function relative risk for physical activity metrics by dosage thresholds among adults with baseline lower-extremity symptoms^a

Physical activity, minutes/week	Improved/high objective gait speed (n = 1,476)	Improved/high PRO (n = 1,629)
------------------------------------	---	----------------------------------

Legacy threshold

Physical activity, minutes/week	Improved/high objective gait speed (n = 1,476)	Improved/high PRO (n = 1,629)
MV-bout ≥ 150 ^b	1.4 (1.3, 1.6)	1.3 (1.2, 1.4)
Optimal threshold		
MV-total ≥ 45 ^c	1.8 (1.6, 2.1)	1.4 (1.3, 1.6)
MV-total ≥ 47 ^d	1.8 (1.6, 2.0)	1.4 (1.3, 1.6)

a Values are the relative risk (95% confidence interval). PRO = patient-reported outcome; MV = moderate to vigorous activity.

b Minutes of MV physical activity acquired in bouts lasting 10 or more minutes.

c Total minutes of MV physical activity. Optimal threshold for improved/high gait speed function.

d Total minutes of MV physical activity. Optimal threshold for improved/high PRO physical function based on the Short Form 12-item medical survey physical component score.

Recognizing that a common threshold has communication advantages for public health applications, we further investigated the predictive ability of both MV-total thresholds for each functional outcome. Specifically, we evaluated if evidence supported a conceptually easier 45 minutes/week target for a common MV-total threshold. Table 2 illustrates the threshold predictive ability of MV-total >45 minutes/week compared to MV-total >47 minutes/week to distinguish improved/high gait speed as identical (RR 1.8 versus 1.8) or PRO physical function (RR 1.4 versus 1.4). The similar performance across the functional outcomes tested supports a common MV-total >45-minute threshold to predict subsequent improved/high function.

DISCUSSION

The primary finding from this longitudinal study of adults with lower-extremity joint symptoms (n = 1,647) supports a minimum threshold of 45 minutes/week physical activity of MV-total activity to improve low function or sustain high function over 2 years. Attaining this evidence-based threshold better predicted improved/high function in gait speed and PRO physical function than the current federal physical activity threshold and represents a less stringent standard than current guidelines (i.e., MV-bout ≥ 150 minutes/week). For adults with lower-extremity joint symptoms who often do little or no moderate activity, a less demanding physical activity target tied to function may be a valuable intermediate benchmark towards meeting the current physical activity guideline.

To our knowledge, this is the first study to investigate aerobic physical activity thresholds related to functional outcomes for adults living with lower-extremity joint symptoms. Evidence supporting the World Health Organization and US physical activity guidelines for adults was initially based on consensus of evidence for cardiovascular benefits related to the 150 MV-bout minute/week threshold.³⁷ An extensive literature now supports broad morbidity and mortality benefits of meeting this guideline. A systematic literature review concluded that engaging in recommended levels of physical activity could reduce the risk of developing cardiovascular disease, stroke, hypertension, colon and breast cancer, type 2 diabetes mellitus, and osteoporosis based on the most methodologically sound studies.³⁸ Moreover,

guideline adherence could result in 20% or greater reduced risk for premature all-cause mortality among adults with chronic disease.³⁸⁻⁴⁰ Despite strong evidence for meeting current physical activity guidelines to support cardiovascular health and a wide range of potential health benefits for the general adult population, many adults with mobility-limiting conditions fail to achieve this goal. Fewer than 11% of US adults with knee OA achieve current physical activity guidelines.⁴¹ This problem motivates investigating potential intermediate thresholds related to different health benefits, in order to encourage adults with lower-joint symptoms to pursue physical activity.

Being physically active can improve function and reduce joint symptoms among adults with lower-extremity conditions. Randomized clinical trials demonstrate the benefit of physical activity programs to improve physical function in adults with lower-extremity conditions, including hip and knee OA.⁴²⁻⁴⁵ Nonstructured moderate activity, such as walking, can improve function and reduce symptomatic pain, fatigue, and stiffness among adults with rheumatic disease.^{46,47}

Longitudinal studies support a dose-response relationship between physical activity and function. A systematic review of the long-term effect of physical activity among older adults having knee pain found no evidence of worsened symptoms related to pain, loss of physical function, or progression in structural disease.⁴⁸ One case-control study concluded that increasing levels of regular physical activity was associated with a lower risk of disease progression to total knee replacement.⁴⁹ Adults with mobility-limiting conditions such as knee OA who achieved current physical activity guidelines by engaging in low-impact physical activity experienced substantial improvement in physical function, pain, and quality of life. Although the benefits from physical activity to improve function are recognized, the minimum time commitment needed to experience health benefits is not known.⁵⁰

Physical activity decreases with older age. Physical activity studies of adults based on objective accelerometer monitoring indicate only 10–15% of community-dwelling adults meet national guidelines, even after adjusting for age-related decline in physical activity capacity.^{6,51} This reality, combined with a dose-response relationship between physical activity and health, motivates clinical advice not to abandon guidelines, but to encourage older adults to pursue achievable incremental increases in physical activity.⁵² People who endure symptomatic joint disease often have a more difficult time being physically active than the general population and are at elevated risk for functional loss.^{52,53} Needed for this large population group is evidence to specify the amount and the intensity of physical activity associated with good functional outcomes.

Our study directly addressed the need for an evidence-based threshold for adults with lower-extremity symptoms by identifying physical activity metrics and thresholds that best predicted improved function or maintenance of high functional ability over a 2-year period. A big data approach using classification prediction trees identified that a minimum threshold of 45 total minutes of physical activity of at least moderate intensity acquired over 1 week predicted improved/high function in both objectively measured and PRO physical function. Sensitivity analyses indicated these MV-total thresholds were stable independent of sex, BMI, the presence of knee OA, and age. This evidence-based threshold predicting good functional outcomes is different from the current guideline in 2 ways. First, the selected MV-total metric captured all weekly time spent in activities of at least moderate intensity, as opposed to the legacy metric that included only MV activity time acquired in bouts lasting at least 10 minutes. For people with lower-extremity symptoms, the removal of the 10-minute bout constraint is a realistic step forward to increase activity levels in a symptomatic population, because those symptoms can inhibit

deconditioned people (like those with joint issues) from being able to sustain 10 minutes of MV physical activity. Second, the evidence-based threshold requires a lower physical activity dose (i.e., fewer weekly minutes of MV activity) than current guidelines. The identified evidence-based MV-total >45 minutes/week threshold related to improved/high function is less stringent than the current aerobic guideline, but does not replace the current guideline, which supports many other health benefits.

Strengths of the study included prospective data collection across multiple sites, the large sample size, the objective assessment of physical activity, and the age and sex diversity of this cohort. Study limitations need to be considered in interpreting results. The OAI sample does not represent the general population. The present sample was composed of adults with lower-extremity joint symptoms from a cohort having or at high risk for developing knee OA. This sample may include a larger proportion of adults with symptomatic knees than the general population with lower-extremity symptoms, which may influence the generalizability of these results. However, the intentional stratified OAI recruitment produced a diverse cohort across age and sex. Although the OAI ascertainment of hip symptoms used a longer time frame than foot, ankle, or knee symptom ascertainment, 90% of people reporting hip symptoms would be in the sample solely due to their additional report of other lower-extremity joints. It is notable that physical activity thresholds held within subgroups, with and without radiographic evidence of knee OA, support the robustness of these findings to disease status. Although an important methodologic strength is the objective measurement of physical activity using accelerometers, it is recognized the accelerometers used cannot capture water activities and may underestimate activities with minimal vertical acceleration/deceleration, such as cycling. However, time spent in these activities was negligible. It is acknowledged that other outcome definitions may yield different thresholds, and unreported treatments or factors may influence outcomes. Causation cannot be inferred from these observational data. Further research is warranted to confirm these findings

The current study supports an intermediate threshold to spend at least 45 minutes/week in accumulated physical activity of at least moderate intensity among adults having lower-extremity joint symptoms. This threshold to support improved/high function represents a less demanding goal than current federal physical activity guidelines in 2 ways. First, all time spent in MV activities contributes to attaining this function-related minimum threshold, in contrast to the current MV-bout threshold, which is only met through activity acquired in bouts lasting at least 10 minutes. Second, a minimum of 45 minutes/week may represent a more feasible activity goal than the current physical activity guideline of 150 minutes/week. Success in meeting the MV-total threshold of 45 minutes/week increased the likelihood of functional preservation in high-functioning persons and functional improvement in those with functional limitations, providing an intermediate goal towards achieving the current aerobic physical activity guideline.

ACKNOWLEDGMENTS

The authors thank the participants from the OAI.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Dunlop had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design

Dunlop.

Acquisition of data

Dunlop, Song, Lee, Semanik.

Analysis and interpretation of data

Dunlop, Song, Lee, Gilbert, Semanik, Ehrlich-Jones, Pellegrini, Pinto, Ainsworth, Chang.

REFERENCES

- 1 Department of Health and Human Services. 2008 physical activity guidelines for Americans. Washington (DC): Department of Health and Human Services; 2008.
- 2 World Health Organization. Global recommendations on physical activity for health. Geneva (Switzerland): WHO Press; 2010. p. 15–35.
- 3 Pate RR, Pratt M, Blair SN, Haskell WL, Macera CA, Bouchard C, et al. Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA* 1995;273:402–7.
- 4 Church TS, Earnest CP, Skinner JS, Blair SN. Effects of different doses of physical activity on cardiorespiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure: a randomized controlled trial. *JAMA* 2007;297:2081–91.
- 5 Bates JH, Serdula MK, Khan LK, Jones DA, Macera CA, Ainsworth BE. Intensity of physical activity and risk of coronary heart disease [letter]. *JAMA* 2001;285:2973.
- 6 Jefferis BJ, Sartini C, Lee IM, Choi M, Amuzu A, Gutierrez C, et al. Adherence to physical activity guidelines in older adults, using objectively measured physical activity in a population-based study. *BMC Public Health* 2014;14:382.
- 7 Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. *Med Sci Sports Exer* 2008;40:181–8.
- 8 Fontaine KR, Heo M, Bathon J. Are US adults with arthritis meeting public health recommendations for physical activity? *Arthritis Rheum* 2004;50:624–8.
- 9 Shih M, Hootman JM, Kruger J, Helmick CG. Physical activity in men and women with arthritis: National Health Interview Survey, 2002. *Am J Prevent Med* 2006;30:385–93.
- 10 Abellan van Kan G, Rolland Y, Andrieu S, Bauer J, Beauchet O, Bonnefoy M, et al. Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people: an International Academy on Nutrition and Aging (IANA) Task Force. *J Nutr Health Aging* 2009;13:881–9.
- 11 Cesari M, Kritchevsky SB, Newman AB, Simonsick EM, Harris TB, Penninx BW, et al. Added value of physical performance measures in predicting adverse health-related events: results from the Health, Aging And Body Composition Study. *J Am Geriatr Soc* 2009;57:251–9.
- 12 Ostir GV, Kuo YF, Berges IM, Markides KS, Ottenbacher KJ. Measures of lower body function and risk of mortality over 7 years of follow-up. *Am J Epidemiol* 2007;166:599–605.
- 13 Rosano C, Newman AB, Katz R, Hirsch CH, Kuller LH. Association between lower digit symbol substitution test score and slower gait and greater risk of mortality and of developing incident disability in well-functioning older adults. *J Am Geriatr Soc* 2008;56:1618–25.
- 14 Keeler E, Guralnik JM, Tian H, Wallace RB, Reuben DB. The impact of functional status on life expectancy in older persons. *J Gerontol A Biol Sci Med Sci* 2010;65:727–33.

- 15 Jinks C, Jordan K, Croft P. Osteoarthritis as a public health problem: the impact of developing knee pain on physical function in adults living in the community: (KNEST 3). *Rheumatology (Oxford)* 2007;46:877–81.
- 16 Stenholm S, Koster A, Valkeinen H, Patel KV, Bandinelli S, Guralnik JM, et al. Association of physical activity history with physical function and mortality in old age. *J Gerontol A Biol Sci Med Sci* 2016;71:496–501.
- 17 Feinglass J, Thompson JA, He XZ, Witt W, Chang RW, Baker DW. Effect of physical activity on functional status among older middle-age adults with arthritis. *Arthritis Rheum* 2005;53:879–85.
- 18 Ip EH, Church T, Marshall SA, Zhang Q, Marsh AP, Guralnik J, et al. Physical activity increases gains in and prevents loss of physical function: results from the lifestyle interventions and independence for elders pilot study. *J Gerontol A Biol Sci Med Sci* 2013;68:426–32.
- 19 Nevitt MC, Sharma L. OMERACT workshop radiography session 1. *Osteoarthritis Cartilage* 2006;14 Suppl A:4–9.
- 20 Eckstein F, Wirth W, Nevitt MC. Recent advances in osteoarthritis imaging: the Osteoarthritis Initiative. *Nat Rev Rheumatol* 2012;8:622–30.
- 21 Sharma L, Cahue S, Song J, Hayes K, Pai YC, Dunlop D. Physical functioning over three years in knee osteoarthritis: role of psychosocial, local mechanical, and neuromuscular factors *Arthritis Rheum* 2003;48:3359–70.
- 22 Mallen CD, Peat G, Thomas E, Lacey R, Croft P. Predicting poor functional outcome in community-dwelling older adults with knee pain: prognostic value of generic indicators. *Ann Rheum Dis* 2007;66:1456–61.
- 23 Thomas E, Peat G, Mallen C, Wood L, Lacey R, Duncan R, et al. Predicting the course of functional limitation among older adults with knee pain: do local signs, symptoms and radiographs add anything to general indicators? *Ann Rheum Dis* 2008;67:1390–8.
- 24 Wright A, Hannon J, Hegedus EJ, Kavchak AE. Clinimetrics corner: a closer look at the minimal clinically important difference (MCID). *J Man Manip Ther* 2012;20:160–6.
- 25 Matthews CE, Ainsworth BE, Thompson RW, Bassett DR Jr. Sources of variance in daily physical activity levels as measured by an accelerometer. *Med Sci Sports Exer* 2002;34:1376–81.
- 26 Semanik P, Song J, Chang RW, Manheim L, Ainsworth B, Dunlop D. Assessing physical activity in persons with rheumatoid arthritis using accelerometry. *Med Sci Sports Exer* 2010;42:1493–501.
- 27 Song J, Semanik P, Sharma L, Chang RW, Hochberg MC, Mysiw WJ, et al. Assessing physical activity in persons with knee osteoarthritis using accelerometers: data from the Osteoarthritis Initiative. *Arthritis Care Res (Hoboken)* 2010;62:1724–32.
- 28 Peterfy C, Li J, Zaim S, Duryea J, Lynch J, Miaux Y, et al. Comparison of fixed-flexion positioning with fluoroscopic semi-flexed positioning for quantifying radiographic joint-space width in the knee: test-retest reproducibility. *Skeletal Radiol* 2003;32:128–32.
- 29 Pepe MS. The receiver operating curve for continuous tests: the statistical evaluation of medical tests of classification and prediction. New York: Oxford University Press; 2004. p. 66–76.
- 30 DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics* 1988;44:837–45.
- 31 Breiman L, Friedman JH, Oshen RA, Stone CJ. Classification and regression trees. Monterey (CA): Wadsworth & Brooks; 1984.
- 32 Esposito F, Malerva D, Semeraro G. Decision tree pruning as a search in the state space: lecture notes in computer science. London: Springer-Verlag; 1993. p. 165–84.

- 33 Pencina MJ, D'Agostino RB Sr, D'Agostino RB Jr, Vasan RS. Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. *Stat Med* 2008;27:157–72.
- 34 Cook NR. Use and misuse of the receiver operating characteristic curve in risk prediction. *Circulation* 2007;115:928–35.
- 35 Salford Systems. CART. Ver. 7.0. San Diego: Salford Systems; 2008.
- 36 Hogan JW, Roy J, Korkontzelou C. Handling drop-out in longitudinal studies. *Stat Med* 2004;23:1455–97.
- 37 Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exer* 2007;39:1423–34.
- 38 Warburton DE, Charlesworth S, Ivey A, Nettlefold L, Bredin SS. A systematic review of the evidence for Canada's Physical Activity Guidelines for Adults [abstract]. *Int J Behav Nutri Phys Act* 2010;7:39.
- 39 Wessel TR, Arant CB, Olson MB, Johnson BD, Reis SE, Sharaf BL, et al. Relationship of physical fitness vs body mass index with coronary artery disease and cardiovascular events in women. *JAMA* 2004;292:1179–87.
- 40 Katzmarzyk PT, Church TS, Blair SN. Cardiorespiratory fitness attenuates the effects of the metabolic syndrome on all-cause and cardiovascular disease mortality in men. *Arch Int Med* 2004;164:1092–7.
- 41 Dunlop DD, Song J, Semanik PA, Chang RW, Sharma L, Bathon JM, et al. Objective physical activity measurement in the Osteoarthritis Initiative: are guidelines being met? *Arthritis Rheum* 2011;63:3372–82.
- 42 Fransen M, McConnell S, Harmer AR, van der Esch M, Simic M, Bennell KL. Exercise for osteoarthritis of the knee: a Cochrane systematic review. *Brit J Sports Med* 2015;49:1554–7.
- 43 Juhl C, Christensen R, Roos EM, Zhang W, Lund H. Impact of exercise type and dose on pain and disability in knee osteoarthritis: a systematic review and meta-regression analysis of randomized controlled trials. *Arthritis Rheumatol* 2014;66:622–36.
- 44 Uthman OA, van der Windt DA, Jordan JL, Dziedzic KS, Healey EL, Peat GM, et al. Exercise for lower limb osteoarthritis: systematic review incorporating trial sequential analysis and network meta-analysis. *BMJ* 2013;347:f5555.
- 45 Messier SP, Mihalko SL, Legault C, Miller GD, Nicklas BJ, DeVita P, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. *JAMA* 2013;310:1263–73.
- 46 Escalante Y, Garcia-Hermoso A, Saavedra JM. Effects of exercise on functional aerobic capacity in lower limb osteoarthritis: a systematic review. *J Sci Med Sport* 2011;14:190–8.
- 47 Callahan LF, Shreffler JH, Altpeter M, Schoster B, Hootman J, Houenou LO, et al. Evaluation of group and self-directed formats of the Arthritis Foundation's Walk With Ease Program. *Arthritis Care Res (Hoboken)* 2011;63:1098–107.
- 48 Quicke JG, Foster NE, Thomas MJ, Holden MA. Is long-term physical activity safe for older adults with knee pain? A systematic review. *Osteoarthritis Cartilage* 2015;23:1445–56.
- 49 Manninen P, Riihimaki H, Heliovaara M, Suomalainen O. Physical exercise and risk of severe knee osteoarthritis requiring arthroplasty. *Rheumatology (Oxford)* 2001;40:432–7.

- 50 Paterson DH, Warburton DE. Physical activity and functional limitations in older adults: a systematic review related to Canada's Physical Activity Guidelines. *Int J Behav Nutr Phys Act* 2010;7:38.
- 51 Tucker JM, Welk GJ, Beyler NK. Physical activity in US: adults compliance with the Physical Activity Guidelines for Americans. *Am J Prevent Med* 2011;40:454–61.
- 52 Sparling PB, Howard BJ, Dunstan DW, Owen N. Recommendations for physical activity in older adults. *BMJ* 2015;350:h100.
- 53 Voelker R. Few adults with knee osteoarthritis meet national guidelines for physical activity. *JAMA* 2011;306:1428–9.