

Does the intensity of daily walking matter for protecting against the development of a slow gait speed in people with or at high risk of Knee Osteoarthritis?

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1 INTRODUCTION

2 Knee osteoarthritis (OA) is a risk factor for a rapid decline in walking or gait speed in middle
3 to older aged adults,¹ and functional limitation in general.² Since a slow gait speed is well
4 recognized as a risk factor for mortality³ and persistent functional limitation in older adults,⁴ it
5 is important to prevent reductions in gait speed in people with knee OA.

6
7 Physical activity is recommended to prevent slow gait and functional limitation in OA.⁵⁻⁷ In
8 particular, daily walking, i.e., taking more steps/day, is underlined as is the single most
9 crucial movement behaviour to encourage,⁸ as it is the most common type of physical
10 activity that older adults employ for exercise.⁹⁻¹² Evidence suggests that walking >6000
11 steps/day can serve to preserve gait speed in knee OA.¹³ However, it is not known whether
12 the *intensity* of steps accumulated is also relevant for preventing a slow gait speed in this
13 population. For instance, walking can be purposeful and of a moderate-to-vigorous intensity
14 (e.g., brisk walking, or walking to load/unload a car), or it can be of a lighter intensity, e.g.,
15 taking a stroll in a park.^{8,14}

16
17 Since the total hours available in one day to participate in physical activity are finite (i.e.,
18 limited to 24 hours) participating in one activity comes at the cost of not engaging in another.
19 For the present study, we are most interested in understanding the effects of replacing not
20 walking for walking at different intensities on incident slow gait speed. Analytically,
21 Isotemporal substitution offers a novel technique to statistically estimate the value of
22 displacing one behaviour with an alternative activity. This is an advance over traditional
23 methods to quantify the association between an exposure and outcome (such as regression
24 models), in which only the effect of “adding”, rather than substituting an activity type can be
25 examined.^{15,16} In particular, isotemporal substitution will enable investigation of the ‘time-
26 substitution effects’ of replacing an identical time period of not walking, with walking at light
27 or moderate-to-vigorous intensities on incident slow gait speed – i.e., the ability to walk >1.0
28 meters/second (m/s) and >1.2 m/s. These thresholds are considered to discriminate those

1 with and without risk of mortality and loss of independent and autonomous functioning within
2 their community, respectively.

3
4 The purpose of this study was therefore to investigate the association of substituting time
5 spent not walking with walking at very-light (i.e., 1–49 steps/minute), light (50–100
6 steps/min), and moderate-to-vigorous walking (>100 steps/min) intensities for incident slow
7 gait speed over a two year period in people with, or at high risk of, knee OA.

8

9 **METHODS**

10 **Study sample**

11 We used data from two longitudinal cohort studies, specifically the Multicenter Osteoarthritis
12 (MOST) study and the Osteoarthritis Initiative (OAI). In both studies, participants were
13 community dwelling adults who have, or who are at high risk of developing knee OA at
14 baseline. Increased risk was identified from age-specific criteria for established risk factors
15 including knee symptoms in the past 12 months,¹⁷ being overweight from gender-specific
16 cut-points,¹⁷ knee injury causing difficulty walking for at least one week,^{17,18} any knee surgery
17 history,¹⁹ family history of a total knee replacement,²⁰ Heberden's nodes,^{17,21} or repetitive
18 knee bending at work or outside of work.²² Detailed descriptions of MOST study and OAI
19 eligibility criteria have been published elsewhere.^{23,24} Briefly, the MOST study enrolled
20 people aged 50 to 79 years, from communities in and surrounding Birmingham, Alabama,
21 and Iowa City. The OAI recruited people aged 45 to 79 years from four clinical sites
22 (Baltimore, Maryland; Pittsburgh, Pennsylvania; Pawtucket, Rhode Island; and Columbus
23 Ohio). Study protocols were approved by the relevant institutional review boards. All
24 participants provided informed consent to participate.

25

26 This study focused on sub-samples of the MOST and OAI cohorts who consented to
27 undertake objective assessment of physical activity (via activity monitors). This occurred for
28 the first time at the 60-month (MOST) and 48-month (OAI) study visits. We also used data
29 collected two years later at the 84-month (MOST) and 72-month (OAI) study visits (Figure

1 1), in order to determine incidence of slow gait speed. For MOST, objective activity monitor
2 data were collected from 2330 individuals between May 2009 and January 2011. For OAI, a
3 total of 2125 participants provided objective activity monitor data between August 2008 and
4 July 2010. For the purpose of this study, 60- and 48-month study visits are considered
5 'baseline' and 84- and 72-months the two-year follow up for MOST and OAI participants,
6 respectively.

7

8 **Measures**

9 **Study exposure**

10 *Intensity of daily walking*

11 Daily walking was measured using an accelerometer-enabled physical activity monitor in
12 both cohorts. For the MOST study, walking intensity was assessed using the StepWatch™
13 activity monitor - a small (70 x 50 x 20mm), waterproof device that is worn around the ankle
14 and records the number of strides taken each minute. To calculate the number of steps, the
15 stride output is doubled. In the OAI study, daily walking was measured via the GT1M
16 Actigraph - a small uniaxial accelerometer that was worn on the right hip and measures
17 acceleration and deceleration along a vertical axis. Both the Stepwatch™ and GT1M
18 Actigraph have been validated for step count against several reference standard measures
19 of step frequency, including in samples of older adults.²⁵⁻²⁷ Participants were provided with
20 written and verbal instructions regarding monitor wear, removal and replacement. In both
21 studies, participants were asked to wear the device during waking hours for 7 consecutive
22 days. They were requested to remove the monitor only for water-based activities (e.g.,
23 swimming, showering), or sleeping.

24

25 Non-wear time was determined by identifying sustained periods of little or zero activity from
26 data recorded by activity monitors. Non-wear criteria was applied in accordance with
27 previous published studies validating non-wear criteria specifically for the StepWatch³⁶ and
28 Actigraph.³⁷ Specifically, in the MOST cohort, we defined non-wear as ≥ 180 minutes of

1 consecutive 0 steps.^{28,29} For the OAI sample, non-wear was identified where the monitor had
2 registered ≥ 90 minutes of consecutive activity counts <100 .²⁹ In both cohorts, we defined a
3 valid day as ≥ 10 hours valid wear time.²⁹

4
5 Walking intensity was classified according to step cadence recorded by the physical activity
6 monitors. Specifically, <1 step/min was defined as not walking, 1 - 49 steps/min as very-light
7 intensity walking, 50 - 100 steps/min as light intensity walking, and >100 steps/min as
8 moderate-to-vigorous intensity walking.^{8,30-32} We split light intensity walking into two
9 categories (very-light and light), as behaviours undertaken between 1 and 100 steps/min are
10 likely to comprise a wide range of behaviours (e.g., standing with incidental movement,
11 household chores, walking at <4 km/hour). As such, it is possible that time spent walking at
12 the lower vs. upper end of the 'light intensity' spectrum may hold different effects for health
13 for people with knee OA.¹⁵

14

15 **Study outcomes**

16 *Slow Gait Speed*

17 Gait speed was measured in both MOST and OAI studies in m/s on the basis of average
18 speed over two 20-meter timed walk tests [i.e., 20 metres \div test time (seconds)].^{13,33} The test
19 was conducted in an unobstructed corridor and timing started when the first foot crossed the
20 start line, and ended after the last foot crossed the finish line. Gait speed has been shown to
21 have high test-re-test reliability in people with knee OA.³³

22

23 We defined two study outcomes from the 20-metre walk:

24 1) *Gait speed <1.0 m/s*: Walking < 1.0 m/s is associated with mortality and limitations in
25 physical functioning among community dwelling older adults.^{3,34}

26 2) *Gait speed <1.2 m/s*: Walking > 1.2 m/s is a minimum speed necessary to cross streets
27 using timed signals.³⁵ Thus, walking at a speed at or above 1.2 m/s is a reasonable proxy
28 for the ability to navigate independently in the community,³⁶ and a speed <1.2 m/s may
29 represent difficulty walking in the community. Several studies in the USA, Canada, and

1 Europe have recently employed this threshold to represent a community walking
2 speed.^{37,38}

3 *Data reduction*

4 Participants who provided ≥ 4 days of valid activity monitor data at baseline were included in
5 present analyses (MOST, N = 1731, OAI, N = 1925).^{39,40} Analyses were further restricted to
6 those without slow gait speed at baseline. For < 1.0 m/s outcome, a total of 1342 and 1551
7 participants in MOST and OAI respectively, were included in the analytic data set. For < 1.2
8 m/s outcome, a total of 878 and 1221, were included for MOST and OAI respectively. **Figure**
9 **1.**

10 11 **Potential confounders**

12 Study covariates were included on the basis of previously associations with physical activity
13 and gait speed,^{41,42} and covariate values collected at our study baseline were included in
14 analyses (MOST 60-month, OAI 48-month) (OAI) study visit as follows; age; sex; body-
15 mass-index (BMI); study site; ethnicity (White, African American, other); educational
16 attainment ($<$ some college vs. \geq college); marital status (married, single, divorced,
17 separated); self-reported comorbidities (Charlson comorbidity index, ≥ 1 vs. none); symptoms
18 of depression symptoms (Centre for Epidemiologic Studies Depression Scale, ≥ 16 vs. < 16);
19 and knee pain on a visual analogue scale (MOST for past 30 days 0 – 100; OAI for past 7
20 days 0-10). All variables were assessed via direct measurement, interview and/or
21 questionnaire. Instruments and data collection procedures have been previously described
22 in detail elsewhere.^{23,24}

23 24 **Statistical analyses**

25 All analyses were conducted separately for MOST and OAI study samples due to
26 differences in study methodologies in regards to exposure variables (i.e., walking intensity
27 measured via the StepWatchTM vs. Actigraph). First, descriptive statistics were computed.
28 Next, regressions were employed to calculate Relative Risk Ratios (RR) using regression
29 models with a log-link function and robust standard errors. In particular, we employed

1 isotemporal substitution within regression models to evaluate the effect (i.e., relative risk
2 reduction) of replacing not walking, with equal periods of very-light, light and moderate-to-
3 vigorous intensity walking, on study outcomes.^{15,16} This analytical approach enables
4 investigation of increasing engagement in different intensities of walking and simultaneously
5 decreasing time spent not walking on the relative risk of developing slow gait speed two
6 years later. In this way, are able to examine the combined effects of displacing minutes of
7 not walking, with equal minutes of walking at specific intensities. This is in contrast to simple
8 regression models, in which only the effect of “adding”, rather than substituting an activity
9 type can be examined.¹⁵ That is, only the independent effects of increasing one behaviour
10 can be investigated, whilst controlling for a constant (and therefore unchanging) level of
11 another.

12
13 We utilised isotemporal models by including a variable for; 1) the total time (i.e., the sum of
14 time spent; not walking + very-light + light + moderate-to-vigorous walking) and 2) four
15 separate variables to represent each unique walking-intensity to the model simultaneously
16 (i.e., one each for; not walking, very-light, light, and moderate-to-vigorous walking). The
17 unique activity variable representing time spent *not walking* was dropped from the model to
18 estimate the effects of replacing not walking, with walking at different intensities.¹⁶

19
20 Before entry into models, all four walking intensity categories were divided by a constant to
21 represent the ‘duration of substitution’, in order to improve the clinical implications of study
22 findings. For example, to estimate the effects of replacing 5 minutes of not walking, with 5
23 minutes of walking at different intensities on study outcomes, all variables were divided by 5
24 to represent an increase of 5 minutes/day within each walking intensity category. We
25 repeated analysis dividing walking categories by 10 and 20 to represent an increase of
26 walking 10 and 20 minutes/day, respectively. All models were adjusted for potential
27 confounders.

28

1 RESULTS

2 Of the 1731 participants included in the MOST analytic dataset, the mean (SD) age was
3 67.2 (7.7) years and 59.8% were women. Of the 1925 participants included in the OAI
4 analytic dataset, the mean (SD) age was 65.1 (9.1) years and 55.2% were women. **Table 1.**
5 Participants not included in the analytic data set, (i.e. those who had baseline but not follow-
6 up data), were in general more likely to be non-white, have pain in the lower body, have less
7 than a college education, have comorbid conditions, and have higher BMI and higher knee
8 pain intensity at baseline compared with those included in the analytic dataset.

9 **Supplemental Table 1.**

10
11 In general, those who did not develop slow gait speed spent more time walking at very-light,
12 light and moderate-to-vigorous intensities at baseline compared with those who developed
13 slow gait speed at 2 years. **Table 2.**

14 15 *Gait speed <1.0 m/s*

16 The cumulative incidence of a gait speed < 1.0 m/s over two years was 8.8% (n = 108/1342)
17 and 4.5% (n = 70/1551) in the MOST and OAI cohorts, respectively. Replacing not walking
18 with 5 to 20 min/day of moderate-to-vigorous walking reduced the risk by 13% to 49% in
19 MOST and 33% to 79% in OAI, which both met statistical significance. **Figure 2.**

20 Replacement with walking 5 to 20 min/day at a light intensity had a 5% to 20% reduction in
21 risk in MOST and 10% to 34% reduction in risk in OAI, and these effects did not meet
22 statistical significance. Replacing time not walking with very-light intensity walking did not
23 materially change the risk of developing a gait speed < 1.0 m/s in both cohorts. For
24 unadjusted effect estimates, see **Supplemental Table 2.**

25 26 *Gait speed <1.2 m/s*

27 The development of a gait speed < 1.2 m/s over two years was 17.8% (n = 156/878) of the
28 MOST study sample, and 13.3% (n = 163/1221) of OAI participants. Replacement with 5 to
29 20 min/day of moderate-to-vigorous walking demonstrated risk reductions between 8% to

1 27% in MOST and 10% to 35% in OAI. However, effects did not meet statistical significance.
2 **Figure 3.** Similarly, replacing not walking, with 5 to 20 min/day of walking at a light intensity
3 or very-light intensity revealed small risk reductions in both cohorts (light = 1-4% in MOST,
4 2-10% in OAI; very-light = 1-2% in MOST, 1-4% in OAI), which were not statistically
5 significant. For unadjusted effect estimates, see **Supplemental Table 2.**

6

7 **DISCUSSION**

8 We investigated the association of substituting time spent not walking with walking at
9 different intensities for protecting against the development of slow gait speeds two years
10 later, in people with or at high risk of knee OA. We found that replacing not walking with
11 equal periods of walking at a moderate-to-vigorous intensity (>100 steps/min) had a small to
12 moderate effect on reducing the risk of developing a slow gait speed <1.0 m/s two years
13 later. However, we found attenuated effects for light intensity walking (50 - 100 steps/min)
14 that did not meet statistical significance, and observed no effect of very-light intensity
15 walking (1 - 49 steps/min).

16

17 Past work employing isothermal substitution analyses has demonstrated the significance of
18 light-intensity physical activity for prevention of poor physical health and reduced risk of
19 mortality among older adults.^{15,43} Such findings have contributed towards the evidence base
20 underpinning recommendations for the promotion of light physical activity among
21 populations for whom regular engagement in higher intensity physical activity may present a
22 challenge (including knee OA).⁴⁴ Arguably our results, which demonstrate that for people
23 with, or at high risk of knee OA, light-intensity walking may not produce the same functional
24 gains as moderate-to-vigorous walking, are particularly important.

25

26 Our findings suggest that walking at a moderate-to-vigorous intensity may be necessary to
27 prevent the development of a slow gait speed <1.0 m/s. This is an important finding given
28 that this critically slow gait speed is a known risk factor for death,³ persistent lower extremity

1 limitation, and hospitalization in older adults.⁴ Thus, preventing the development of slow gait,
2 from taking more moderate-to-vigorous steps/day is noteworthy for people with knee OA,
3 who are already at high risk of developing functional limitation.

4

5 These findings extend previous work regarding recommendations for daily step
6 accumulation in knee OA (i.e., >6000 steps/day),¹³ by adding the caveat that steps may
7 need to be at a moderate intensity in order to significantly protect against critically slow gait
8 speed. One way to increase such steps is to use a joint step and time goal. Indeed, there is
9 expert consensus to indicate that setting step cadence goals - in addition to step frequency
10 goals - might help individuals engage in more moderate-to-vigorous physical activity.⁸ For
11 example, a previous study investigating messaging of physical activity goals for Latina
12 women found a goal of 3000 steps in 30 minutes had the best increase in time spent in
13 moderate-to-vigorous physical activity, compared to a step goal of walking 10,000 steps/day
14 or a self-selected step goal.⁴⁵ Considering the emerging widespread use of commercially
15 available fitness trackers to record steps among the general population, we believe our
16 findings are particularly timely.

17

18 One reason why moderate-to-vigorous walking, relative to lighter intensity walking may be
19 protective against slow gait, is because of the significant physiological response required by
20 the lower-body musculature to generate faster more frequent walking. It is well evidenced
21 that moderate-to-vigorous physical activity is associated with increased muscular strength,⁴⁶⁻
22 ⁴⁸ and that higher lower-extremity muscular strength reduces the risk of functional decline
23 among at risk cohorts.^{49,50} Our findings are consistent with the Australian Diabetes, Obesity
24 and Lifestyle Study, which found steps accumulated at a moderate-to-vigorous intensity
25 were more consistently, and strongly linked to lower-extremity muscular strength than steps
26 taken at a light intensity.⁴⁷

27

1 Still, it is noteworthy that whilst our analyses revealed only small associations for light-
2 intensity walking that did not meet statistical significance, the size of the risk reductions were
3 comparable for replacement of not walking with 20 minutes of light-intensity walking vs.
4 5 minutes of moderate-to-vigorous intensity walking (i.e., 20% vs 13% (MOST), and 34% vs
5 33% (OAI), respectively). This is perhaps because these replacement durations are more
6 comparable at the relative level (i.e., typically between a 40-100% increase). Thus, it is
7 possible that trading not walking with light-intensity walking of longer durations, may offer an
8 intermediate step to promoting engagement in moderate-to-vigorous intensity walking.
9 Indeed, the avoidance of time spent in no or very-light activity for short time periods each
10 day, may be a first realistic goal for people with knee pain and co-existing mobility issues.

11
12
13 Strengths of this study include parallel analyses of longitudinal data from two large-scale
14 cohort studies – MOST and OAI and the objective assessment of daily walking in both
15 cohorts. There are a number of limitations to the present study. First, isotemporal
16 regression models permit investigation of only theoretical relationships, and do not represent
17 observed changes in physical activity. In addition, as the confidence intervals for all effect
18 sizes are wide, the reported associations between walking intensity and risk of developing
19 slow gait speed may be much smaller (or larger) than suggested by the point estimates.
20 Results should therefore be interpreted with some caution. Second, there is a potential for
21 reverse-causation, i.e., individuals who walk faster are able to achieve moderate intensity
22 with less effort than those who walk slower. We mitigate this by only including study
23 participants who are without slow gait speed at our study baseline. However, it is still
24 possible classification bias at baseline in regards to baseline gait speeds may have
25 influenced study findings – i.e., participants with a gait speed just above the critical
26 thresholds (1.0 and 1.2 m/s) may be at a greater risk of falling below the threshold after two
27 years, than participants with a much higher baseline gait speed. Thus, to definitively test the
28 effect of replacing variable time periods of not walking, with walking at different intensities on
29 gait speed, a controlled clinical trial is required. Such a trial may be impractical, however,

1 given the low incidence of our study outcomes, <20%, and the associated cost of a RCT.
2 Third, it is not known if walking at a moderate-to-vigorous intensity was accumulated in
3 bouts e.g., continuous walking episodes, or across interrupted minutes of walking. Finally,
4 we only evaluated our study outcome over two years. It is likely a higher incidence may
5 occur with a longer follow-up period. Nevertheless, these findings may provide support that
6 walking at a moderate-to-vigorous intensity (for longer durations) is associated with
7 maintenance of gait speed above critical levels in people with, or at high risk of knee OA.
8 Indeed, where moderate-to-vigorous walking can be encouraged or maintained from knee
9 OA onset, our findings highlight the positive consequences of a cyclic relationship between
10 walking intensity and gait speed.

11

12 **Conclusions**

13 We found that increasing time in moderate-to-vigorous walking may prevent slow gait speed
14 in people with or at high risk of knee OA. These findings may support the importance of
15 recommending a moderate-to-vigorous walking intensity in addition to a step goal, in order
16 reduce the risk of developing critical slow gait speeds in this population. These
17 recommendations need to be confirmed in controlled clinical trials.

18

19 **Author contributions**

20 SF (s.a.m.fenton@bham.ac.uk) and DW (dkw@udel.edu) had full access to all of the data in
21 the study and take responsibility for the integrity of the data and the accuracy of the data
22 analysis. SF, JLD, AR, AA, RK and DW: *study concept and analytical design*. SF, TN and
23 DW: *analysis and interpretation of data*. SF and DW: *drafting of the manuscript*. SF, TN, DD,
24 MN, MD, JD, RK, AA, AR, WZ, CEL, JT, GK and DW: *critical revision of the manuscript for*
25 *important intellectual content*. SF and DW: *statistical analysis*. SF, TN, DD, MN, MD, JD, RK,
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27

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7 review, or approval of the manuscript.

8

9 **Conflict of interest**

10 All authors declare no conflicts of interest.

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