Stepping Forward: A Scoping Review of Physical Activity in Osteoarthritis

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### <u>Abstract</u>

Physical Activity (PA) is recommended to mitigate the symptoms of osteoarthritis (OA), however this modality remains an unfamiliar construct for many patients and clinicians. Moreover, there can be confusion over the nuanced differences in terminology, such as such as exercise, sedentary behavior, and moderate intensity. The purpose of this scoping review is to provide a basic overview of PA including terminology, summarize the importance of PA for adults with OA, and discuss current gaps in the literature. Broadly, PA is defined as "any bodily movement produced by skeletal muscles that results in energy expenditure", and exercise is considered a type of PA that is planned, structured, and repetitive. Robust literature shows that PA has a modest protective effect on pain, functional limitation, and disability for OA, which is in addition to positive effects on a broad range of outcomes from mood and affect to mortality and morbidity in the general population. Recommendations are provided for which measurement instruments can be used clinically and from a research perspective to record PA, as well as metrics to employ to summarize daily activity.

### Introduction

An estimated 240 million adults worldwide have painful osteoarthritis (OA), which includes 10% of men and 18% of women over the age of 60.(1) Physical activity (PA), defined as energy expenditure from skeletal muscle above a resting level,(2) plays an important role for OA, namely as a recommended management strategy. However, PA remains an unfamiliar construct for many patients, clinicians, policymakers, and investigators alike. Moreover, there can be confusion over the nuanced differences in terminology, such as the differences between PA and exercise, sedentary behavior and inactivity, and steps/day and moderate intensity activity.

To clarify these questions, this scoping review will begin with a basic overview of PA, including how it is defined and measured in research. Next, we will summarize the importance of PA to disease, pain, and physical function outcomes for adults with OA. Lastly, we will discuss current gaps in the literature for PA for adults with OA. We searched the PubMED database for publications on "physical activity"[MeSH Terms], "exercise"[MeSH Terms] and "osteoarthritis"[MeSH Terms]. We restricted our search to articles, originally published in English, until June 1, 2022. We also added several original studies to provide more detailed support of the findings of the articles, based on the authors' familiarity with the literature. We highlight that this search was performed to inform our scoping review, but we did not employ a systematic approach in identifying key articles.

### What exactly is Physical Activity?

Caspersen and colleagues defined PA as, "any bodily movement produced by skeletal muscles that results in energy expenditure".(2) They further distinguish exercise as bodily movement that is planned, structured, and repetitive. Therefore, PA encompasses all energy expenditure, and exercise is a special sub-type of PA involving dedicated time to expending energy, i.e., working out. Importantly, PA captures how much time is spent in daily behaviors such as walking, and gives us an accurate picture about what someone actually *does*. This is in contrast to performance-based tests (e.g., gait speed) that tell us what someone is capable of doing.

### How is Physical Activity measured?

Wearable monitors and patient reported questionnaires are the two primary means of measuring PA. The advantage of using wearable monitors is access to detailed metrics regarding time spent in different intensities of PA and the number of steps/day taken. While these measures of PA can also be estimated from patient reported

questionnaires, they are less precise than wearable monitors and are subject to recall bias.

Wearable monitors come in research-grade and consumer-grade types, and are worn on specific body sites. For example, a popular research-grade monitor called the Actigraph GT3X is most often worn around the waist with an elastic band. (Figure 1) In contrast, consumer-grade monitors, such as the Fitbit, are often worn around the wrist. Even simple consumer-grade pedometers can be used to measure PA.(3) A major advantage of consumer-grade monitors is that they are less expensive than research-grade monitors. Of note, an increasing number of studies are using consumer-grade monitors to report PA (steps/day) in clinical research studies.(4) A limitation of consumer-grade monitors is that they have limited validity to measure time spent in moderate-to-vigorous intensity PA, which is a common intensity-based physical activity outcome employed in the literature.(5,6)

The length of time that study participants must wear the monitor is an important consideration when measuring PA. One common and agreed upon methodology is described by Troiano et al who used a monitor to measure PA in the National Health and Nutrition Examination Survey (NHANES).(7) These guidelines recommend one week (7 days) of monitoring, with a minimum of 4 valid days to be included in an analytic dataset. A valid day is  $\geq$  10 hours of monitor wear. Thus, a disadvantage of using wearable monitors is that participants need to wear the monitors for the majority of a day and for several days, which can be burdensome.

As well, consideration should be given to the fact that consumer-grade monitors give users feedback regarding their PA, which may positively influence their behaviors. Research-grade monitors do not provide feedback; however, we still observed a 'Hawthorne effect' i.e., when participants began wearing a monitor, they slightly increased their PA (8). Nevertheless, using steps/day summaries provided in all consumer-grade monitors should suffice for clinicians seeking a snapshot measure of their patient's physical activity.

# What are common metrics of Physical Activity?

Steps/day is one of the commonly employed measures of PA. There is a high level of face validity, as taking a step is readily apparent, and both consumer- and research-grade monitors can produce this metric. The most standardized measure of energy expenditure is quantified using a Metabolic Equivalent or MET. The MET represents the ratio of energy expended for a given activity relative to resting. The resting value of 1.0 MET represents 3.5 ml of oxygen consumed per kilogram of body weight per minute.(9)

Another classification of energy expenditure is using the terms light, moderate, and vigorous intensity. Time spent in moderate intensity activity has strong ties to positive health outcomes(10). Light intensity is considered METs between 1.5 and < 3.0. Moderate intensity refers to energy expenditure >between 3.0 and 6.0 METs, and Vigorous intensity is > 6.0 METs. In order to improve interpretation of energy expenditure corresponding with daily life activities, Dr. Barbara Ainsworth and colleagues created a compendium of common daily physical activities and their associated MET values(11) and made this available online. Example activities from the compendium of common daily physical activities and associated MET values are listed in the table.

The current PA guidelines from the Department of Health and Human Services from the United States recommends all adults spent at least 150 minutes/week in moderate-to-vigorous intensity PA.(10) The term 'inactivity' technically applies to those who do not meet this guideline(12) which includes a wide range of those who participate anywhere from 1 minute/week to 149 minutes/week. Perhaps more important is to consider that inactivity is distinctly different than sedentary behaviors. Sedentary behaviors have received more attention in the past few years, e.g., the phrase 'sitting is the new smoking', although the literal interpretation of this phrase has been debunked.(13) Sedentary behaviors are defined as < 1.5 METs while sitting or reclining during waking hours.(14)

## Why is Physical Activity Important for OA?

The benefits of PA mitigate many disease specific symptoms such as functional limitation, in addition to providing general health benefits relevant to adults with OA, such as improved sleep, mood, muscular strength, and less risk of mortality. Studies show that supervised strengthening exercises and aerobic walking, especially when combined with weight loss, lessen pain and improve physical function(15). We previously found from observational studies that greater PA, i.e., taking more steps/day, is related to less risk of developing functional limitation among adults with (or at risk for) knee OA.(16,17) In particular, our group found approximately 6,000 steps/day best discriminated between those who did and did not develop functional limitation, e.g., difficulty with getting up from a chair or out of bed over two years(16). Even light intensity PA, which includes activities such as gardening and taking a slow walk, prevents the development of functional limitation for adults with knee OA.(17)

These disease-specific findings extend what is already known about the benefits of PA from the general population. That is, there is strong evidence that regular PA has a wide range of health benefits from reduced blood pressure to improved sleep and mood.(10)

The benefits of PA increase with age; that is, older adults who are physically active can mitigate losses in muscular strength(18), and improve physical function(19) and participation in important daily life activities.(20) They can move better, have less risk of falls, and are better able to live independently compared with their inactive counterparts(21). For example, using data from 16,741 women with a mean age of 72 years, Dr. I-Min Lee and colleagues reported those who took approximately 4,400 steps/day had significantly lower risk for all-cause mortality compared with those who took < 2,700 steps/day. Moreover, further reductions in mortality were observed up to 7,500 steps/day.(22)

Lastly, current evidence suggests sedentary behaviors have negative effects on all-cause mortality and cardiovascular disease,(10) though it remains unclear if these effects are truly independent of the positive effects of PA as some literature reports a relationship,(23) while others do not.(24) One of the first published studies in 2012 showed a relation between sitting and mortality, following 222,497 adults > 45 years of age from Australia with a mean follow up time of 2.8 years, finding a dose-response relationship between sitting time and risk of all-cause mortality within physical activity strata. Namely within strata of moderate-to-vigorous intensity PA measured by questionnaire ranging from 0 to > 300 minutes/week, those with greater time spent sitting had higher mortality compared to those with less sitting.(23) In contrast, a more recent systematic review of over 1,000,000 adults from 16 studies found that daily sitting time was not associated with all-cause mortality for those who were active.(24)

# What is the intersection of PA with Obesity in OA?

Obesity has strong ties as a risk factor for OA, which can be modified by PA. Previous studies have examined the association of obesity with PA, and found a strong graded relation between increasing BMI and less PA. For example, our group has found increasing BMI to be associated with fewer steps/day in a large cross-sectional study using data from the Multicenter Osteoarthritis (MOST) study.(25) A similar relationship has been observed using data from the Osteoarthritis Initiative (OAI).(26) These findings support the notion that adults with knee OA who are obese tend to be less active on average. Studies show that exercise-only intervention do reduce weight, but this effect is modest and diet specific interventions are recommended to better target weight loss.(27) Weight Loss is important for adults with knee OA, as previous studies have shown the best improvements in clinical outcomes of pain and physical function were in those who receive both exercise and diet interventions, rather than exercise alone.(15,28) Research does not suggest, however, that exercises need to be non-weightbearing for people who are obese. A recent trial comparing weight bearing versus non-weight bearing exercises in adults with knee OA who were obese found no

differences in pain and physical function, though there were fewer adverse events in the weight bearing group.(29) It is noteworthy that while obesity is a risk factor for the development of knee OA, literature to date shows that participating in exercise interventions and greater PA is not at all linked to faster progression of OA. This is discussed in more detail in the next section.

# What is the relation of PA with the development of knee OA?

Data from studies that investigate recreational PA, i.e., activity occurring outside of work, does not support the common general public view that OA is the consequence of "wear and tear", i.e., overuse of the joint, and that further use only worsens existing damage.(30) While there are some studies that indicate high levels of PA are associated with structural damage of the knee, it is unclear if such structural damage actually leads to OA, and most studies do not support the finding that PA leads to OA.(31)

Data from studies have investigated the relation of walking and running with the development of knee OA. In short, there is no evidence that walking or recreational running increases the risk of developing radiographic OA, knee pain, or symptomatic knee OA. For walking, Felson and colleagues reported that adults who were normal weight to overweight and reported walking at least 9 miles/week (i.e., about 180 minutes/week, which satisfies many guidelines for physical activity) did not have increased risk of joint space loss or incident knee OA over a 9-year period.(32) Also, data from large observational cohorts that used monitors to measure walking reported that adults with mild to moderate knee OA could walk at least 10,000 steps/day without increased risk of structural worsening over 2 years.(33,34) For running, evidence from systematic reviews and meta analyses does not point to recreational running increasing the risk for knee OA, but rather the opposite. For example, a meta analysis including 17 studies with over 110,000 study participants found those who ran for recreation had less risk of knee OA than non-runners.(35) For elite runners, the risk of OA may be not be increased compared to non-runners, though this may hold true for those who are uninjured.(36) For making clinical decisions, we highlight a narrative review that poses specific recommendations for patients who are runners versus those who are not running.(37) This review recommended those who were already runners should be encouraged to continue running while taking measures to prevent injury, while nonrunners should be encouraged to engage in walking. These are important messages for patients since walking is the most common type of physical activity employed for exercise in adults, (38) and exercise highly recommended for the treatment for knee OA.(39)

For participation in physical activity other than walking or running, a recent review concluded that recreational sport was not consistently related to the progression of radiographic or symptomatic knee OA.(40) This is in contrast to elite-level soccer, powerlifting, wrestling, and recreational American football, which may be associated with knee OA from a recent systematic review.(41) The relationship between these sports and knee OA is challenging to study, however, due to the confounding effect of traumatic injury and its association with knee OA.(42) Nevertheless, clinicians should continue to recommend physical activity and exercise to their patients with knee OA, with emphasis on those activities that are at a recreational level.

For occupational PA, specific work-related tasks appear to influence the risk of symptoms and disease incidence. Namely, there seems to be a positive relationship between the frequency of knee bending with knee pain, especially when combined with heavy lifting. A meta-analysis of 66 studies found adults who had jobs with frequent knee bending were 61% more likely to have knee pain compared to those with more sedentary jobs,(43) and another study reported that combining heavy lifting with kneeling increased risk for knee pain by 1.8 to 7.9 times.(44) More recently, Lo and colleagues reported that walking while working with materials increases the OA risk of incidence by 90% compared with those who primarily sit during work.(45) It is important to note that PA was measured using questionnaires in all of these studies. As well, there is a possibility that previous knee injury could moderate the relation of knee bending with knee OA, which further supports the need to prevent knee injury as much as possible in occupational settings.

At present, there is no conceptual model of how PA contributes to OA in terms of negative changes in structure and symptoms including pain and functional limitation. There is a possibility of a 'U' shape relationship between loading and the development of knee OA, whereby underloading in addition to overloading is detrimental to knee health. This is based on the notion that knee cartilage requires a minimum amount of load to remain healthy,(46) and that low levels of physical activity are common in adults with knee OA. We recently reported on preliminary evidence of the relation of underloading, characterized by low steps/day, with worsening cartilage damage.(47) However, little is known about the relationship between low levels of physical activity, i.e., underloading, and the development of knee OA, as most studies have focused on high-intensity activities.(48,49)

In sum, these findings support the notion that frequent local loading contributes to the development of knee pain.(50) Namely, certain occupational tasks, including repeated knee bending and carrying heavy materials appear to result in enough excessive loading to increase the risk of developing knee OA and pain. However, the loading that

occurs from recreational activities appears to be below that which leads to the development of knee OA and symptoms.

Why is inactivity so prevalent in OA, and how to encourage taking MORE steps in the right direction

Physical activity promotion is paramount for adults with knee OA. This is because many with knee OA are in a vicious cycle of pain and inactivity leading to decreased strength and mobility, which then lead to more pain and inactivity. However, the 'causes' of inactivity are not so straightforward as PA is a behavior that relies not only on physical capacity, but also a complex array of psychological factors such as self-efficacy,(51) positive affect,(52) and motivation(53) to name a few. Encouraging small increases in physical activity, e.g., taking more steps/day can help facilitate an exit from this cycle or prevent it from starting. Accomplishing this can take on many forms. For example, a recent Editorial by Li and colleagues(54) highlighted how the Canadian 24-hour movement guidelines attempt to help increase activity by specifying types of low intensity or sedentary activities that should be replaced with higher intensity activities, e.g., walking.(55) Another approach we have highlighted is to simply make a goal of walking for at least 10 minutes/day, everyday, as this duration of activity is associated with health benefits for adults with osteoarthritis.(56) Regardless of the approach, the message to be active from health professionals is important.

Next Steps: What is not known about PA and knee OA

Moving forward, there are many areas of need within the fields of rehabilitation-, OA-, and PA-research. First and perhaps most importantly, there is great need to develop effective interventions that specifically target and promote PA for adults with OA. We previously found less than 10% of adults with knee OA meet recommended levels of PA,(57) i.e. 150 min/week of moderate intensity.(10) While previous studies have shown that wearable monitors are an effective strategy to increase PA in the general population,(58) to date there are no effective strategies to increase PA in adults with knee OA. Even total knee replacement, the definitive treatment for knee OA does not increase PA!(59)

Second, little is known about changes in PA following common interventions for OA. The absence of PA measures in the context of clinical trials is particularly problematic for adults with OA. Any change in PA following intervention is missed, which is unfortunate since sedentary behaviors are common in this patient population(60). As well, positive changes in PA may be masked in trials reporting no changes in pain. For instance, participants may in fact become more active after an intervention due to a

reduction in pain and as a consequence increase their walking or PA. However, because of the increased activity their knee pain may remain unchanged from baseline values. Lastly, those who already regularly exercise may respond differently to an intervention than those who are inactive due to additive or synergistic effects of exercise not being known. Thus, there is a need to better investigate changes in and the additive effects of PA in clinical intervention studies for knee OA.

### Conclusion

PA is an important health outcome for adults with OA. The measurement of PA has evolved to include affordable consumer grade monitors, which can be used to capture estimates of walking, i.e., steps/day. As well, research-grade monitors provide reliable and valid estimates of steps/day and time at different intensities of physical activity. Overall, there is an unclear relationship between PA and the development of OA. In the workplace, excessive loading appears related to the presence of knee pain, however the relation of recreational PA with the development of knee OA is not established and may not exist. Regardless, the benefits of PA for the symptoms of OA including pain and physical function are well established. There remains an important public health need to develop, test, and refine interventions to increase PA in adults with OA.

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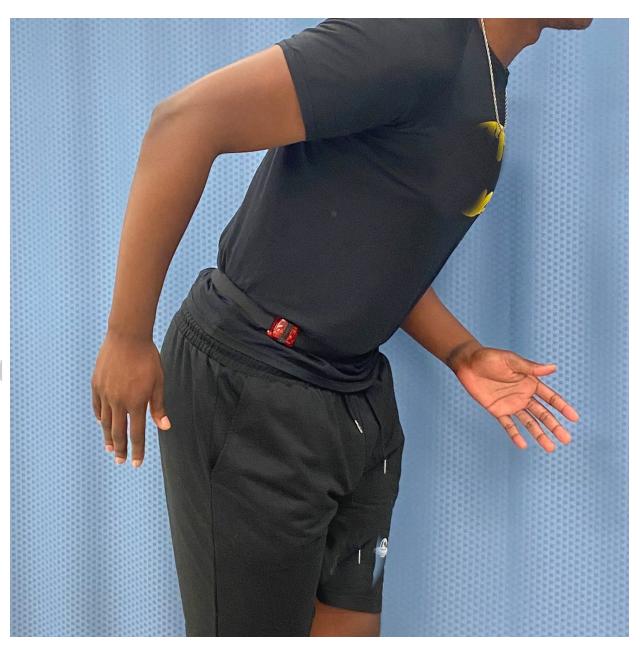
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Daily Activity	MET Value	Intensity of Physical Activity
Sitting watching TV	1.3	Sedentary
Walking around the house	2.0	Light Intensity
Mowing the lawn while walking with a power mower	5.0	Moderate Intensity
Shoveling Snow by hand	6.0	Vigorous Intensity