

# **Associating Knee Osteoarthritis with Fall Risk: Implications for Interventions**

BY

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THESIS

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This thesis is dedicated to the love of my life, Jeffrey. Thank you for being my voice of reason,  
my best friend, and my supplier of endless encouragement.

This thesis is also dedicated to my grandmother, Lois Plotts. Thank you for showing me how to  
fight and how to always appreciate the happiness in life. Keep fighting.

GOD IS WITH HER. SHE WILL NOT FALL.

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## LIST OF ABBREVIATIONS

OA	Osteoarthritis
MTC	Minimum toe clearance
CDC	Centers for Disease Control
RR	Relative risk
CI	Confidence interval
<i>OR</i>	Odds ratio
<i>ACR</i>	American College of Rheumatology
<i>aOR</i>	Adjusted odds ratio
<i>HR</i>	Hazard ratio
IQR	Interquartile range
VAS	Visual Analog Scale
BMI	Body Mass Index

## SUMMARY

The purposes of this dissertation research, which focused on trip-related falls, were to identify the biomechanical risk factors that may be responsible for the increased fall risk of people with knee OA, and to establish if people with knee OA would benefit from an intervention that specifically targets the ability to perform recovery stepping responses. The first investigation showed that women with knee OA are at a notably, and clinically meaningfully, increased risk for trip-related falls compared to women without knee OA. As trips are the primary cause of falls for older adults, this finding stresses the need to determine if the modifiable biomechanical causes of falls for those with and without knee OA are similar.

A trip-related fall is the result of two sequential, mostly independent events: (1) a loss of dynamic stability (e.g. a trip over an uneven surface), followed by (2) an insufficient recovery stepping response that fails to restore dynamic stability. The probability of the first event occurring increases for adults who display a low toe clearance during gait. The results from the first investigation showed no differences in minimum toe clearance (MTC) between people with and without knee OA. This finding suggests that trip-related falls occurring by individuals with knee OA may be due to inadequate recovery stepping responses.

Prior to this dissertation, recovery stepping responses following trips had not been assessed for individuals with knee OA. The second investigation subjected women with and without knee OA to two types of large postural perturbations – a laboratory-induced trip and a treadmill-delivered perturbation that simulates a trip. While the women with knee OA did not have higher fall rates following either type of perturbation, when compared to the control group they displayed impaired recovery kinematics related to control of the trunk. These trunk

## SUMMARY (continued)

kinematics have previously been established for healthy middle aged and older adults as variables that distinguish fallers from non-fallers following laboratory-induced trips and treadmill-delivered disturbances that simulate a trip. Furthermore, trunk kinematics are modifiable using task-specific perturbation training where individuals practice the motor skills required to avoid a fall by being exposed to repeated postural perturbations requiring a step(s) to avoid a fall. These findings suggests that task-specific perturbation training, which have previously shown to prospectively decrease trip-related falls by 50%, could be extended to reduce fall risk in people with OA.

The third investigation was successful in showing that task-specific perturbation training is effective and can improve kinematics related to the recovery stepping response in women with knee OA. During the one-session training protocol, women were subjected to large, treadmill-delivered postural perturbations; a large pre-training perturbation, 20 smaller “training” perturbations, and then a final post-training perturbation that was identical to the pre-training perturbation. The training allowed women to practice the actual motor skill of avoiding a fall following a simulated trip. Both the OA and the control group demonstrated improvements in recovery kinematics related to the trunk from pre- to post-training. In addition, the skill of successful recovery from a large perturbation was acquired in less than 10 trials for both groups. Following the point at which the recovery task was assumed to have been acquired (i.e. when performance plateaued) there were no significant differences in the variability of the recovery response between groups. The similarity in performance suggests that women with knee OA can improve performance following large postural disturbances simulating a trip to the same extent

## **SUMMARY (continued)**

as otherwise healthy middle aged and older adults. These results support the utility of using task-specific training as a means to address the increased fall risk in people with OA.

These three investigations contribute to the existing falls literature as they are preliminary findings extending work that has been previously conducted using healthy older adults to those who appear to be at high fall risk – adults with knee OA. Beginning to understand the mechanisms underlying the increased fall risk reported by those with OA can guide future research and clinical practice regarding how to best address this increased risk. This dissertation supports the utility of implementing task-specific perturbation training as a fall prevention intervention in people with knee OA. This could result in significant reductions in the number of falls, fall-related injuries, medical care costs, and subsequently, could improve the quality of life of people with knee OA.

# 1 Introduction

## 1.1 Significance

Falls by older adults are a leading public health problem, with one out of every three older adults reporting a fall in the last year (1). Falls are associated with mortality, disability, decreased independence, early admission to nursing homes (2) and, in 2012 were associated with \$30 billion in direct medical care costs (1). These economic and clinical consequences of falls stress the need for effective strategies that are cost-conscious and easy to implement to reduce their occurrences. A growing body of literature suggests that people with osteoarthritis (OA) are at approximately 25% greater risk of falls compared to their age-matched counterparts without OA, and of greater concern, are at 20% increased risk of fracture (3). Unfortunately, the underlying mechanisms of the increased fall and fracture risk reported in this population are currently unknown and strategies to prevent falls are currently not a part of disease management for individuals with knee OA. As arthritis is an age-related disease, the continued aging of our population has driven a significant increase in the number of people with OA (4). This results in a greater absolute number of falls and fall-related injuries. In light of this, there is a need to identify modifiable and causal risk factors for falls, and to determine whether adults with OA fall for the same biomechanical reasons as otherwise healthy adults. This would lead to opportunities to develop, or improve upon, existing interventions to reduce the absolute number of falls. The work done for this dissertation is significant as it is the first to explore and identify biomechanical mechanisms which may increase fall risk for people with knee OA. These findings will further extend the understanding of strategies that can be used to reduce fall risk in older adults in general.

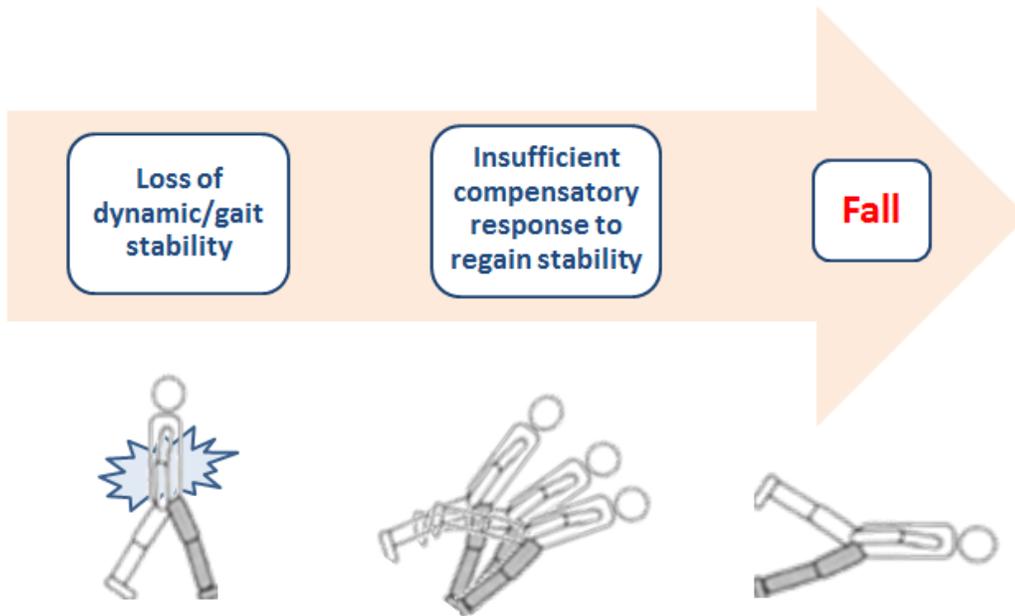
## 1.2 **Background**

### 1.2.1 **Falls by older adults**

The 33% of older adults (age 65 and older) reporting a fall in the last year has increased from 28% in 1981 (5). This suggests that efforts to reduce the number of falls have not been successful. Moreover, the rate of injurious falls by adults over age 65 increased 2.4% per year from 2001-2009 (1) suggesting not only that older adults are falling more often, but that the consequences of the falls have become more serious. Indeed, 20-30% of falls results in moderate to severe injuries, which can directly result in disability and reduced quality of life, and consequently can increase mortality risk (2). Older adults are also five times more likely to be hospitalized for injuries due to falls than for injuries from other causes (6). The economic costs of falls on the healthcare system are particularly worrisome. In 2020, the direct medical-care costs of falls are expected to reach US\$67 billion (7), up from just US\$19 billion in 2006 (8). Unfortunately, the number of falls and the associated injuries and costs will only continue to increase due to the growing number of older adults, predicted to double by 2030 to a total of 70 million (9). Reducing the occurrences of falls, and particularly, reducing injurious falls is an essential and complex undertaking for biomedical and gerontological researchers. In fact, Healthy People 2020 (10) declared one of its targets to reduce emergency room visits due to falls by older adults by 10%. If in 2010, there was over US\$20 billion spent in medical care costs for falls resulting in emergency room visits (11), then a 10% decrease in the number of falls resulting in emergency room visits could result in lives saved and nearly \$2 billion saved in US health care costs.

### 1.2.2. **Biomechanical factors related to falls**

Falls that occur during locomotion are the most common type of falls reported in community-dwelling older adults (12). Specifically, trips and slips are amongst the most common causes of falls, making up 39-77% of falls by older adults (12-15). Trips and slips are typically due to external disturbances (e.g. icy or uneven surfaces) and require some type of compensatory response following the disturbance to maintain upright stability. Conceptually, a fall can be considered a result of two sequential events: (1) a loss of dynamic stability followed by (2) an insufficient recovery response that fails to restore dynamic stability (Figure 1). These two events are independent, in that the risk of becoming unstable from either an internal or external disturbance is not related to the ability to restore stability and avoid a fall (16). This stresses the need to assess both events separately when determining an individual's fall risk.



**Figure 1.** Schematic depicting the sequence of events leading to fall. The first event, a loss of dynamic stability (e.g. a trip over an uneven surface) followed by the second event, an insufficient recovery response that fails to restore dynamic stability (e.g. a recovery step that fails to re-establish stability).

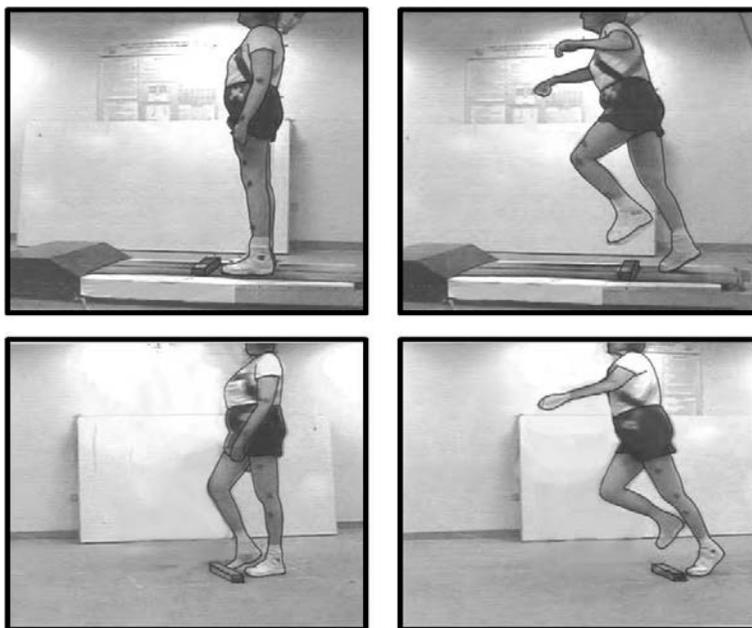
Following a loss of dynamic stability, a fall will only occur if a compensatory response is unsuccessful. Depending on the nature of the instability (e.g. a trip, slip, limb buckle, syncope etc.) and the environment (e.g. handrails available, other hazards close by, etc.), there are various compensatory responses that could be utilized. Most common are the postural (no step) response, a grasping reaction (reaching to grasp on to a nearby handrail or wall), and a stepping response (17). As most falls by older adults occur during locomotion, this dissertation will focus on stepping responses, which are commonly utilized following trips. Following a trip while walking

in the forward direction, the body rotates in the same direction as the walk, with the stance foot serving as the “global” axis of rotation. In this situation, an anteriorly-directed step(s) is required to restore dynamic stability. Following a trip, the ability to arrest and reverse trunk flexion (i.e. go from a trunk flexion velocity to a trunk extension velocity) is a determinant of a fall following laboratory-induced trips (18, 19) as it acts to decelerate the forward falling body and aid in successful recovery. Indeed, trunk flexion velocity and trunk flexion angle at recovery step completion (the instant the recovery foot makes contact with the ground) are two kinematics which have been shown to discriminate those who fell following a laboratory-induced trip from those who successfully recovered (19). Performing a recovery step having sufficient length also distinguished (during-step) fallers from non-fallers as it assists in establishing a stable base for the upcoming step(s) (19) (Figure 2).

While laboratory-induced trips have a strong ecological validity as they closely represent what a trip looks like in the community, treadmill-delivered perturbations can be used to mimic laboratory-induced trips (20) and offer a number of advantages over that of laboratory-induced trips. Treadmill-delivered perturbations may be delivered by accelerating the treadmill belt(s) without warning, as subjects stand (or walk) on a treadmill. This type of perturbation results in recovery kinematics similar to those following laboratory-induced trips (20) (Figure 3). Further, the same recovery kinematics that discriminate fallers from non-fallers have been identified for both the laboratory-induced trip and the treadmill-delivered perturbation (20). An additional benefit to using treadmill-delivered perturbations is that they can be administered repeatedly and in varying magnitudes. Thus, these perturbations can be used by populations of varying fall-risk, and can be utilized for training purposes (described in the later sections).



**Figure 2.** Schematic showing general kinematic differences between a faller and non-faller following a laboratory-induced trip. The top panel represents an individual able to successfully recovery from the trip (i.e. non-faller). The bottom panel represents an individual who did not perform a successful recovery step (i.e. faller). Note that in the non-faller, the trunk angle is less than that of the faller at recovery step completion (right-hand images). Further, the non-faller exhibits a trunk extension velocity at recovery step completion (arrow in the counterclockwise direction) compared to the faller exhibiting a trunk flexion velocity (clockwise arrow) in the bottom figure. Finally, note that the non-faller has a longer step length compared to the faller. These three kinematics (trunk angular velocity, trunk flexion angle, and step length) at recovery step completion have consistently discriminated fallers from non-fallers following laboratory-induced and treadmill-delivered trips (19, 20). (Figure from Pavol et al., 2001 (19)).



**Figure 3.** Similarities between a laboratory-induced trip and a treadmill-delivered perturbation. Images on the left-hand side show the individual prior to the perturbation. Note the similarities in the trunk angle. The right-hand images show the kinematics induced by the perturbation. Note the similarities in recovery kinematics, primarily trunk angle, during both recovery responses. These similarities support the utility of using a treadmill-delivered perturbation as a surrogate for a laboratory-induced trip.

### 1.2.3 Falls by adults with Osteoarthritis

Individuals with arthritis, in general, have a 2.5-times greater fall risk than that of age-matched, otherwise healthy controls according to a recent meta-analysis based on sixteen prospective studies (21). In agreement with this finding, the Centers for Disease Control and Prevention (CDC) recently reported on nearly 350,000 older adults with self-reported arthritis from around the US, who were 2.5 times more likely experience multiple falls than those without

arthritis, and are also at a 2.5-times increased risk for fall-related injuries (22). Consequently, the CDC has stressed that clinicians should be aware of the link between arthritis and falls and that disease management should evaluate and address the increased risk (22).

While the above mentioned studies suggest that arthritis is a significant risk factor for falls, there are many different forms of arthritis, (i.e. rheumatoid arthritis, osteoarthritis, gout, lupus, etc.), and a number of different joints that can be affected (i.e. fingers, knees, hips, spine, etc.). Unfortunately, information on the type of arthritis and the joints involved were not provided/available in the above-mentioned studies (21, 22). Recently, more studies have focused specifically on osteoarthritis (OA) and particularly, OA of the lower extremity (TABLE 1). Collectively, these studies support the notion that these individuals are at an increased risk for falls and fall-related injuries compared to their otherwise healthy counterparts. Of note, a large prospective multi-center study of over 50,000 post-menopausal women (40% of whom self-reported OA) showed that those with OA were at 1.25 and 1.2 times greater fall risk and risk for fracture, respectively (3). This increased risk remained significant even after adjusting for multiple confounders, including age, body mass index (BMI), medication use, region of origin, and other comorbidities. However, this study had three limitations: (1) women were not asked to specify which joint was affected, (2) OA was self-reported rather than physician/radiographically diagnosed at baseline, and (3) although the study was prospective in nature, falls were assessed retrospectively each year – leaving room for recall bias. The third limitation regarding the tracking of falls is a common, and challenging, issue for many studies examining fall risk in older adults. Although time and labor intensive, calendars which are filled out daily by participants on whether or not a fall occurred (and then mailed to study personnel monthly) have shown to be the most accurate, and preferred method for prospective fall tracking (23).

This dissertation will focus on OA of the knee as the knee is the most commonly affected weight bearing joint for OA, with radiographic knee OA and symptomatic radiographic knee OA affecting 37.4% and 12.1% of Americans over age 60, respectively (24). Following a review of the literature, only two studies were found considering the influence of physician-diagnosed knee OA (diagnosis occurring at study baseline by a study physician) on prospectively measured falls. These studies reported anywhere from a 1.3-2.7-times increased fall risk for those diagnosed with knee OA compared to a control group (25, 26). In fact, one of these two studies (26) had an especially strong study design, using daily fall calendars (the “gold standard”) to track falls. With the increasing obesity levels and general aging of the US population, the number of individuals with knee OA, as well as the absolute number of falls and fall-related injuries is only expected to increase. In light of this, determining the underlying mechanisms for the increased fall risk reported in people with knee OA is warranted, as this will assist in determining the best strategy for decreasing their fall risk.

**TABLE I. SUMMARY OF STUDIES OF FALLS AND FRACTURE RISK FOR PEOPLE WITH VARIOUS FORMS OF ARTHRITIS <sup>a</sup>**

Reference	Subjects	Arthritis Diagnosis	Fall/fracture assessment	Findings <sup>b</sup>	Summary: Do results support OA as increased fall/fracture risk?
<i>Prospective Study Design</i>					
Campbell et al., 1989 (25)	761 men and women $\geq 70$ yrs	Physician exam for knee arthritis	One-year prospective monitoring (monthly phone call)	Knee arthritis was significantly associated with future falls for men and women (women: RR=1.8, CI=1.1-2.8, men: RR=2.7, CI=1.3-5.3)	Yes - knee arthritis increases future fall risk is associated with future falls
Arden et al., 1999 (27)	5,552 women $\geq 65$ yrs	Self-reported OA; radiographic hip OA	One-year prospective monitoring for falls and fracture (phone call every 4 months)	OA increased risk of falls (RR=1.4, CI=1.2-1.5); radiographic hip OA did not increase fall risk (RR=0.70, CI=0.5-0.95). OA did not increase risk of fracture.	Yes - self-reported OA increases fall risk, but not fracture risk
Bergink et al., 2003 (28)	2,773 men and women $> 55$ yrs	Radiographic knee OA	Prospective monitoring of fracture over 5.7 yrs (yearly followup)	Knee OA increased risk of vertebral (OR=2.0, CI=1.1-3.4) and non-vertebral fractures (OR=1.5, CI=1.1-2.0)	Yes - knee OA increased risk for fracture
Kelsey et al., 2010 (26)	765 men and women $\geq 70$ yrs	Physician exam for knee OA (ACR criteria)	One-year prospective monitoring (daily calendars)	Knee OA increased risk of falls (RR=1.30, CI=1.03-1.62)	Yes - knee OA increases fall risk

TABLE I (continued)

Reference	Subjects	Arthritis Diagnosis	Fall/fracture assessment	Findings <sup>b</sup>	Summary
<i>Case Control Study Design (fallers vs. non-fallers)</i>					
Granek et al., 1987 (29)	446 men and women $\geq 65$ yrs housed in long-term care facility	OA from medical records (not site specific)	Fall incident reports	OA increased risk of falls (OR=2.3, $p=0.0003$ )	Yes - OA at increased fall risk
<i>Retrospective Study Design</i>					
Blake et al., 1988 (14)	1,042 men and women $>65$ yrs	Self-reported arthritis or "rheumatism" (not specific type or site)	One-year fall history	Arthritis one of four variables to significantly discriminate fallers from non-fallers	Yes - arthritis discriminates fallers from non-fallers
Nevitt et al., 1989 (30)	325 men and women $\geq 60$ yrs with fall history	Self-reported arthritis (not specific type or site)	One-year fall history	Arthritis increased risk of multiple falls (aOR=2.7, CI=1.3-5.6)	Yes - arthritis increases fall risk
Sturneiks et al., 2004 (31)	684 men and women $\geq 75$ yrs	Self-reported lower extremity OA	One-year fall and injurious fall history	OA increase risk for falls (RR=1.22, CI=1.03-1.46) and injurious falls (RR=1.27, CI=1.01-1.60)	Yes - lower extremity OA increases risk of fall and fracture
Arden et al., 2006 (32)	6,641 men and women $\geq 75$ yrs	Self-reported knee pain and/or OA	6-month fall and fall-related fracture history over 6 semi-annual interviews	Knee pain increased risk of falls (HR=1.26; CI=1.17-1.36) and fractures (HR=1.20; CI=1.18-3.37); OA did not increase fall risk (HR=1.12; CI=0.97-2.88) but did increase risk of fracture (HR=1.61, CI=1.09-2.36)	Equivocal - knee pain increases risk of falls and fracture; self-reported OA increases risk of fracture

TABLE I (continued)

Reference	Subjects	Arthritis Diagnosis	Fall/fracture assessment	Findings <sup>b</sup>	Summary
<i>Retrospective Study Design (continued)</i>					
Levinger et al., 2011 (33)	35 patients pre-TKR and 27 control	Clinical diagnosis of knee OA	One-year fall history	OA may increase risk for falls (48% report falls in OA group; 30% report falls in control group (not significantly different)	Equivocal – OA had increased risk for falls (although, was not significant)
Muraki et al., 2011 (34)	1,657 men and women	Radiographic knee OA; self-reported knee OA	One-year fall history	Women with knee pain had increased risk for multiple falls (aOR=1.87, CI=1.06-3.28); Radiographic knee OA did not increase fall risk (aOR=1.31, CI=0.70-2.43)	Equivocal - knee pain, but not radiographic knee OA, increased fall risk
Prieto-Alahambra et al., 2013 (3)	51,386 women ≥55yrs	Self-reported OA (not specific site)	One-year fall and fracture history	OA had increased risk of falls (aOR=1.24, CI=1.22-1.26) and fractures (aOR=1.21, CI=1.13-1.30)	Yes - OA increased risk for falls and fractures
Dore et al., 2014 (35)	1,619 men and women	Radiographic symptomatic knee OA	One year fall history	Symptomatic knee and hip OA increased risk for falls (Knee: aOR=1.39, CI=1.02-1.88; Hip; aOR=1.60, CI=1.14-2.24)	Yes- knee OA at increased risk for falls
Barbour et al., 2014 (22)	338,734 women ≥45yrs	Self-reported arthritis (not specific type or site)	One-year fall history	Arthritis increased risk of multiple falls and fall-related injuries (significant)	Yes – arthritis significantly increases fall and fall-injury risk

<sup>a</sup> Top section includes studies with prospective designs, followed by case-control (fallers vs. non-fallers) and retrospective designs. Studies were identified by searching using the search terms “arthritis” and “falls” in PubMed and Google Scholar and then evaluating

and including studies that compared fall risk of people with 'arthritis' and/or 'joint pain' to a control group. Studies that only reported fall rates in an arthritis group without comparison to a control group were excluded. This was not a systematic review.

<sup>b</sup> Each section is ordered chronologically from least to most recent. Risk, when provided, was presented as odds ratio (OR), adjusted odds ratio (aOR), risk ratio (RR) or hazard ratio (HR) with 95% confidence interval, when reported (CI).

### 1.2.3.1. Risk factors for falls by adults with OA

While the evidence showing OA to be a significant risk factor for falls continues to accumulate, the mechanisms underlying the increased risk are largely unknown. Several established, general risk factors for falls by older adults include decreased muscle strength, impaired gait, and impaired postural stability (21). Other risk factors for falls by older adults include the use of sedatives, cognitive impairments, lower-extremity disability, pain, obesity, and foot problems (36-38), all of which are likely more prevalent in a clinical populations as compared to community-dwelling older adults (39). Indeed, many of these risk factors are commonly manifested in people with knee OA. Thus, knee OA may not be an *independent* risk factor for falls, but rather, OA may interact with other risk factors such that the cumulative effect amplifies, or exacerbates, the risk of falling (40). Indeed, fall risk scales linearly with the number of risk factors present, with those displaying four or more risk factors having a risk of falling in the next year as high as 78% (36).

As mentioned previously, a fall during gait is the result of two sequential, independent events; (1) a loss of dynamic stability and (2) an insufficient recovery response that fails to restore dynamic stability. Many characteristics and symptoms associated with knee OA – primarily, gait and balance impairments, strength deficits, pain levels, and high obesity rates – could affect one or both of these events, increasing the risk of an impending fall (40) (TABLE II). Consequently, while any factor that negatively affects one, or both, of these events could help explain the increased fall risk seen in this population, those which effect the latter event (the recovery response) are potentially of greater impact as a failed recovery response will certainly result in a fall. Identifying those factors which impair the recovery response, specifically the recovery stepping response, could provide a potential target for fall prevention interventions.

**TABLE II. RISK FACTORS FOR FALLS, HOW THEY MANIFEST IN PEOPLE WITH LOWER EXTREMITY OA AND HOW THEY COULD IMPAIR STABILITY, THE RECOVERY STEPPING RESPONSE, OR BOTH. <sup>a</sup>**

<b>Fall risk factors <sup>b</sup></b>	<b>How variable is manifested in OA</b>	<b>Could this risk factor increase the likelihood of an individual becoming unstable? <sup>c</sup></b> <i>How?</i>	<b>Could this further impair the recovery stepping response?</b> <i>How?</i>
Gait impairments	Slower walking velocity, shorter stride length, wider step width, longer double support time (41-44)	<b>No known evidence</b> <i>Although the extent to which changes in gait are associated with, or cause falls, is not clear, certain gait parameters could theoretically cause someone to lose balance during gait</i>	<b>No known evidence</b> <i>There is no evidence, and no obvious mechanism, supporting the notion that impaired gait kinematics could affect the recovery stepping response</i>
Balance impairments	Larger static/dynamic postural sway (45-47)	<b>Yes</b> <i>An increase in postural sway infers that for a given perturbation, there is an increase in the likelihood of the individual becoming unstable because their center of mass will be closer to the limits of their base of support</i>	<b>No</b> <i>Measures of static and dynamic stability are not been related to the ability to recover from postural disturbances (16)</i>
Muscle weakness	Weaker knee extensors and hip abductors, as well as increased knee instability, associated with knee buckling (44, 47-49)	<b>Yes</b> <i>Poor balance has been associated with lower extremity muscle weakness and knee buckling (49)</i>	<b>Yes</b> <i>A recovery stepping response requires large muscle strength and power requirements to avoid a fall (50)</i>

TABLE II (continued)

Fall risk factors <sup>b</sup>	How variable is manifested in OA	Could this risk factor increase the likelihood of an individual becoming unstable? <sup>c</sup> <i>How?</i>	Could this further impair the recovery stepping response? <i>How?</i>
Pain	Primary symptom of OA (51)	<b>Correlational relationship</b> <i>Although there is no direct relationship, pain is related to increased postural sway (see balance impairments above)(52)</i>	<b>No known evidence</b> <i>Although there is no current evidence that individuals experiencing pain have impairments in their recovery responses, it is certainly plausible to believe that pain, or the anticipation of pain, could cause negative changes to the recovery stepping response(40)</i>
Proprioceptive deficits	Decreased feedback on lower limb position and orientation (47, 53-55)	<b>Correlational relationship</b> <i>Although there is no direct relationship, decreased proprioception is related to increased postural sway (see balance impairments above)(56)</i>	<b>No know evidence</b> <i>Although there is no evidence that poor proprioception could cause deficits in the recovery response, it is plausible that delayed or absent afferent information about an external perturbation could influence the compensatory response</i>
Gait Variability	Greater variation in step length, step width, and double support time (57)	<b>No known evidence</b> <i>Although gait variability has been linked to falls, the mechanisms are unclear (58)</i>	<b>No known evidence</b> <i>There is no known evidence that increased gait variability effects stepping response. However, if gait variability reflects underlying motor control issues, there could be a relationship - this, however, this has not been studied.</i>

TABLE II (continued)

Fall risk factors <sup>b</sup>	How variable is manifested in OA	Could this risk factor increase the likelihood of an individual becoming unstable? <sup>c</sup> <i>How?</i>	Could this further impair the recovery stepping response? <i>How?</i>
Obesity	Most modifiable risk factor for OA	<b>Correlational relationship</b> <i>Although there is no direct relationship, obesity is related to increased postural sway (see balance impairments above)(59)</i>	<b>Yes</b> <i>Obese individuals have impaired recovery responses following trips compared to their normal weight counterparts (60)</i>

<sup>a</sup> Table adapted from Hoops et al., 2012 (40)

<sup>b</sup> Risk factors selected are those discussed in Hoops et al., 2012 (40)

<sup>c</sup> Stability can refer to either static or dynamic/gait stability. Static postural stability is a condition defined by a person's center of mass being within the boundaries of the base of support and is commonly measured by assessing ones "postural sway" during quiet standing. Dynamic/gait stability is a condition defined by both the position of the center of mass and the velocity relative to the base of support and thus can be applied to dynamic activities and gait. Poor dynamic/gait stability could increase the likelihood of one becoming unstable given a perturbation during a dynamic task.

It is well established that individuals with knee OA have impaired static postural stability compared to their healthy counter parts, as measured by increased static postural sway and reduced single-leg stance time (45-47, 52, 61). These deficits are likely related to osteoarthritic changes that occur as a result of the disease affecting all the structures of the joint – including the ligaments, capsule, tendons, and surrounding muscle (62). Postural control in dynamic situations may also be associated with characteristics associated with OA. In one study, patients with asymptomatic knee OA were asked to stand on an oscillatory platform which could deliver sudden small perturbations during stance (63). Indeed, the group with knee OA was less able to respond to the perturbations and restore equilibrium compared to a control group, determined by a significant decrease in the Lehr's dampening ratio, a value representing balancing capacity following a sudden perturbation (63). The authors suggest that this deficit could be due to reduced muscle strength or decreased joint mobility, both commonly manifested in those with knee OA. Another possible explanation for the decreased balancing capacity could attribute to proprioceptive deficits observed in those with OA (47, 64). Proprioception involves mechanoreceptors which can be reduced or damaged in knees affected by OA, which could impair the afferent sensory information about the perturbation, and consequently, could alter the compensatory response.

It is important to stress that static and dynamic postural measures do not reflect how individuals adapt to changes in the environment and cannot give any information about an individual's ability to perform a successful recovery step(s) in response to external perturbations such as a trip or a slip (16). Consequently, even though people with OA are likely at greater risk for becoming posturally or dynamically unstable, given what is known about "specificity" (discussed in later sections), it is prudent to assess the ability to perform recovery responses

when exposed to destabilizing perturbations to better identify those that are at a particularly high risk for falls.

#### 1.2.3.2. *Relating OA to the recovery stepping response*

There have been no published studies assessing the recovery stepping response in people with OA. As discussed previously, following a trip, a successful recovery step requires deceleration and ideally, reversal of the trip-induced trunk flexion (18, 19) and a step of adequate length to reestablish a new base of support (19). There are several characteristics associated with knee OA that may influence the ability to perform a successful stepping response following a loss of dynamic stability (40).

Following a laboratory-induced trip, knee buckling (i.e. the knee of the recovery limb flexes after ground contact) was associated with falling (19). To avoid knee buckling from occurring following a trip, rapid eccentric contraction of the quadriceps is needed to negate the rapid flexion that can occur at or just after recovery step foot contact. Individuals with knee OA have both reduced eccentric and concentric quadriceps strength (43, 65) which may interfere with the ability to perform a step and the ability to generate the appropriate amount of muscle force to negate a fall. Knee buckling is common during undisturbed gait in people with knee OA, occurring in 12% of patients in the last year (49) and has also been related to fear of falling, poor physical function and low balance confidence (49). Consequently, knee buckling could contribute to the increased fall risk. The stepping response can also result in high and rapid compressive loading at the knee joint (66). Thus, individuals with knee OA may be reluctant to step due to a “fear” of pain from excess loading, or in the event that they do step, may do so with impaired recovery kinematics. One additional factor which may affect the stepping response of

people with OA is obesity. Obesity is particularly common in people with knee OA with one study showing as few as 17% of their OA population to be normal weight, with the remaining being overweight, obese or severely obese (67). Rosenblatt and Grabiner (2012) report that 46.2% obese individuals fell in response to a laboratory-induced trip compared to only 25% of healthy-weight subjects. Most notably, two-thirds of the obese fallers failed to even initiate a stepping response (60). The authors concluded that the failure to initiate a recovery step is particularly important as it could increase impact force with the ground consequently increasing the risk of a fall-related injury.

#### 1.2.4 **Fall-prevention interventions**

##### 1.2.4.1. *Fall prevention interventions for healthy older adults*

*Task specificity* has been studied in the field of motor learning as far back as 1956 and can be summarized as: “*performance of one task will be maximized if the training best mimics the sensory motor and environmental conditions of the task*” (68). Over the last decade, task-specific interventions have been utilized for fall prevention with much success. These types of interventions involve practicing the motor skills required to avoid a fall by subjecting individuals to repeated perturbations using treadmills, sliding platforms, and/or waist pulls that are large enough to require a recovery stepping response to avoid a fall. Treadmill-based programs particularly have resulted in favorable and encouraging results. Grabiner et al. assigned 52 community-dwelling women to either a training or control group, where the training group received four training sessions over 4 weeks, each consisting of an individualized training of up to 30 forward-directed postural disturbances of varying magnitude (69). The women were then subjected to a laboratory-induced trip, where the number of falls in the training group was 86% lower to that of the control group (OR=0.13,  $p < 0.001$ ) (69). In another study of 46 healthy young

adults, one session of 24 perturbations using a sliding platform to induce slip-like perturbations also resulted in trained subjects falling less following a laboratory-induced slip (70).

Treadmill perturbation interventions are likely effective as they quickly modify kinematics that are associated with successful recovery responses, and they can be retained to prospectively reduce falls. Bieryla et al. reported that one session of training forward-directed steps (i.e. simulating trips) using a treadmill resulted in improved recovery kinematics, mainly related to the trunk (71). In another study, 65 older adults were exposed to five identical treadmill-delivered perturbations which required at least one forward-directed step to avoid a fall (20). Thirty-five percent of the subjects fell following their initial, “untrained” perturbation, while all adults were able to successfully recover following the fifth, and final, perturbation. Those subjects who failed on their initial attempt successfully modified their recovery response by altering their trunk kinematics, such that there was a decrease in the trunk flexion angle and trunk flexion velocity at recovery step completion, and by increasing the length of their recovery step. These kinematic improvements gained from task-specific perturbation training have also shown to be retained for up to 4 months (72, 73). The most convincing evidence of the efficacy of this type of training is a result from a recent one-year prospective study showing that 4 sessions of task-specific perturbation training was able to decrease trip-related fall rates by 50% (74).

In summary, the kinematic improvements gained from task-specific perturbation training can be quickly learned, can be transferred, can be retained, and can prospectively decrease fall rates. Currently, exercise programs incorporating a balance component are said to prospectively reduce falls by 30% (75). Adding task-specific perturbation training to existing exercise programs could significantly reduce fall rates, and possibly fall-related injury rates, in older

adults. Grabiner et al. quantified that if the success of fall prevention interventions could be increased by just 5%, this could result in the prevention of over 1.1 million falls and \$580 million in annual medical care costs (76). Further, these authors stated that it is believed that task-specific training could increase the efficacy of fall-prevention interventions by much more than 5% (76), thereby having even greater reductions in the number of falls and the associated costs.

#### 1.2.4.2. *Fall prevention interventions for individuals with OA*

Many strategies commonly recommended for the treatment and management of OA, including exercise, weight loss, pain-relief, and total knee replacements could potentially reduce their increased risk for falls and/or fall-related injuries. Indeed, several studies have studied the effect of various interventions on fall risk by people with OA, although there remains a need for interventions where falls and/or fall injury is the primary outcome measure.

Similar to the benefits of exercise-based intervention on fall risk seen in otherwise healthy older adults, exercise significantly decreases fall risk by people with knee OA. In 2015, Mat et al. (2015) conducted a systematic review evaluating the effectiveness of various exercise interventions on fall risk for people with knee OA (77). Their review included 15 randomized controlled trials, concluding that strength training, Tai Chi, and aerobics can improve balance and/or reduce fall risk for older adults with knee OA. When pooled together, the authors found that these interventions improved fall risk by 45% (pooled standardized mean difference = 0.55, 95% CI: 0.41-0.68). However, the authors noted that there were no studies with large enough sample sizes to determine actual reductions in the number of falls, thus were limited to the use of fall-related measures to assess fall risk (e.g. timed-up and go test, sit-to-stand test, gait speed,

Berg's balance scale, etc.), limiting the strength of this finding. Individual studies examining the effects of exercise programs on fall risk scores for people with knee OA have mixed results. Hale et al. (2012) used a twice-per-week water based program focusing on balance, finding no significant reductions in fall-risk, measured using a timed-up and go test (78) while Song et al. (79) and Shen et al. (80) found significant improvements in walking kinematics, knee extensor muscle endurance, and balance as a result of Tai Chi. Unfortunately, whether exercise interventions can reduce the absolute number of falls or can improve the ability to perform recovery responses when exposed to destabilizing perturbations for people with knee OA remains to be studied.

Pain relief has also been proposed as a method to decrease fall risk in those with OA. Using intra-articular pain relieving injections (a combination of a fast-acting local anesthetic, a slow-acting long-term glucocorticoid, and a quick-acting, short-term glucocorticoid) to reduce pain in patients with knee OA, Pandya et al. (2007) then had subjects walk over a platform and assessed their ability to avoid a suddenly appearing 'virtual' obstacle (i.e. a light beam) and evaluated obstacle avoidance success rates (i.e. their ability to step over, without any part of their foot/shoe making contact with, the virtual obstacle/beam) (81). Following the injection, patients with knee OA were 37% more effective at clearing the virtual obstacle; however, this was still 20% lower than a group of control subjects (81). Although the ability to avoid an obstacle is considerably different than the ability to perform a recovery response to maintain dynamic stability, this study may suggest that people with symptomatic and asymptomatic knee OA are at increased likelihood to trip on an obstacle, therefore necessitating a recovery response. Another study assessing the effect of pain relief on fall risk, observed knee OA patients before and after a total knee replacement, showing that although pain levels significantly improved, patients who

reported a fall in the three months prior to surgery had an 8-fold increase in the risk of falling post-operatively (82). In the aggregate, these studies suggest that pain reduction, alone, is not an effective method in reducing fall-risk for people with knee OA.

The above mentioned interventions have been limited as they have not been specific to the task of recovering dynamic stability following large perturbations that mimic the types of disturbances that occur during locomotion in the community. As discussed previously, task-specific perturbation training has been successful in preventing prospective falls in healthy older adults (74). A number of the risk factors for falls by individuals with OA are the same as the risk factors for falls in healthy older adults, such as balance/gait deficits and strength declines (40). Thus it is likely that the task-specific perturbation interventions which have been successful in older adults, should also work in an OA population. For people with knee OA, there is no published evidence of a task-specific fall prevention intervention having been conducted. An ideal program for an individual with OA would be to implement task-specific perturbation training to improve recovery responses, in addition to using traditional disease management exercise programs. Exercise programs significantly improve pain, strength, and quality of life measures for people with knee OA (83-85), which consequently would assist in reducing the number of fall-related risk factors (i.e. pain, strength/balance deficits, etc.) for those with knee OA. Adding perturbation training would further negate fall-risk by improving the ability to successfully perform recovery steps in response to unexpected perturbations.

### 1.3 **Purpose**

The purposes of this dissertation research, which focused on trip-related falls, were to identify the biomechanical risk factors that may be responsible for the increased fall risk of

people with knee OA, and to establish if people with knee OA would benefit from an intervention that specifically targets the ability to perform recovery stepping responses.

The underlying *rationale* for this dissertation was that identification of clinically modifiable risk factors which are causally related to falls by individuals with knee OA will provide clinicians with tools to better identify OA patients who will most benefit from task-specific perturbation training targeting the recovery stepping response. This would result in fewer falls by – and fewer fall related injuries sustained by – individuals with knee OA.

This dissertation is made up of three chapters, all of which address research questions that are related and work towards the overall purpose. The purposes of each chapter are as followed:

Study 1 (Chapter #2): The purposes of this study were to document the occurrences of trip-related falls by people with knee OA compared to a control group and to characterize the relationship between MTC, MTC variability and trip-related falls by people with knee OA.

Study 2 (Chapter #3): The purpose of this study was to determine the extent to which knee OA negatively affects the recovery stepping response following a laboratory-induced trip and a large treadmill-delivered postural perturbation simulating a trip.

Study 3 (Chapter #4): The primary purpose of this study was to determine whether task-specific perturbation training improves recovery step performance in people with knee OA. A secondary purpose of this study was to determine the rate and extent that women

with knee OA were able to learn to perform a successful recovery following a large postural perturbation.

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## **PREFACE TO CHAPTERS TWO, THREE, AND FOUR**

Chapters two, three, and four are preliminary studies determining the extent to which knee OA influences the likelihood of a trip occurring, the kinematics associated with the recovery stepping response, and the trainability of the recovery stepping response, respectively. A total of 50 middle-aged and older women, 25 of which has self-reported physician-diagnosed knee OA and 25 of which acted as control subjects, participated in all three studies. Subjects who participated in all three studies did so over the course of one visit to the University of Illinois at Chicago Biomechanics Laboratory. The visit took between 2-3 hours and all subjects were given adequate rest breaks when needed throughout the visit. No women complained about the duration of their visit to the lab. Some women did not complete all parts of the studies. The reasons for not completing included pain, anxiety about the treadmill, and investigator decision.

It should be noted that the studies in this dissertation are preliminary and were underpowered to detect differences in fall rates (both retrospectively reported fall rates, and fall rates following laboratory induced trips and treadmill delivered postural perturbations). Further, women in the OA group for the current study had relatively low pain scores, thus future work is needed including women with a larger range of OA severity to confirm and generalize the present findings.

## **2 Causes of falls by individuals with knee OA: influence of minimum toe clearance**

### **2.1 Introduction**

With one out of every three older adults sustaining a fall each year (1) and older adults also making up the fastest growing demographic in America (2), falls and fall-related injuries are a significant and growing concern for older adults. Falls are associated with early morbidity and mortality and, in 2012, cost the US healthcare system upwards of \$30 billion in direct medical care costs (3, 4). The clinical and financial consequences of falls and fall-related injuries by older adults stress the need to develop, or improve upon, strategies to reduce the occurrence of falls and fall-related injuries.

One strategy to reduce the absolute number of falls by older adults may be to determine the sub-population who is at an increased risk for falls, and to focus on identifying and treating causal fall mechanisms. One population that has an increased risk of falls and fall-related injuries are those that have lower extremity osteoarthritis (5, 6). The knee is the most commonly affected weight bearing joint for osteoarthritis (OA) and knee OA is present in nearly 37% of Americans (7). Further, Knee OA reportedly increases fall risk by 30% (6). Unfortunately, the reason(s) why individuals with knee OA tend to fall more than their otherwise healthy counterparts is unknown. As OA is an age-related disease (8) and is highly related to obesity (9), the prevalence of knee OA, and the falls associated with knee OA, are expected to increase due to the growing age, and dramatic increase in obesity levels, of the US population. Consequently, addressing the increased fall risk in people with knee OA would likely reduce the absolute number of falls in older adults.

For healthy, community-dwelling older adults, most falls occur during locomotion (10), with nearly 50% of falls being due to trips (10-12). Similarly, one retrospective study of 106

patients with hip OA identified trips, followed by slips, as the most common causes of falls reported in the last year (13). This study, however, was specific to patients with hip OA, which compared to knee OA makes up a smaller percentage of the population. Further, the authors did not compare the reported fall rates to a control group (i.e. patients without OA) to determine if their patient group was at an increased risk of a specific type of fall. To date, the causes of falls for people with knee OA, specifically, have not been studied. Determining whether trip-related falls occur for individuals with OA to the same extent as otherwise healthy older adults, and if so, whether the mechanisms explaining the trip-related fall risk are similar, may assist in extending interventions previously shown to decrease trip-related falls in the community (14) to this population.

During gait, an individual is particularly susceptible to tripping at the instant of minimum toe clearance (MTC). MTC occurs when the vertical distance between the swing foot and the ground is at a local minimum (15). Having a low mean or median MTC could increase the probability of the swing foot making contact with an unseen hazard thereby causing a trip or stumble (16) which could result in a fall in the event of an unsuccessful recovery response. As most people take thousands of steps per day, assessing measures of variability are also important when determining one's likelihood of tripping during gait (16, 17). Having a low average MTC and/or a high MTC variability could both increase the probability of a trip/stumble occurring (17). Indeed, for healthy older adults, retrospectively reported fallers have a lower MTC (mean:  $12.0 \pm 0.7$  mm vs.  $15.2 \pm 1.0$  mm,  $p < 0.001$ ) and increased MTC variability (coefficient of variation: 0.29 vs. 0.25) compared to non-fallers (18). MTC is sensitive to changes in knee, hip, and ankle kinematics (15, 19, 20), which are commonly different in individuals with knee OA (21), thus could affect their MTC. To date, only one study has quantified MTC in patients with

knee OA (22) finding no differences in the average MTC compared to a control group. This study collected data on only 5 steps and did not, and could not accurately, assess MTC variability. Consequently, more comprehensive analyses of MTC in individuals with knee OA are warranted to determine this population's likelihood of becoming dynamically unstable due to a trip.

There were two purposes of the study. The first was to document the occurrences of trip-related falls by people with knee OA compared to a control group and, second, to characterize the relationship between MTC, MTC variability and trip-related falls by people with knee OA. It was hypothesized that people with knee OA would report significantly more trip-related falls in the year preceding their participation in the study compared to the control group. It was also hypothesized that MTC would be significantly lower, and MTC variability would be significantly larger, in the OA group compared to the control group. An additional, explorative aim of this study was to determine the occurrence of frequent stumbling or subjective feelings of unsteadiness in the year preceding participation in the study to determine if it was related to MTC and MTC variability.

## 2.2 **Methods**

### 2.2.1 **Participants**

Fifty women, aged 50 and older who were divided equally into a self-reported OA group and a control group, participated in this study (OA group:  $60.8 \pm 6.9$  yrs,  $163.8 \pm 5.7$  cm,  $82.6 \pm 14.4$  kg; control group:  $(60.4 \pm 7.8$  yrs,  $163.0 \pm 6.2$  cm,  $76.6 \pm 18.9$  kg). Women responded by phone to fliers which were posted around the community, and were asked a series of questions determining their eligibility in the study. Women in the OA group answered "yes" to the

following question: “*Have you been told by your doctor or physician that you have osteoarthritis or degenerative joint disease in your knees?*”. To be considered as a participant in the control group women had to answer “no” to each of the following questions: (1) “*Have you been told by your doctor/physician that you have osteoarthritis or degenerative joint disease in your knees?*”, (2) “*Have you taken any medications for joint pain in the last year?*” and (3) “*Have you experienced any joint pain in your knees, hips, ankles, or lower back in the last year?*”.

Exclusion criteria for all women included: self-reported inability to walk for 15 minutes without stopping, knee or hip replacements, or having received any pain relieving injections in the last 6 months. All protocols were approved by the University of Illinois at Chicago Institutional Review Board and all participants provided written informed consent prior to participation.

### 2.2.2 **Protocol**

Each woman had their age, height, weight, and most affected or dominant leg recorded. Each woman was asked to evaluate the severity of pain in their knees, which was scored 0-100 on a 100 mm visual analog scale (VAS).

Women then completed a questionnaire asking about their fall history. Women were asked “*Have you experienced a fall in the last year? (yes/no)*”, and “*If yes, have you experienced more than one fall in the last year (yes/no)*”. If the participant answered yes to one or both questions, they were then asked to describe the circumstances of their fall (i.e. trip on the sidewalk, slip on ice, knee gave out, etc.). Subject responses were later classified into one of 4 categories based on their responses: trips, slips, knee buckling, and other. To address the occurrence of frequent stumbling or feelings of unsteadiness, all women were also asked to

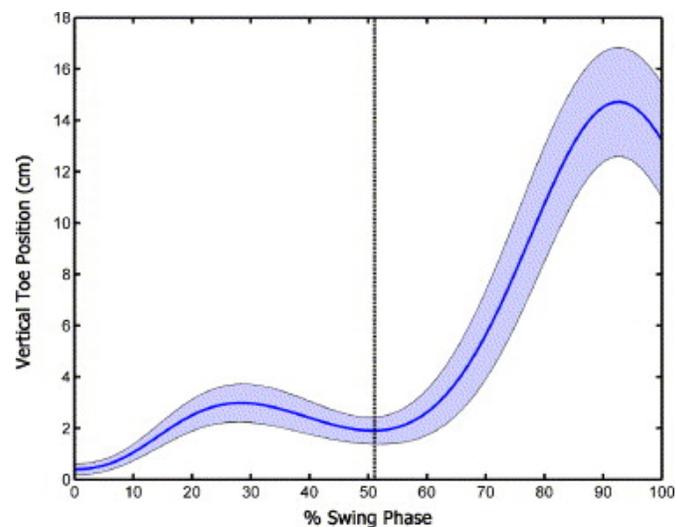
answer yes or no to the question “*have you stumbled multiple times in the last year or do you often feel unsteady on your feet?*” (23).

Women were then asked to walk on a treadmill for up to 10 minutes wearing their own comfortable walking shoes. Two women from the OA group dropped out of the study prior to treadmill walking due to pain or being afraid of walking on the treadmill. All women walked on the treadmill at a self-selected speed, which was determined by increasing the speed of the treadmill gradually, until the participant informed the investigator they had reached their comfortable walking speed. While participants were encouraged to walk for 10 minutes, some women were unable to do so and the trial was stopped prematurely. Accurate estimation of step kinematic variability requires at least 400 steps (24). Thus, only women who completed 400 steps or more were included in the analyses. All women were also asked if they had prior experience walking on a treadmill. To remove the possibility that prior experience walking on a treadmill could affect MTC, only women who responded “yes” were considered for the analyses. Consequently, after removing those who did not have 400 steps and those who did not have prior treadmill experience, only 19 women in the OA group and 22 women in the control group were included in the subsequent MTC analyses.

### **2.2.3 MTC and MTC variability**

All participants had a passive reflective marker placed on the shoe over the second metatarsal (i.e. the toe marker), which is the anatomical location defined in the Helen Hayes Marker configuration (25). An 8-camera 3D motion capture system operating at 120 Hz (Motion Analysis Co.) tracked the motion of the toe marker, which was then used to compute MTC and MTC variability. For each step, MTC was calculated as a local minimum in the vertical

trajectory of the toe marker of the swing foot relative to the vertical portion of the same marker at the initiation of the swing phase (i.e. toe off) (19). If there was no local minimum, the value at 50% of the swing phase was determined, as this is approximately when MTC occurs (15) (Figure 4).



**Figure 4.** Swing limb vertical displacement of the toe marker during the swing phase of gait (figure taken from Moosabhoy et al., 2006 (20)). This figure represents able-bodied walking. The shaded area on either side of the mean represents one standard deviation. The vertical line (at ~52%) indicates the time of MTC (local minimum). Note that this local minimum is around 50% of the swing phase. For individuals who do not display a local minimum, MTC was taken at 50%.

#### 2.2.4. Data/Statistical Analyses

All statistical analyses were performed using IBM SPSS 22.0 (Armonk, NY). For all statistical analyses, the significance level was set at 0.05. T-tests were used to test for differences in subject characteristics between the OA and control groups.

To address the first hypothesis that people with knee OA would report significantly more trip-related falls in the year preceding their participation in the study compared to the control group, a chi-square test was used to compare the proportion of women in the OA group who had reported at least one trip-related fall in the last year to that of the control group. Due to the small sample size, effect sizes were calculated, where a larger effect size represents a stronger effect of OA on fall occurrences. Effect sizes were estimated using phi ( $\phi$ ), the square root of the chi-squared statistic divided by the sample size. Values of  $\phi$  equal to 0.1, 0.3, and 0.5 represent small, medium and large effects, respectively (26). Additionally, to distinguish between statistical and clinical significance, a method suggested by Hopkins (27) was used. This method provides the probability that the observed effect is substantive, that is, above the clinically relevant value which is suggested as a relative risk of 1.2 or more (27, 28) based on the observed p-value, and the calculated relative risk and 95% confidence interval.

To address the second hypothesis that MTC would be significantly lower, and MTC variability would be significantly larger, in the OA group compared to the control group, the mean and median MTC was computed separately for each limb and subject. MTC variability was also calculated using standard deviation of the mean and the IQR. Prior to addressing the second hypothesis, paired t-tests were used to determine whether there were differences between MTC and MTC variability of the most- and least-affected limb in the OA group, and between the

dominant- and non-dominant limb in the control group. Significant between-limb differences would dictate testing the second hypothesis by comparing the most-affected limb of the OA group to the non-dominant limb of the control group. In the absence of between-leg differences the MTC values for each leg would be pooled. Differences in MTC and MTC variability within the OA group were also compared between those who did report a trip-related fall in the last year and those who did not using independent t-tests. Similarly, in the event of a between-limb difference, the limbs would be separated during the analysis.

An additional, explorative, aim of this study was to determine the occurrence of frequent stumbling or subjective feelings of unsteadiness in the year preceding participation in the study and to determine if it was related to MTC and MTC variability. A chi-squared test was used to compare the proportions of women who answered yes to the question “*have you stumbled multiple times in the last year or do you often feel unsteady on your feet?*” (from this point forward, referred to as “frequent stumbles/unsteadiness”) compared to those who answered no. Independent t-tests to quantify differences in MTC and MTC variability between those who had and had not reported frequent stumbling/unsteadiness in the OA group were also used.

### 2.3 **Results**

The OA group was similar to the control group with respect to descriptive characteristics. The OA and control were not significantly different in age, height, or weight ( $p > 0.05$ ) (TABLE III).

**TABLE III. SUBJECT CHARACTERISTICS (MEAN  $\pm$  SD) AND RETROSPECTIVELY-REPORTED FALLS AND FALL CAUSES IN KNEE OA AND CONTROL GROUP.**

	<b>Knee OA (n=25)</b>	<b>Control (n=25)</b>
<b>Age (yrs)</b>	60.8 $\pm$ 6.9	60.4 $\pm$ 7.8
<b>Height (cm)</b>	163.8 $\pm$ 5.7	163.0 $\pm$ 6.2
<b>Weight (kg)</b>	82.6 $\pm$ 14.4	76.6 $\pm$ 18.9
<b>VAS (mm)</b>	25.4 $\pm$ 22.4	4.21 $\pm$ 8.04*
<b>Frequent stumbling/unsteadiness, n (%)</b>	15 (60%)	7 (28%)*
<i>Causes of falls (n, %) <sup>a</sup></i>		
<b>Trips</b>	12 (48%)	6 (24%)
<b>Slips</b>	13 (52%)	8 (32%)
<b>Knee Buckling</b>	2 (8%)	0
<b>Other</b>	3 (12%)	6 (24%)
<b>No falls reported</b>	6 (24%)	9 (36%)

\*significant difference OA vs control,  $p < 0.05$

<sup>a</sup> Number of women who reported having at least one of the following fall types in the last year

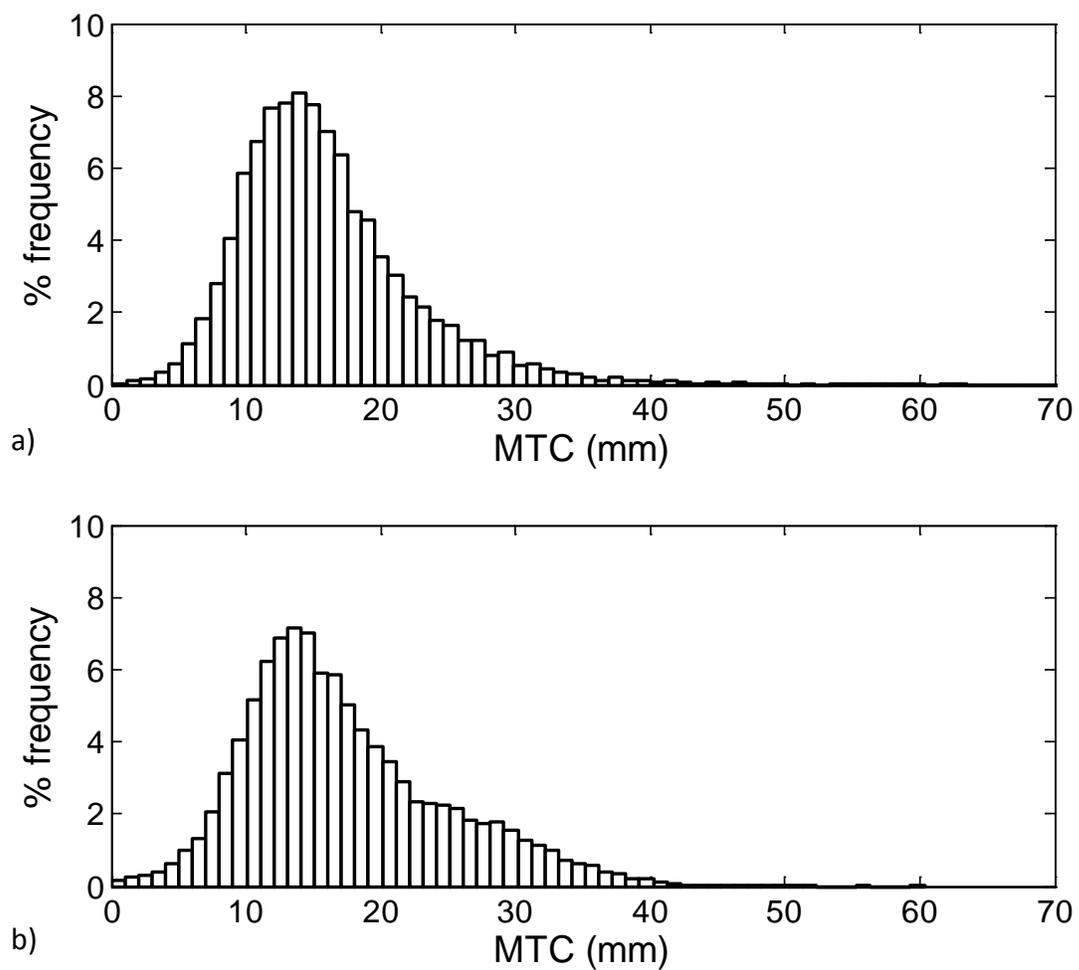
### 2.3.1 Retrospective fall causes

More women in the knee OA group reported falls compared to the control group. Specifically, there were twice as many women in the knee OA group who reported having at least one trip-related fall in the last year (48% vs. 24%) (TABLE III). This difference approached, but did not achieve, statistical significance ( $p=0.077$ ,  $\phi=0.3$ ;  $RR=2.0$ ; 95% CI on RR, 0.89-4.49). This corresponds to a 90.2% probability that OA results in a clinically important increased risk of trip-related falls. After documenting other fall causes, both groups had a large percentage of

women reporting at least one slip-related fall (52% in the OA group vs. 32% in the control group). Two women in the OA group (8%) also reported falls resulting from limb buckling, compared to zero in the control group.

### 2.3.2 **MTC and MTC variability**

Knee OA did not have an effect on MTC or MTC variability. MTC frequency distributions were similar for both groups (Figure 5). There were no significant differences in MTC or MTC variability between the most-affected and least-affected limbs in the OA group or between the dominant and non-dominant limb in the control group (TABLE IV). As a result, subsequent between-group analyses were conducted on the pooled data from the two limbs. Independent t-tests did not show any significant differences in MTC or MTC variability between the OA and control group (TABLE V).



**Figure 5.** MTC histogram of the (a) OA group (14,566 total steps from 19 subjects), and (b) control group (23,233 total steps from 22 subjects)

Having a trip-related fall in the last year did not affect MTC for women with knee OA. Within the OA group, there were no significant differences in MTC and MTC variability between the women who reported having at least one trip-related fall in the last year and those who had none (Table VI).

TABLE IV. BETWEEN LIMB DIFFERENCES IN MTC AND MTC VARIABILITY.

	Knee OA			Control		
	Most-affected knee	Least-affected knee	p-value	Non-dominant limb	Dominant limb	p-value
<b>Mean (mm)</b>	16.19 ± 6.09	15.20 ± 4.62	0.18	17.12 ± 7.42	16.73 ± 5.69	0.65
<b>Median (mm)</b>	15.87 ± 5.96	14.96 ± 4.56	0.21	16.96 ± 7.38	16.57 ± 5.58	0.65
<b>SD (mm)</b>	3.77 ± 1.63	3.76 ± 1.07	0.91	3.52 ± 0.92	3.48 ± 1.09	0.78
<b>IQR</b>	4.88 ± 1.91	4.50 ± 1.25	0.13	4.56 ± 1.21	5.45 ± 1.52	0.54

SD=standard deviation; IQR=interquartile range

\*p<0.05

TABLE V. MTC AND MTC VARIABILITY IN THE OA AND CONTROL GROUP (MEAN  $\pm$  SD)

Parameters	OA (n=19)	Control (n=22)
Mean (mm)	15.69 $\pm$ 5.18	16.93 $\pm$ 6.30
Median (mm)	15.39 $\pm$ 5.06	16.83 $\pm$ 6.23
SD (mm)	4.05 $\pm$ 1.47	3.94 $\pm$ 1.27
IQR	5.16 $\pm$ 1.80	5.29 $\pm$ 2.15

SD=standard deviation; IQR=interquartile range

\*p<0.05

TABLE VI. DIFFERENCES IN MTC AND MTC VARIABILITY (MEAN  $\pm$  SD) BETWEEN WOMEN IN THE OA GROUP WHO DID AND DID NOT REPORT A TRIP-RELATED FALL IN THE LAST YEAR AND BETWEEN THOSE WHO DID AND DID NOT REPORT FREQUENT STUMBLING/UNSTEADINESS IN THE LAST YEAR

	Trip-related fall (n=10)	No trip-related falls (n=9)	Frequent stumbling/ unsteadiness (n=11)	No stumbling/ unsteadiness (n=8)
Mean (mm)	15.05 $\pm$ 5.54	16.41 $\pm$ 4.97	13.48 $\pm$ 3.39**	18.74 $\pm$ 5.85
Median (mm)	14.83 $\pm$ 5.56	16.02 $\pm$ 4.68	13.26 $\pm$ 3.47**	18.33 $\pm$ 5.62
SD (mm)	3.64 $\pm$ 0.92	4.51 $\pm$ 1.86	3.43 $\pm$ 0.84**	4.91 $\pm$ 1.76
IQR	4.65 $\pm$ 1.11	5.73 $\pm$ 2.28	4.34 $\pm$ 1.01**	6.29 $\pm$ 1.09

SD=standard deviation; IQR=interquartile range

\*p<0.05 between trip-related fall and no-trip related falls

\*\*p<0.05 between reporting frequent stumbling/unsteadiness and not

### 2.3.3 **Frequent Stumbling or Feelings of Unsteadiness**

The presence of knee OA had an effect on the reporting of frequent stumbling/unsteadiness over the last year. Significantly more women in the OA group reported frequent stumbling/unsteadiness in the year preceding participation compared to the control group ( $X^2=5.20$ ,  $p=0.023$ ,  $\phi=0.3$ ) (TABLE III). There were significant differences in MTC and MTC variability between those who did and did not report frequent stumbling/unsteadiness (TABLE VI), with those who did having significantly lower MTC and significantly less MTC variability compared to the women who did not ( $p<0.05$ ).

## 2.4. **Discussion**

The purposes of this study were to document the occurrences of trip-related falls by people with knee OA compared to a control group and to characterize the relationship between MTC, MTC variability and trip-related falls by people with knee OA. The first hypothesis was that people with knee OA would report significantly more trip-related falls in the year preceding their participation in the study compared to the control group. Although twice the number of women in the OA group reported a trip-related fall in the year preceding their participation in the study compared to the control group, this difference did not achieve statistical significance. However, subsequent analyses determined this difference to be clinically meaningful. The second hypothesis that MTC would be significantly lower, and MTC variability would be significantly larger, in the OA group compared to the control group was not supported. Neither MTC nor MTC variability were significantly different between the two groups. An explorative aim of this study was to determine the occurrences of stumbling and subjective feelings of unsteadiness in the year preceding participation in the study to determine if it was related to

MTC and MTC variability. It was found that individuals with knee OA who reported frequent stumbling/unsteadiness had lower MTC compared to those who did not. The results suggest that although women with knee OA may be particularly at risk for trip-related falls compared to a control group, this is not due to differences in MTC. This suggests that the increased risk for trip-related falls by people with knee OA may be due to inadequate recovery stepping responses following a trip.

#### 2.4.1. **Retrospective fall causes**

While knee OA is considered a significant risk factor for falls (5), no studies have determined the causes of falls in this population. This is the first study to show meaningful differences in the number of women with OA who report trip-related falls in the last year compared to otherwise healthy women. Although this difference only approached significance ( $p=0.077$ ), a subsequent analysis to determine whether this was a clinically significant difference found that there was over a 90% probability that knee OA results in a clinically important increase in trip-related fall risk. A medium-sized effect was also observed, further suggesting that knee OA may particularly increase the risk of trip-related falls. The small sample size, the medium effect, and calculated clinical significance of the current study may explain the nonsignificant statistical findings, warranting future studies with larger sample sizes. Slips were also common in this study, with the OA group reporting almost twice as many slip-related falls as the control group. Both trips and slips require compensatory responses – typically in the form of forward- or backward-directed recovery stepping response, respectively – to regain dynamic stability and avoid a fall. Consequently, the nearly twice as high occurrence of trip- and slip-related falls by people with knee OA compared to controls could reflect an inability to perform both forward- and backward-directed recovery stepping responses.

There were two falls reported as a result of limb buckling from the OA group compared to zero in the control group. Indeed, limb buckling is a common characteristic for people with OA, occurring in nearly 11% of individuals every three months, and 35% of the time it results in a fall (29). While the small sample size makes it difficult to determine if this difference is non-random, targeting limb buckling as a potential factor to reduce fall-risk in people with knee OA would not likely be as effective as interventions specific to trips and/or slips as they make up a larger proportion of falls occurring in the community. Indeed, interventions to reduce trip-related falls have been developed and are particularly effective, reducing their occurrences by 50% in otherwise healthy middle aged and older adults (14). This is especially important as it is greater than the 30% reduction in prospective falls that is commonly reported using exercise-based interventions (30).

#### 2.4.2. **MTC and MTC variability**

While there was a clinically meaningful increase in the number of women in the OA group reporting trip-related falls, we could not relate this to differences in MTC. This finding expands on that of Levinger et al. (2011) who reported no difference in MTC between an OA and control group based on 5-steps (22). The current study provided a more comprehensive analysis of MTC, utilizing up to ten minutes of continuous walking data, and including measures of stride-to-stride variability, finding no differences in MTC or MTC variability between the OA and control group. This finding suggests that the likelihood of people with knee OA making contact with an obstacle during gait (e.g. tripping on an uneven surface while walking) is similar to otherwise healthy individuals. Thus, rather than an increased incidence of tripping, inadequate recovery stepping responses may explain the occurrence of trip-related falls in this population. This is further supported by the finding that within the knee OA group, there were also no

differences in MTC or MTC variability between women who did and did not report having a trip-related fall in the past year.

The study design was cross-sectional and thus, should be interpreted with caution. There is no prospective evidence showing that small MTC is causally-related to trip-related falls. In fact, one study reports *greater* MTC values in older adults who reported having a history of falls compared to age-matched individuals which could reflect an adaptation by high fall-risk individuals to reduce the likelihood of a trip (31). It is possible that during gait, because individuals with OA report frequent stumbling/unsteadiness, they adapt their gait such that the resulting MTC values are closer to that of control subjects. Indeed, in a study examining MTC in adults who were asked to step over obstacles, those in the knee OA group displayed a higher toe clearance in the trailing limb crossing the obstacle (32). The authors suggested that this was an adaptation to reduce the probability of the foot hitting the obstacle (32). Similar to these findings, it is possible that women with knee OA in the current study alter their gait in this way to decrease their risk of making contact with an unseen obstacle.

#### **2.4.3. Frequent Stumbling or Feelings of Unsteadiness**

No studies have addressed the extent to which people with knee OA report frequent stumbling or feelings of unsteadiness. In the current study, more than double the women in the OA group reported frequent stumbling/unsteadiness compared to the control group. The occurrences of frequent stumbling/unsteadiness could be attributed to the fact that these women had significantly reduced MTC. Indeed, Teno et al. (33) prospectively followed nearly 600 community-dwelling older adults finding that those who reported more than one stumble in the previous month, had a 2.3-times increased risk of falling over the next year (aOR=2.3,

95%CI=2.9-12.2) . Further, Srylgy et al. (34) had healthy, community-dwelling older adults log daily, for 12 months, whether they had a fall or a “misstep” that day (missteps were defined as “a trip, slip, or other loss of balance in which recovery occurred to prevent a fall”). They reported that adults who reported multiple missteps were nearly 4-times more likely to fall prospectively (34). One limitation of the current study is the nature in which the question of stumbling/unsteadiness was asked. Subjects were asked to answer yes or no to: “*have you stumbled multiple times in the last year or do you often feel unsteady on your feet?*”. This question could be interpreted differently between subjects as “frequent stumbling” is likely very different than “often feeling unsteady on ones feet”. Nevertheless, women who answered “yes” to the question likely they find themselves in more occurrences where some type of recovery response is necessary to recover dynamic stability, thus increasing their likelihood of a fall occurring.

#### 2.4.4 **Conclusion**

In conclusion, the occurrence of trip-related falls by individuals with knee OA was notably higher compared to women without knee OA. The greater number of trip-related falls could not be attributed to between-group differences in MTC or MTC variability. Consequently, the increased risk of falls by people with OA reported in the literature, particularly trip-related falls, may occur due to inadequate recovery stepping responses.

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### **3 Knee osteoarthritis negatively affects the recovery step following large forward-directed postural disturbances**

#### **3.1 Introduction**

Osteoarthritis (OA) affects nearly 26 million Americans (1) and is the leading cause of disability (2). Specifically, the knee is the most common weight-bearing joint affected by OA and symptomatic knee OA is estimated to affect 12.1% of Americans over the age of 70 (3). As OA is highly associated with both aging and obesity (4), the number of Americans affected by OA is expected to increase as both the population ages and as obesity rates continues to rise, increasing the healthcare costs and disability associated with OA, making it a concern for the US healthcare system.

Just as aging is associated OA, it is also associated with increased fall risk (5, 6). Each year, 33% of older adults (age 65+) will experience a fall (7), resulting in over 2 million reported injuries and 20 thousand mortalities (8). In 2014, falls were estimated to cost the US nearly 45\$ billion in medical care costs (8). Indeed, people with OA, specifically lower extremity OA, have increased fall rates compared to their otherwise healthy counterparts (9-15). A recent prospective study of over 50,000 post-menopausal women reported that OA increased the risk of falls and fracture by 25% and 20%, respectively (16). In summary, given the general aging of our population, both OA and falls are growing concerns for older adults and for the US healthcare system, stressing the need for effective interventions that can reduce fall rates, particularly falls by those with OA.

Unfortunately, the mechanisms behind this increased fall and fracture risk reported in those with OA are unknown. A fall is the result of two sequential, independent events. The first

event, an initial loss of dynamic stability, which may result from a trip or slip, is followed by the failure to execute a sufficient recovery response such as a grasping or stepping response that restores dynamic stability. Only in the event that a recovery response is insufficient, will a fall occur. Following small postural perturbations that do not require a step, Kiss et al. reported that individuals with knee OA were less capable of responding to perturbations compared to age-matched controls, determined by a significant decrease in the Lehr's dampening ratio, a value representing balancing capacity following a sudden perturbation (17). However, small postural perturbations are not informative of the ability to respond to a large perturbation, such as a trip or a slip, which account for over 50% of falls occurring by older adults (18), as these commonly depend on successful recovery stepping responses. In the lab, how adults respond to trips can be studied by subjecting participants to laboratory-induced trips where an obstacle suddenly appears and obstructs the motion of the swing limb during gait causing a trip, or using a treadmill, where the treadmill belts accelerate rapidly causing forward rotation of the body, simulating a trip and necessitating a recovery step(s) to restore dynamic stability. In healthy older adults, the failure to limit trunk motion and perform a recovery step of sufficient length following both these types of perturbations have consistently discriminated fallers from non-fallers (19-21). To date, recovery stepping responses by people with knee OA following large postural disturbances have not been studied.

Pain, a hallmark symptom of OA, may partially explain this increased risk as it can negatively influence coordination, postural sway, muscle strength and power, and proprioception (22, 23). These deficits provide possible mechanisms by which pain could influence dynamic stability and/or a recovery stepping response (22). Further, self-reported OA and frequent reported knee pain, but notably, not radiographic evidence of OA, have been related to

retrospective fall risk (11, 24). Specifically, a study of nearly 750 older adults showed that those who reporting having “pain that interfered with performance of daily activities” were significantly more likely to fall than those with lower levels of pain (25). As pain is associated with significant changes in gait kinematics for those with knee OA (26, 27), it is plausible that pain associated with knee OA could also influence kinematics related to the recovery stepping response.

The purpose of this study was to determine the extent to which knee OA negatively affects the recovery stepping response following a laboratory-induced trip and a large treadmill-delivered postural perturbation simulating a trip. There were three hypotheses. The first hypothesis was that women with knee OA would have a higher fall rate compared to a control group following both types of perturbations. The second hypothesis was that recovery kinematics following a laboratory-induced trip and a treadmill-delivered postural perturbation would be impaired in an OA group compared to a control group. The recovery kinematics of interest were trunk angle at recovery step completion, trunk angular velocity at recovery step completion, and the initial recovery step length, as these have discriminated fallers from non-fallers in previous studies (19, 20). The third hypothesis was that, in women with OA, pain would be significantly associated with recovery kinematics.

## 3.2 **Methods**

### 3.2.1 **Participants and Protocol**

Twenty-five women aged 50 and older who had self-reported knee OA volunteered to participate in this study ( $60.8 \pm 6.9$  yrs,  $163.8 \pm 5.7$  cm,  $82.6 \pm 14.4$  kg) after responding to fliers posted around the community. During a phone screening, these women responded “yes” to the

question “*Have you been told by your doctor or physician that you have osteoarthritis or degenerative joint disease in your knee(s)?*”. A control group of 25 women without self-reported knee OA ( $60.4 \pm 7.8$  yrs,  $163.0 \pm 6.2$  cm,  $76.6 \pm 18.9$  kg) also volunteered to participate in the study. These women answered “no” to each of the following questions during the phone screening: (1) “*Have you been told by your doctor or physician that you have osteoarthritis or degenerative joint disease in your knee(s)?*”, (2) “*Have you taken any medications for joint pain in the last year?*” and (3) “*Have you experienced any joint pain in your knees, hips, ankles, or lower back in the last year?*”. Exclusion criteria for all women included: inability to walk for 15 minutes without stopping, knee or hip replacements, or having received any pain relieving injections in the last 6 months. All protocols were completed in a single laboratory visit. Women in the OA group were allowed to take their normal, daily pain medications. The protocol was approved by the University of Illinois at Chicago Institutional Review Board and all participants provided written informed consent prior to participation.<sup>1</sup>

Upon visiting the lab, all women had their height and weight measured, from which BMI was calculated. Women were asked to evaluate the severity of knee pain, scored as 0-100 on a 100 mm visual analog scale (VAS). Women also completed the Knee Injury and Osteoarthritis Outcomes (KOOS) questionnaire. The KOOS questionnaire is a validated and reliable patient-report measurement assessing an individual’s opinion about their knees and associated problems (28). The KOOS questionnaire is composed of 5 subscales: Pain, Symptoms, Function in daily living (ADL), Function in Sport and Recreation (Sport/Rec), and knee-related quality of life (QOL). In each subscale, higher scores indicate fewer knee-related problems or symptoms.

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<sup>1</sup> These are the same subjects that were used in Chapters #2 and #3

Women were subjected to two types of large postural perturbations: a laboratory-induced trip (19) and a treadmill-delivered postural perturbation (20, 21), both described below. These two types of perturbations each have their own inherent advantages. The laboratory-induced trip has high ecological validity as it represents the types of trips that would occur in the community where objects suddenly appear without notice. On the other hand, the treadmill-delivered perturbation guarantees that the initial conditions are experimentally controlled, ensuring that each subject receives a perturbation of equal magnitude. For both perturbations, women wore their own comfortable walking shoes and were fit to a safety harness. The safety harness ensured that in the event a subject fell, the hands or knees were not able to make contact with the floor/treadmill belt (29) (see harness in Figure 7). However, depending on the length of the harness rope, there was a degree of ambiguity in determining whether subjects were assisted in their recovery responses. Therefore, a successful recovery was one in which the participant was able to unambiguously recover dynamic stability without use of the safety harness.

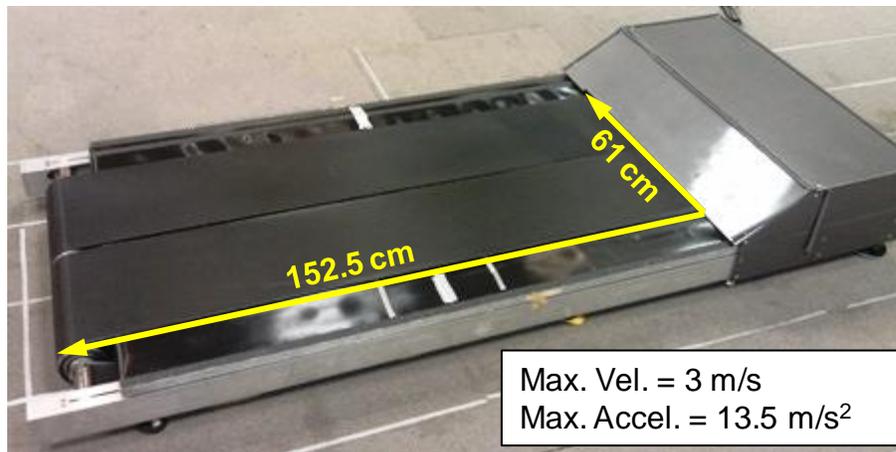
### 3.2.2 **Laboratory-induced trip**

Subjects performed walking trials at a self-selected speed along a 22-meter walkway during which they were aware that during an unspecified trial they would be tripped. During all trials, a decoy tripping rope was positioned in the gait path to divert attention away from the location at which the trip would occur. After ~10-15 walking trials, a trial was selected for the trip where a mechanical obstacle was manually triggered by an investigator and rose 5 cm to obstruct the motion of the swing foot. Only one attempt was made to trip each participant. The outcome of the trip was documented as a “fall”, “recovery”, or “miss”. Misses occurred when the mechanical obstacle was triggered at an inappropriate time and the subject was not tripped. These trials were excluded from subsequent analyses.

Trips were categorized by the recovery strategy used (19, 30). A *lowering strategy* occurs when the tripped limb is immediately lowered to the ground and acts as the support limb as the contralateral foot is used to complete the initial recovery step. An *elevating strategy* occurs when the tripped limb is used as the recovery limb. Both recovery strategy and walking speed can affect kinematics following a laboratory-induced trip (19). Consequently, a regression analysis (see: statistical analyses, pg 65) was used to control for these variables during the statistical analyses.

### 3.2.3 **Treadmill-delivered Postural Perturbation**

Women received a treadmill-delivered postural perturbation, similar to that used in Owings et al. (2001) and Grabiner et al. (2012) (20, 21). The perturbation was such that the recovery kinematics required to avoid a fall were comparable to those required following a laboratory-induced trip (e.g. the ability to control trunk kinematics at recovery step completion and to perform a step of adequate length) (20). Participants stood with their arms to their side, feet positioned shoulder width apart and heels aligned on a microprocessor-controlled, stepper motor-driven, dual-belt treadmill (ActiveStep™, Simbex, Lebanon, NH) (Figure 6).



**Figure 6.** The microprocessor-controlled, stepper motor-driven, dual-belt treadmill (ActiveStep™, Simbex, Lebanon, NH).

None of the women in the study had prior experience receiving treadmill-delivered postural perturbations. Participants were informed that the treadmill would move “sometime in the next minute” and, when it moved, to “do whatever they could to recover their balance”. When initiated by the investigator, the treadmill accelerated in the posterior direction to 1.00 m/s in about 170 ms causing the subject to become unstable in the forward direction. The treadmill then maintained a constant velocity of 1.00 m/s for 5 sec before decelerating for 2.00 sec back to zero m/s. The perturbation was such that it required at least one step to restore dynamic stability (Figure 7). Recoveries were classified as either successful (non-fallers) or not-successful (fallers).



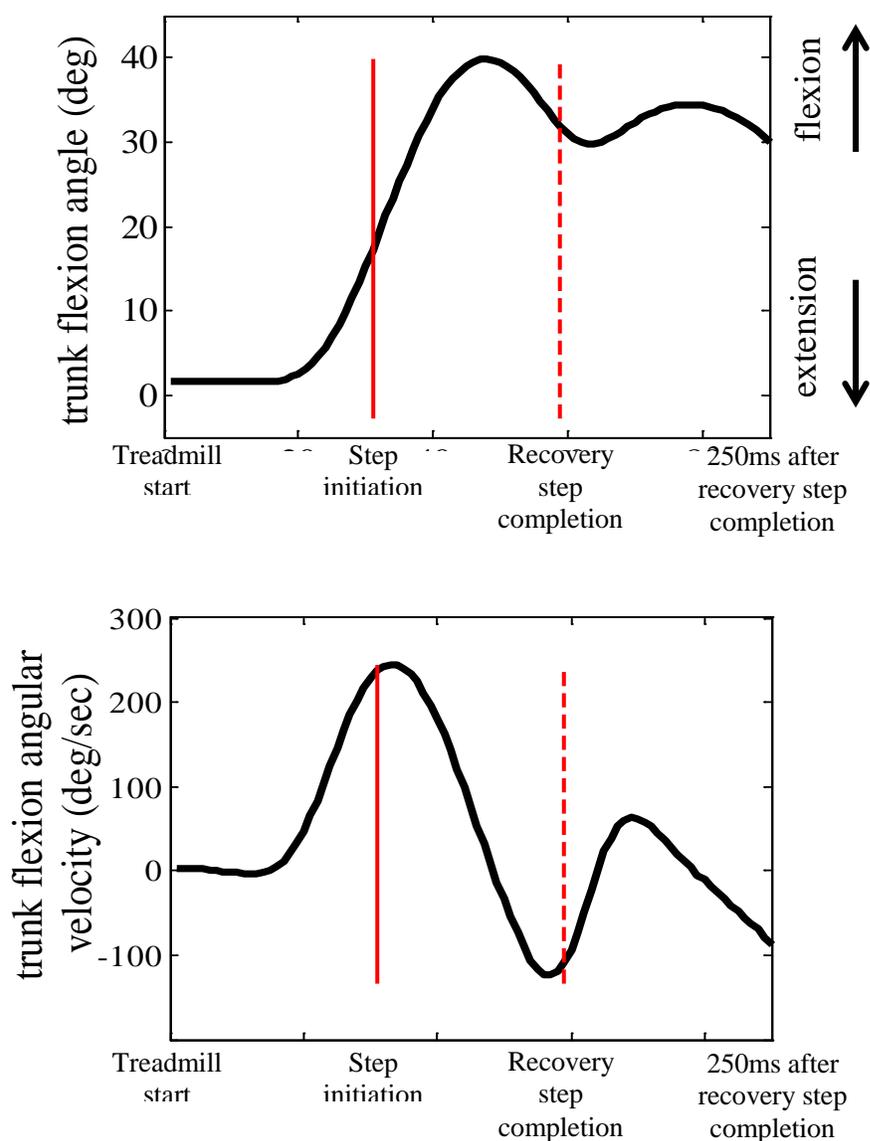
**Figure 7.** Subject recovering from a forward-directed postural perturbation which requires multiple steps to regain dynamic stability. Subjects begin by standing quietly with arms to the side (1). Treadmill then accelerates in the posterior direction causing forward rotation of the body (2). The subject then must initiate a step and control the forward rotation of the trunk during the recovery response (2-3). Recovery step completion is the instant at which the heel or toe (whichever came first) of the recovery foot makes contact with the treadmill surface (3). Following recovery step completion, several additional steps are initiated to re-establish dynamic stability (4).

### 3.2.4 Kinematics of the recovery stepping response

Twenty-two passive reflective markers were placed on the arms, legs, and torso using the Helen Hayes marker configuration (31). An 8-camera 3D motion capture system operating at 120 Hz (Motion Analysis Co., Santa Rosa, CA) was used to record the motions of the reflective markers. Marker data was collected and edited using Cortex 2.5.2 software (Motion Analysis Co., Santa Rosa, CA) and raw coordinate data were filtered using a recursive fourth-order Butterworth filter with a cutoff frequency of 6 Hz. Kinematics associated with the recovery

stepping responses for both the laboratory-induced trip and the treadmill-delivered perturbation were calculated from the motion capture data off-line using custom code in Matlab (MathWorks, Natick, MA) and using OrthoTrak 6.6 clinical gait analysis software (Motion Analysis Co., Santa Rosa, CA).

Trunk flexion/extension angle at recovery step completion, trunk angular velocity at recovery step completion, and step length were the kinematics of interest given their ability to statistically discriminate fallers from non-fallers following trips (19, 20). Step completion was manually assessed from the raw motion capture data and was considered the instant at which either the heel or toe of the recovery foot first made contact with the treadmill surface or ground. Trunk angle at recovery step completion was calculated relative to the trunk angle prior to the perturbation (see Figure 2 for exemplar subject). Trunk angular velocity at step completion was extracted from the time series computed as the first derivative of the trunk angle (Figure 8). A negative trunk angular velocity indicated trunk extension. Step length was expressed as a percentage of body height and calculated as the distance between the centroids of the recovery and stance foot at the time of recovery foot contact. Walking speed during the laboratory-induced trip was computed by determining the average rate of horizontal displacement of the sacral marker over the 500ms prior to contacting the obstacle.



**Figure 8.** Trunk flexion (top) and trunk angular velocity (bottom) taken from an exemplar subject who successfully recovered following a treadmill-delivered postural perturbation. The solid vertical line represents step initiation (manually identified as the instant the recovery foot leaves the treadmill surface). The dotted vertical line represents recovery step completion (instant at which the heel or toe of the recovery foot first made contact with the treadmill surface). Note that maximum trunk flexion angle (local maximum between step initiation and step completion) occurred prior to recovery step completion, after which trunk began to extend (evidenced by a negative trunk extension angular velocity). This “trunk control” represents an ideal recovery response where the individual has arrested the perturbation-induced forward trunk rotation.

### 3.2.5 Statistical Analyses

All statistical analyses were performed using IBM SPSS 22.0 (Armonk, NY). To test the first hypothesis that women with knee OA would have higher fall rates than women without knee OA, chi-squared tests were used to compare between-group fall rates. This was done separately for the laboratory-induced trips and treadmill-delivered perturbations.

To test the second hypothesis that recovery kinematics following a laboratory-induced trip and a treadmill-delivered postural perturbation would be impaired in an OA group compared to a control group, separate analyses were conducted for the laboratory-induced trip and the treadmill-delivered perturbations. For both perturbations, kinematics of the women in the OA group who were able to successfully recovery (i.e. the non-fallers) were compared to the non-fallers in the control group. For the laboratory-induced trip, because walking speed and recovery strategy used can influence recovery kinematics (19), separate linear regressions were used to determine the effect of knee OA on each dependent variable while controlling for the walking speed prior to the trip and recovery strategy using the following equation:

Recovery kinematic =  $\beta_0 + \beta_1 * \text{group} + \beta_2 * \text{walking speed} + \beta_3 * \text{strategy}$ , where:

Recovery kinematic = dependent/variable of interest (e.g. trunk angle at recovery step completion)

$\beta_0$  = intercept (constant)

$\beta_1$  = either an increase or decrease in the dependent variable for OA versus control (coded as a 1 for OA and a 0 for control)

$\beta_2$  = either an increase or a decrease in the dependent variable, per unit difference in walking speed (continuous variable)

$\beta_3$  = either an increase or decrease in the dependent variable for lower versus elevating strategy (coded as a 0 for lowering and a 1 for elevating)

A significant  $\beta_1$  suggested that knee OA had a significant effect on the recovery kinematic after controlling for walking speed and strategy used. Additionally, for the treadmill-delivered postural perturbation, independent t-tests were used to detect differences in recovery kinematics between the non-fallers in the OA group and the non-fallers in the control group.

Additionally, independent t-tests were used to determine whether there were significant differences in recovery kinematics between fallers and non-fallers. This was done separately for the OA and control groups to determine whether the underlying biomechanical causes that lead to trip-related falls by people with knee OA were similar to those of otherwise healthy controls. This analysis was performed for both the laboratory-induced trips and the treadmill-delivered disturbances.

To test the third hypothesis that for women with OA, pain would be significantly associated with recovery kinematics, Pearson correlation coefficients were computed to determine the extent to which the KOOS scores were related to recovery kinematics. For this analysis, only recovery kinematics from the treadmill-induced perturbation were used, as it ensured that each subject was given a perturbation of equal magnitude. For all statistical analyses, the significance level was set at 0.05.

### 3.3 **Results**

Women in the OA group did not differ from the control group in any anthropometrics. The between group differences in age, height, weight and BMI were not significant (TABLE VII). The OA group had significantly higher VAS scores and significantly lower KOOS scores (worse pain/function) compared to the control group.

**TABLE VII. DESCRIPTIVE CHARACTERISTICS FOR OA AND CONTROL GROUP**

	<b>OA group (n=25)</b>	<b>Control group (n=25)</b>
<b>Age (years)</b>	60.8 (6.9)	60.4 (7.8)
<b>Height (m)</b>	1.64 (0.57)	1.63 (0.62)
<b>Weight (kg)</b>	82.60 (14.36)	76.60 (18.86)
<b>BMI (kg/m<sup>2</sup>)</b>	30.91 (5.91)	28.70 (6.40)
<b>VAS (mm)</b>	25.38 (22.4)	4.2 (8.0)
<b>KOOS score</b>	299.71 (98.2)	464.96 (54.5)

#### 3.3.1 **Fall Outcomes**

Knee OA did not have an effect on fall outcomes. The between-group differences of the number of women who fell following the laboratory-induced trip and treadmill-delivered perturbations did not achieve statistical significance. During the laboratory-induced trip, there were five “misses” in the OA and 5 misses in the control group. Of the remaining women, 3 of 20 (15%) women in the OA group fell and 5 of 20 (25%) women in the in the control group fell.

This between-group difference in the proportion of fallers was not significant ( $X^2=0.70$ ,  $p=0.40$ ). For the treadmill-delivered postural perturbation, two women from the OA group were not included in the subsequent statistical analysis. One of these women did not receive any treadmill perturbations (investigator decision; subject fell following laboratory-induced trip, was emotionally apprehensive, and investigator felt the treadmill-portion of the protocol was unnecessary) and the other woman received a perturbation of different magnitude (investigator error). Of the remaining women, following the treadmill-delivered perturbation, seven of 23 (30%) women in the OA group fell and five of 25 (20%) women in the control group fell. The between-group difference in the proportion of fallers was not significant ( $X^2=0.860$ ,  $p=0.35$ ).

### 3.3.2 **Recovery kinematics following laboratory-induced trips**

Knee OA had an effect on recovery step kinematics during the laboratory induced trip. Although women with knee OA walked significantly slower during the laboratory-induced trip trial (OA group:  $1.10 \pm 0.20$  m/s; control group:  $1.22 \pm 0.123$ ,  $p=0.03$ ). After adjusting for walking speed and recovery strategy, the trunk angular velocity at recovery step completion of the knee OA group was, on average,  $60.7$  deg/sec faster than that of the control group ( $\beta=60.713$ ,  $SE=20.225$ ,  $p=0.006$ ). In this regression model, the strategy used had a significant effect on trunk angular velocity at step completion. On average, an elevating strategy was associated with increased trunk flexion velocity ( $\beta=60.583$ ,  $SE=19.868$ ,  $p=0.005$ ). The effect of knee OA on the remaining kinematic variables, after controlling for walking speed and strategy, was not significant.

When comparing fallers to non-fallers for both the OA and control group (TABLE VIII), due to the small number of fallers using an elevating strategy (one in each group), statistical

comparisons between fallers and non-fallers were not carried out. However, the observed data shows that, in general (a few exceptions), the fallers in the OA and control group had larger trunk flexion angles at recovery step completion compared to the non-fallers and trunk angular velocity. Further, the fallers (OA and control) displayed a trunk flexion velocity at recovery step completion while the non-fallers for both groups displayed either a trunk extension velocity (observed in those using lowering strategy) or a reduced trunk flexion velocity (observed in the elevating strategy).

**TABLE VIII. RECOVERY KINEMATICS FOLLOWING THE LABORATORY-INDUCED TRIP.**

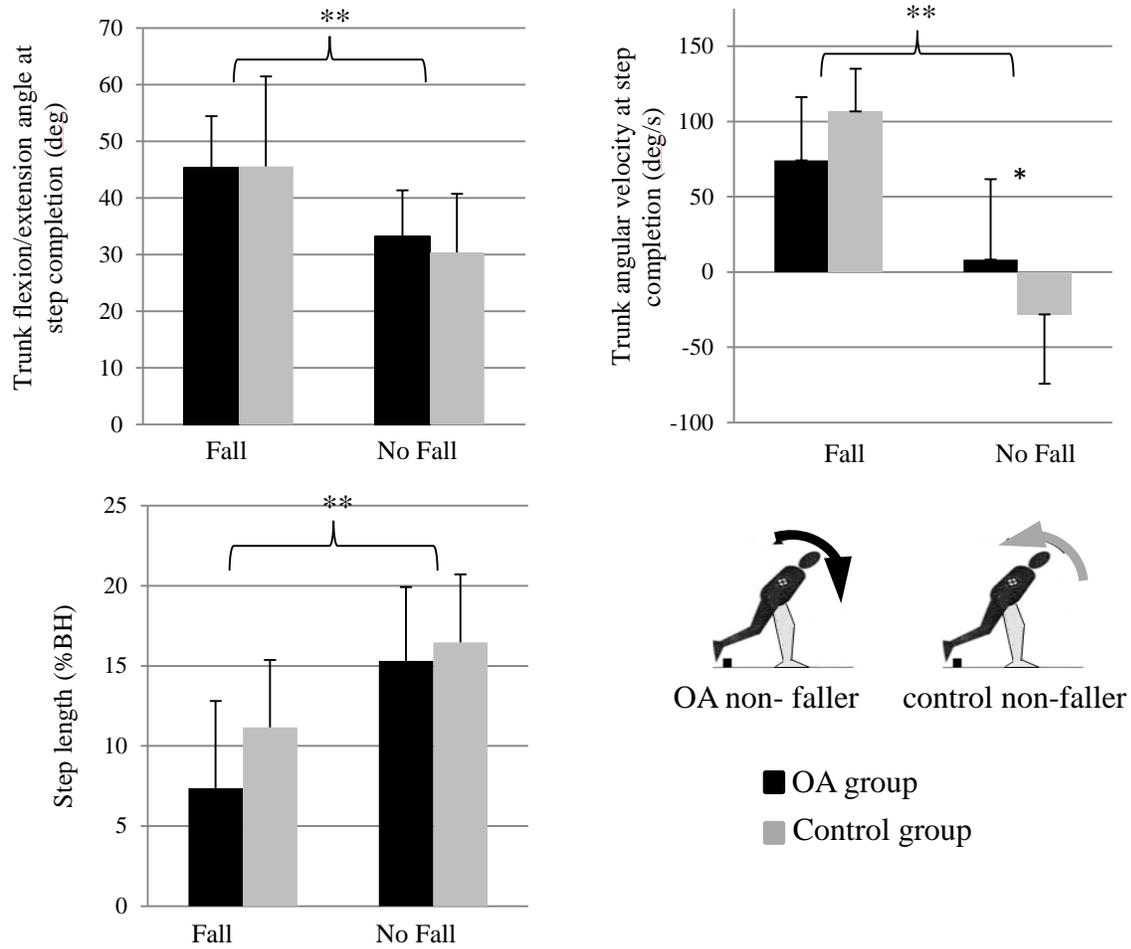
	<b>OA non-fallers (n=17)</b>		<b>control non-fallers (n=15)</b>		<b>OA fallers (n=3)</b>		<b>control fallers (n=5)</b>	
	Lower- ing n=10	Elevat- ing n=7	Lower- ing n=7	Elevat- ing n=8	Lower- ing n=2	Elevat- ing n=1*	Lower- ing n=4	Elevat- ing n=1*
Walking speed (m/s)	1.12 (0.16)	1.22 (0.23)	1.24 (0.14)	1.23 (0.10)	0.80 (0.04)	1.13	1.24 (0.05)	1.01
Trunk angle at recovery step completion (deg)	29.60 (9.44)	20.73 (6.50)	22.02 (7.19)	22.94 (7.38)	33.08 (16.45)	17.42	40.09 (11.05)	37.95
Trunk angular velocity at recovery step completion (deg/sec)	-12.13 (50.94)	50.64 (36.46)	-68.81 (28.71)	0.15 (85.69)	45.35 (17.15)	86.30	29.27 (72.63)	0.58
Step length (%BH)	0.57 (0.10)	0.27 (0.09)	0.64 (0.07)	0.34 (0.14)	0.46 (0.02)	0.07	0.52 (0.12)	0.45

\* due to only 1 faller in each group utilizing an elevating strategy, only that subjects value is reported

### 3.3.3 **Recovery kinematics following treadmill-delivered postural perturbation**

Following the treadmill-delivered postural perturbation, women with knee OA exhibited significantly impaired control of the trunk compared to the control group. Following the treadmill-delivered perturbation, the non-fallers of the OA group displayed a trunk flexion velocity at recovery step completion that was significantly different than the trunk extension velocity displayed in the control group (Figure 9B) ( $p=0.037$ ). No other recovery step kinematics were significantly different between the OA and control group. Notably, three of the six fallers in the OA group did not initiate a recovery step. That is, the safety harness was engaged prior to the stepping foot leaving the treadmill belt. In contrast, none of the five women in the control group who fell failed to initiate a recovery step. A post-hoc Fisher exact test did not reveal these proportions to be significantly different ( $p=0.18$ ).

Fall outcome did have an effect on recovery kinematics. Within both the OA and control groups, all three recovery kinematics were significantly impaired in the fallers compared to the non-fallers ( $p<0.05$ , Figure 9).



**Figure 9.** Between- and within- group differences in trunk angle (A), trunk angular velocity (B), and step length (C) following the treadmill-delivered perturbation (mean (SD)). Schematic in the lower right panel (adapted from Pavol et al. (19)) depicts the trunk flexion velocity occurring at step completion in the OA non-fallers, compared to the trunk extension velocity occurring in the control non-fallers.

\*\*Significant ( $p < 0.05$ ) difference exists between both the OA fallers and OA non-fallers and between the control fallers and control non-fallers

\* Significant ( $p < 0.05$ ) difference exists between OA and control group

### 3.3.4 **KOOS**

Pain did not have an effect on recovery step kinematics. Pain, as measured from the KOOS subscale, was not significantly associated with any recovery kinematics following the treadmill-delivered perturbation (TABLE IX). However, the relationships between recovery kinematics and other KOOS subscales (symptoms, ADL, and sport, and the total score) were significantly correlated or approached significance ( $0.05 < p < 0.10$ ).

TABLE IX. PEARSON CORRELATION COEFFICIENTS FOR THE OA GROUP BETWEEN KOOS SCORE AND RECOVERY KINEMATICS FOLLOWING THE TREADMILL-DELIVERED POSTURAL PERTURBATION.

	<b>Trunk angle at step completion (deg)</b>	<b>Trunk angular velocity at step completion (deg/sec)</b>	<b>Step length (%BH)</b>
<b>KOOS Total</b>	-0.406*	-0.309	0.418*
<b>KOOS Pain</b>	-0.322	-0.293	0.275
<b>KOOS Symptoms</b>	-0.303	-0.363*	0.422*
<b>KOOS ADL</b>	-0.382*	-0.340	0.454**
<b>KOOS Sport/Recreation</b>	-0.472**	-0.133	0.358
<b>KOOS QOL</b>	-0.297	-0.278	0.342

\*\* $p < 0.05$

\* $0.05 < p < 0.10$

### 3.4 **Discussion**

The purpose of this study was to determine the extent to which knee OA negatively affects the recovery stepping response following a laboratory-induced trip and following a large treadmill-delivered postural perturbation simulating a trip. The hypothesis that women with knee OA would have higher fall rates following both types of perturbations compared to a control group was not supported, as the between-group differences in fall rates did not achieve significance for either perturbation. The second hypothesis, that recovery kinematics following a laboratory-induced trip and a treadmill-delivered postural perturbation would be impaired in an OA group compared to a control group was partially supported. Indeed, women in the OA group displayed impaired kinematics related to control of the trunk following both types of perturbations. The third hypothesis that in women with OA, pain would be significantly associated with recovery kinematics was not supported.

#### 3.4.1 **Fall Outcomes**

There were no significant differences in fall rates between the OA and control group following both a laboratory-induced trip and a treadmill-delivered postural perturbation. The failure to show a between-group difference in the number of fallers could be explained by several reasons. First, during the laboratory induced trip, the OA group was walking significantly slower than the control group. It has been shown previously that healthy older adults who walk faster are more likely to fall following a laboratory-induced trip compared to their slower-walking counterparts (19). Specifically, in a study of 79 healthy, community-dwelling older adults, a 0.16 m/s faster walking speed resulted in a 2.5-times increased risk of a fall occurring following a trip (OR=2.56, 95%CI=1.11-5.86) (32). This is because walking velocity contributes to the speed of the forward rotation of the body after the trip (33), thus requiring a greater

extension moment to arrest and reverse the forward rotation of the body to avoid a fall. During the laboratory-induced trip trial, women in the knee OA group walked at a speed that was, on average, 10% slower than the control group. It is possible that had subjects been required to walk at similar walking speeds, more women in the OA group would have sustained falls. However, a strength of using the laboratory-induced trip is that it is likely generalizable to trips that may occur in the community (where unseen obstacles could cause stumbles/trips). Thus, it would have been unreasonable matching walking speeds between groups would not be representative of what may be occurring in the community. A second explanation for the failure to detect significant differences in fall rates is that the study was underpowered to detect differences in fall-rates as significant. Indeed, while the number of fallers was greater in the OA group following the treadmill-delivered perturbation compared to the control (7/23 vs. 5/25), the difference did not achieve statistical significance. The observed power for the comparison was 0.29, well below the standard 0.80. Based on the observed fall rates (30% vs. 20%), to achieve power at the 0.80 level with  $\alpha=0.05$ , ninety-seven subjects in each group (N=194) would be needed – a value well beyond the scope and feasibility of this dissertation research. The large sample size required to see significant differences in fall-rates was anticipated in the design of this study. Consequently, sample size was chosen such that it was powered to detect differences in recovery step kinematics between groups.

#### **3.4.2 Differences in recovery step kinematics between the knee OA and control groups**

Characterizing the extent to which people with knee OA are able to perform recovery step(s) associated with avoiding a trip-related fall is central to explaining why people with knee OA are at an increased fall risk. Women with knee OA were hypothesized to have impaired recovery kinematics following large postural perturbations compared to women in a control

group. This hypothesis was partially supported by the finding that, at recovery step completion, the OA non-fallers displayed a trunk flexion velocity following both the laboratory-induced trip and treadmill-delivered perturbation while the control non-fallers displayed a trunk extension velocity.

As mentioned previously, the failure to limit trunk motion following both laboratory-induced trips and a treadmill-delivered perturbations simulating trips have consistently discriminated fallers from non-fallers (19, 20, 34, 35). In healthy young subjects, trunk flexion velocity at recovery step completion could accurately classify 92.3% of the time successful vs. failed stepping responses following large (substantially larger than those used in the present study) treadmill-delivered perturbations (35). Similarly, in healthy community-dwelling middle aged and older adults, a logistic regression approach found that trunk flexion at recovery step completion was one of two kinematics that contributed to sensitively classifying falls and recoveries (sensitivity=0.67, specificity=0.98) (21). Collectively, these studies stress the central role of the trunk control in avoiding a fall from occurring. The influence of knee OA on control of the trunk following large postural perturbations had not been previously reported. In the present study, even the women in the OA group who successfully recovered from the perturbations did so with impaired control of the trunk (displayed trunk flexion velocity at recovery step completion). This implies that women with knee OA are less able to arrest, and reverse, the forward-directed angular momentum resulting from a perturbation prior to step completion. This could suggest that given a larger perturbation, or in instances where they are unaware that they will be receiving an upcoming perturbation (which is known to have a negative effect on trunk kinematics and fall outcome (36)), women with knee OA may be less likely to perform a successful recovery stepping response. However, the mechanisms by which

OA could affect kinematics related to the trunk, particularly following perturbations, is currently unknown.

### 3.4.3 **Differences in recovery step kinematics between fallers and non-fallers**

Consistent with previous findings (19-21), fallers in both groups had significantly worse recovery step kinematics compared to the non-fallers. This was observed only following the treadmill-delivered postural perturbation, as the laboratory-induced trip did not have enough fallers to run statistical analyses. The results support the premise that the underlying biomechanical causes that lead to trip-related falls by people with knee OA are similar to those of otherwise healthy controls. Indeed, those in the OA who fell had a 27% greater trunk flexion angle at recovery step completion and displayed a larger trunk flexion velocity at step completion compared to those who did not fall. Similarly, the fallers in the control group had a 33% larger trunk flexion angle at recovery step completion compared to the non-fallers, and displayed a trunk flexion velocity while those who recovered displayed a trunk extension velocity. This is an important, and novel, finding as it suggests trip-specific training, which has previously shown to improve the same recovery kinematics studied here (21), and reduce trip-related fall risk in otherwise healthy women (37), could also effectively reduce trip-related fall risk women with knee OA by improving the recovery stepping response.

### 3.4.4 **Recovery step kinematics: injury risk**

An unexpected and interesting finding of the current study was that 50% of fallers in the OA group failed to initiate a recovery stepping response following the treadmill-delivered postural perturbation while all women in the control group initiated a step (Figure 10). Lower extremity OA has been associated with an increased risk of fall-related fracture (9, 16, 38), which is thought to reflect the higher incidence and/or greater severity of falls (9). The present

results support the explanation that individuals with OA may have a greater severity of falls. Because a recovery step assists in decelerating the forward falling body (19), the absence of a recovery step increases the likelihood of an unimpeded fall to the ground, likely contributing to larger ground forces at either the wrist/forearm or at the hip (39). Indeed, similar observations have been reported in obese older adults and have been used to explain the increased fall-related injury risk (40). Thus, training focusing on improving recovery step performance may not only reduce trip-related fall risk, but could also reduce the likelihood of a fall-related injury occurring.



**Figure 10.** Left: subject initiated a recovery step shortly after the treadmill belt acceleration. Right: subject failed to initiate a recovery step in response to the treadmill belt acceleration. For this subject, engagement of the safety harness occurred before a recovery foot left the treadmill surface.

#### 3.4.4 **Effect of pain on recovery kinematics**

Whether people with more severe OA-related knee pain are at increased fall risk is unknown. Pain is associated with gait impairments (26, 27), balance deficits (41), and reduced muscle strength (41, 42), all of which are age-related risk factors for falls (43). In the present study, higher levels of pain were hypothesized to be associated with impaired recovery kinematics. This hypothesis was not supported, implying that the level of self-reported/perceived pain does not influence key recovery kinematics following large postural perturbations. This may indicate that the women with OA in the present study may have prioritized recovery of dynamic stability over perceived pain. Indeed, a “posture-first” hierarchy (44) has been proposed during dual-task conditions. These studies have shown that during a dual task, in which subjects are asked to respond to perturbations while performing a secondary cognitive or motor task (e.g. counting, pointing), that they focus their attention towards the postural task and that performance of the secondary task is negatively affected (44-46). The current study is the first to suggest that recovery stepping responses may receive higher priority with respect to attention over perceived pain.

Determining key characteristics associated with OA that may assist in identifying those at high fall risk would greatly assist clinicians in determining who would benefit most from a fall-prevention intervention. Although scores on the pain subscale of the KOOS were not associated with recovery kinematics, other subscales did reveal significant associations. Specifically, the KOOS sport/recreation and KOOS ADL subscales were significantly correlated with trunk flexion angle at step completion and recovery step length, respectively, signifying that those reporting lower (worse) KOOS scores, had a larger trunk flexion angle and shorter step length during trip recovery. While the Pearson correlation coefficients were statistically significant, they

were quite small, with a KOOS subscale score only accounting for, at best, 22% of the variation in recovery kinematics (KOOS sport/recreation vs. trunk flexion angle,  $r=0.472$ ,  $p<0.005$ ). Nevertheless, these significant correlations warrant further study of the utility of KOOS in determining fall risk in people with knee OA.

#### 3.4.5 **Conclusion**

In conclusion, following trips under controlled laboratory conditions and large postural perturbations simulating trips, both which require stepping responses to avoid falling, women with knee OA did not have a statistically higher incidence of falls compared to control subjects. However, the results demonstrate, for the first time, that knee OA is associated with significant and biomechanically meaningful differences in the recovery stepping response that increase fall risk, specifically, in those variables related to the ability to restore control of the trunk. Moreover, some women with OA failed to initiate a recovery stepping response completely. Both of these performance impairments could independently increase the likelihood of a fall and/or a fall-related injury. Performance of the recovery stepping response is amenable to training (21, 47). Consequently, incorporating training focused on improving the recovery stepping response (21) may likely reduce fall- and fall-related injury risk. If the event this is true, incorporating this type of training in the clinical management of people with knee OA is warranted.

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## 4 Task-specific perturbation training improves the recovery stepping responses by people with knee osteoarthritis

### 4.1 Introduction

Task-specific training is based on the hypothesis that “*performance of one task will be maximized if the training best mimics the sensory-motor and environmental conditions of that task*” (1). This premise has been adapted by researchers to develop novel fall prevention interventions during which participants practice the motor skills required to avoid a fall by being exposed to repeated postural perturbations that require stepping to avoid a fall. These task-specific interventions have resulted in improved kinematics associated with the recovery stepping response. Specifically, the improvements include reducing the trunk flexion angle and trunk flexion angular velocity at recovery step completion and increasing the length of the initial recovery step (2, 3). This is important because these kinematics have consistently discriminated fallers from non-fallers following laboratory-induced trips and treadmill-delivered postural perturbations (4, 5).

The most encouraging evidence of the effectiveness of task-specific perturbation training is that the acquired motor skill demonstrates transfer and reduces falls in the community (3, 6, 7). Rosenblatt et al. compared prospective fall rates between women who participated in four sessions of task-specific perturbation training and a control group (6). The women in the training group were they were exposed to up to 30 perturbations each session. In the one-year following completion of the training, the occurrence of prospectively-measured trip-related falls in the community was reduced by 50% compared to that of the control group (6). Another study by Pai et al. compared prospective fall rates in 212 community-dwelling older adults who were

randomly assigned to either a training group, who was exposed to 24 laboratory-induced slips, or a control group who only received a single slip (7). Interestingly, and contrary to the construct of specificity, although one session of slip-training did not significantly reduce the occurrence of slip-related falls one year following training, older adults did significantly reduce their annual all-cause fall risk by 50% (34% to 15%,  $p < 0.05$ ). Consequently, Pai et al. suggested that perturbation training may be effective by training proactive and reactive mechanisms for controlling dynamic stability that are generalizable across conditions outside of the training context (7). Nevertheless, the reductions in fall rates reported in Rosenblatt et al. and Pai et al. are especially important given that they exceed the 30% reduction in all-cause fall rates commonly reported using exercise interventions (8). This suggests that adding task-specific training to conventional exercise-based interventions could have a significant effect in reducing the number of falls.

People with knee osteoarthritis (OA) are at a 1.3-times (i.e. 30%) increased fall risk compared to otherwise healthy older adults (9). The study mentioned previously by Rosenblatt et al. (6), specifically excluded women with underlying musculoskeletal disorders, and the study by Pai et al. (7) using a medical history questionnaire, only included women who were presumably healthy. Given that people with knee OA are at increased fall risk, they may also be candidates for participation in such an intervention. Furthermore, people with knee OA display many of the same risk factors for falls that have been identified for the general population of older adults (10), including strength and balance deficits, pain, and gait impairments. It is likely that task-specific perturbation training, shown to be successful in otherwise healthy older adults, should also work in an OA population. To date, there is no published evidence of a task-specific fall prevention intervention for people with knee OA having been conducted.

According to Fitts and Posner's model of learning, as an individual practices a motor skill, the learner will acquire the basic movement pattern and performance will become more consistent from trial-to-trial (11). Hurt et al. had healthy young adults practice the motor skill of avoiding a fall by exposing them to 30 laterally-directed disturbances and determining how many trials were needed before performance became consistent from trial-to-trial. Hurt et al. measured performance by quantifying kinematics variables associated with the recovery task and assessing how they changed throughout the 30 trials. On average, in ~10 disturbances, the subjects were able to maintain a constant level of performance (i.e. the value of the kinematic variable plateaued), hereinafter referred to as the time of "skill acquisition" (12). It is unknown how many trials are required for older adults before performance becomes consistent following repeated forward-directed perturbations, and if people with OA would require the same number of trials for skill acquisition. As a motor skill is acquired, performance is first modified towards less variability as the individual begins to refine the movement to perform the task consistently and efficiently (13). Whether people with OA can consistently perform, i.e. can perform with a low degree of variability from trial-to-trial, the kinematics associated with successful recovery following repeated perturbations to the same extent as people without knee OA has not been studied. During gait, Kiss et al. observed that people with knee OA display increased variability of spatial-temporal variables, particularly increases in step length variability, compared to controls, and suggested that this may indicate an inability to reproduce comparable limb-coordinated movements from stride-to-stride (14). It is possible that the inability to perform consistent movements repeatedly during walking for people with knee OA could also translate to an inability to perform consistent movements when recovering from repeated perturbations. The extent that people with knee OA can reproduce the kinematics associated with successful

recovery responses following postural perturbations compared to people without knee OA could influence how perturbation training is implemented for people with knee OA. For example, if individuals with knee OA display greater trial-to-trial variability in the kinematics associated with successful fall recovery, this may warrant feedback from the individual administering to the patient on how to best perform a successful stepping response.

The primary purpose of this study was to determine whether task-specific perturbation training improves recovery step performance in people with knee OA. It was hypothesized that a single session of perturbation training would improve the ability of people with knee OA to restore control of the trunk during the initial recovery step and to perform a sufficiently long initial recovery step following large treadmill-delivered postural perturbations. A secondary purpose of this study was to determine the rate and extent that women with knee OA were able to learn to perform a successful recovery following a large postural perturbation. The hypothesis was that women with knee OA would require the same number of trials to acquire the kinematics associated with successful recovery, and upon skill acquisition, would display greater trial-to-trial variability of recovery kinematics. To address this hypothesis, the number of trials needed for skill acquisition and the trial-to-trial variability of each recovery kinematic upon skill acquisition (where increased variability signifies a lesser degree of skill acquisition) in women with knee OA were compared to that of healthy controls.

## 4.2. **Methods**

### 4.2.1 **Participants**

Twenty-five women, aged 50 and older ( $60.8 \pm 6.9$  yrs,  $163.8 \pm 5.7$  cm,  $82.6 \pm 14.4$  kg) who had self-reported knee OA volunteered to participate in this study after responding to fliers

posted around the community. During a phone screening, women had to respond “yes” to the question “*Have you been told by your doctor or physician that you have osteoarthritis or degenerative joint disease in your knees?*”. A control group of 25 women without knee OA ( $60.4 \pm 7.8$  yrs,  $163.0 \pm 6.2$  cm,  $76.6 \pm 18.9$  kg) were also recruited from the community. These women answered “no” to each of the following questions during their phone screening: (1) “*Have you been told by your doctor or physician that you have osteoarthritis or degenerative joint disease in your knees?*”, (2) “*Have you taken any medications for joint pain in the last year?*” and (3) “*Have you experienced any joint pain in your knees, hips, ankles, or lower back in the last year?*”. Exclusion criteria for all women included: self-reported inability to walk for 15 minutes without stopping, knee or hip replacements, or having received any pain relieving injections in the last 6 months. All protocols were approved by the University of Illinois at Chicago Institutional Review Board and all participants provided written informed consent prior to participation.<sup>2</sup>

#### 4.2.2 **Protocol**

Upon visiting the lab, all participants had their height and weight measured, from which BMI was calculated. Subjects in the knee OA group were asked which knee generally gave them the most pain/discomfort. All women were asked to evaluate the severity of knee pain, scored as 0-100 on a 100 mm visual analog scale (VAS) and were asked to fill out the Knee Injury and Osteoarthritis Outcomes (KOOS) questionnaire (15) to further assess their function and pain levels. Functional mobility was assessed using a timed 10-meter walk test at both a self-selected comfortable walking speed and their maximum walking speed (16). Women first performed the 10-meter walk test at comfortable walking speed. Subjects were informed that they should walk

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<sup>2</sup> These are the same subjects that were used in Chapters #2 and #3

“at a comfortable, leisurely speed as if you were walking to the store”. The second test was done while walking as quickly as possible. Subjects were informed to “walk as fast as you can without running”. Subjects performed three trials of each and the average speed for each test was calculated. Finally, subjects completed a timed 5-time sit-to-stand test (5xSST) (17) to assess lower extremity strength and functional mobility. For this test, subjects were asked to “stand up straight as quickly as you can 5 times without stopping in between with your arms folded across your chest”. The time it took to complete 5 repetitions was recorded.

Women stood on a microprocessor-controlled, stepper motor-driven, dual-belt treadmill (ActiveStep™, Simbex, Lebanon, NH) (Figure 6) with their arms to the side, feet positioned shoulder width apart and heels aligned while wearing a safety harness. The treadmill was used to deliver no more than 22 postural perturbations for which the belt accelerated posteriorly, i.e., opposite of the direction the subject was facing, causing each participant to become dynamically unstable in the forward direction. The first <sup>3</sup> and last perturbations (hereby referred to as the pre- and post-training disturbances) were of equal magnitude, accelerating to 1.00 m/s in about 170 ms, then maintaining a constant velocity of 1.00 m/s for 5 sec before decelerating for 2.00 sec back to zero m/s. The perturbation was such that it elicited at least one forward directed step to restore dynamic stability. The middle 20 training perturbations were smaller than the pre- and post-training perturbations, accelerating to 1.25 m/s in 300 ms and maintaining a constant velocity for 170 ms before decelerating back to 0 m/s for 100 ms. All 20 training perturbations required at least one step to restore dynamic stability. For all trials, the women were instructed

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<sup>3</sup> The first perturbation was the same as the large treadmill-induced postural perturbation that is used in Chapter #3, pp. 60.

“when the treadmill moves, do whatever you can to recovery your balance”. No feedback about their performance during any of the trials was provided.

Twenty-two passive reflective markers were placed on the arms, legs, and torso using the Helen Hayes marker configuration (18). The three-dimensional marker positions were recorded using an 8-camera motion capture system operating at 120 Hz (Motion Analysis, Santa Rosa, CA). Marker data was collected and edited using Cortex 2.5.2 software (Motion Analysis Co., Santa Rosa, CA) and raw coordinate data were filtered using a recursive fourth-order Butterworth filter with a cutoff frequency of 6 Hz. Kinematics associated with the recovery stepping responses for both the laboratory-induced trip and the treadmill-delivered perturbation were calculated from the motion capture data off-line using custom code in Matlab (MathWorks, Natick, MA) and using OrthoTrak 6.6 clinical gait analysis software (Motion Analysis Co., Santa Rosa, CA).

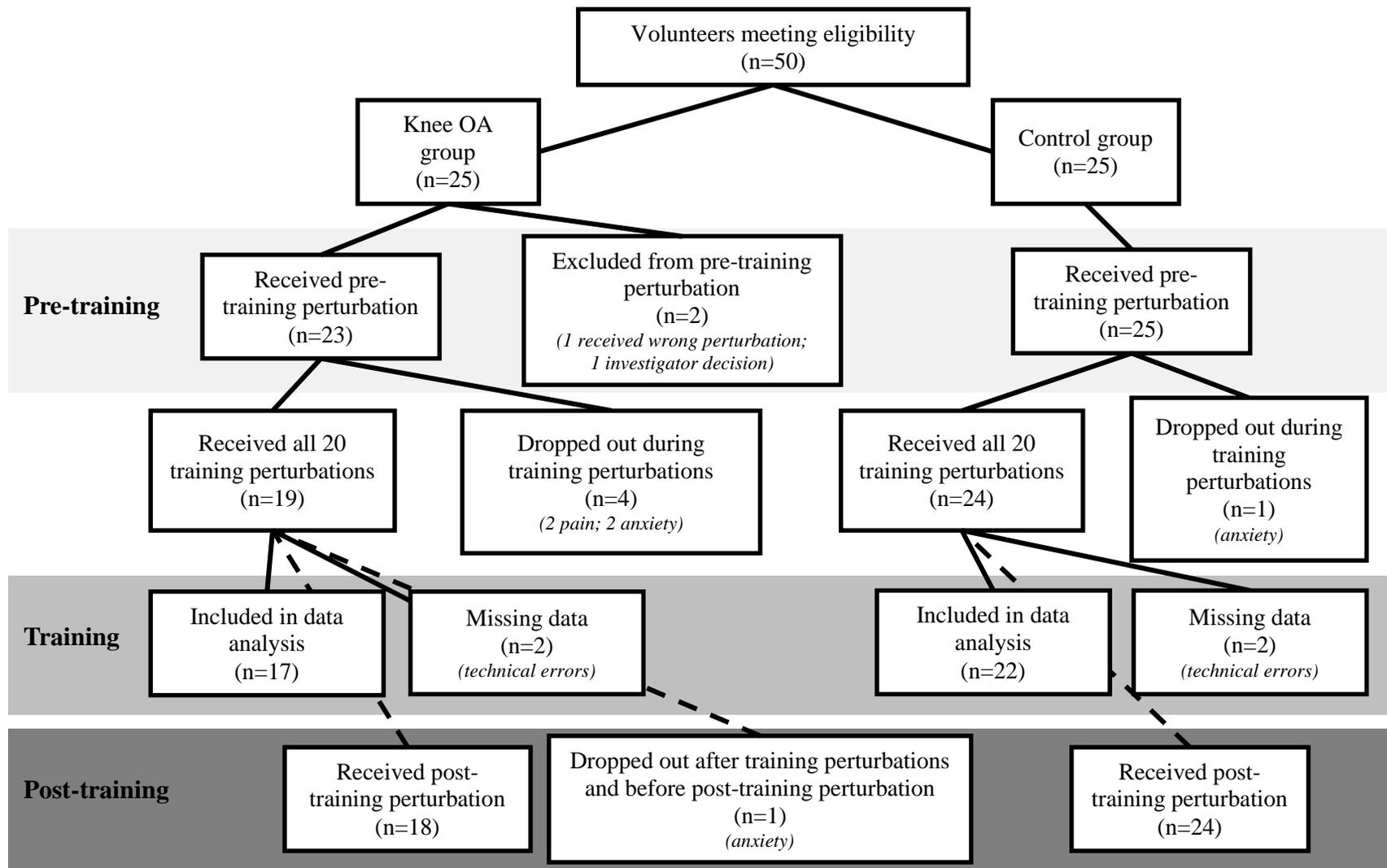
Trunk angle at recovery step completion, trunk angular velocity at recovery step completion, and the initial recovery step length were the key dependent variables of interest given their ability to discriminate fallers from non- fallers following trips (4, 5). Step completion was considered the instant at which the heel or toe (whichever came first) of the recovery foot made contact with the treadmill surface and was manually assessed from the raw motion capture data. Trunk angle (degrees) at recovery step completion was calculated as the trunk angle at the instant the step completion relative to the trunk orientation prior to the perturbation. Trunk angular velocity was computed as the first derivative of the trunk angle at step completion. A negative trunk angular velocity indicated the subject was in trunk extension. Step length was expressed as a percentage of body height and calculated as the distance between the centroids of

the recovery and stance foot at the time of recovery foot contact. Which foot the subject stepped with (most- or least-affected) was also documented for each trial.

#### 4.2.3 **Statistical/data analysis**

All statistical analyses were done using IBM SPSS 22.0 (Aramonk, NY). Significance level for all analyses was set at 0.05. Independent t-tests were used to compare between-group (OA vs. control) subject characteristics, pain scores, and functional test scores (e.g. 10-meter walk test and 5xSST). To compare fall rates between the OA and control groups following the pre- and post-training perturbations, separate chi-squared tests were used. Two women from the OA group did not receive the pre-training perturbation thus were excluded from this analysis (see Figure 11, light grey region). One of these women received a perturbation of different magnitude (technical error), and the second woman was withdrawn from the perturbation-portion of the study by the investigator as it was believed the perturbations could unnecessary pain or anxiety.

To test the first hypothesis that single session of perturbation training would improve the ability of people with knee OA to restore control of the trunk during the initial recovery step and to perform a sufficiently long initial recovery step following large treadmill-delivered postural perturbations, separate paired t-tests were used to assess changes in each recovery kinematic between the pre- and post-training perturbations. Six women dropped out of the study during the training perturbations (see Figure 11). The reasons included: pain (n=2), anxiety (n=3). One woman completed all 20 training disturbances then dropped out prior to receiving the post-training perturbation due to anxiety.

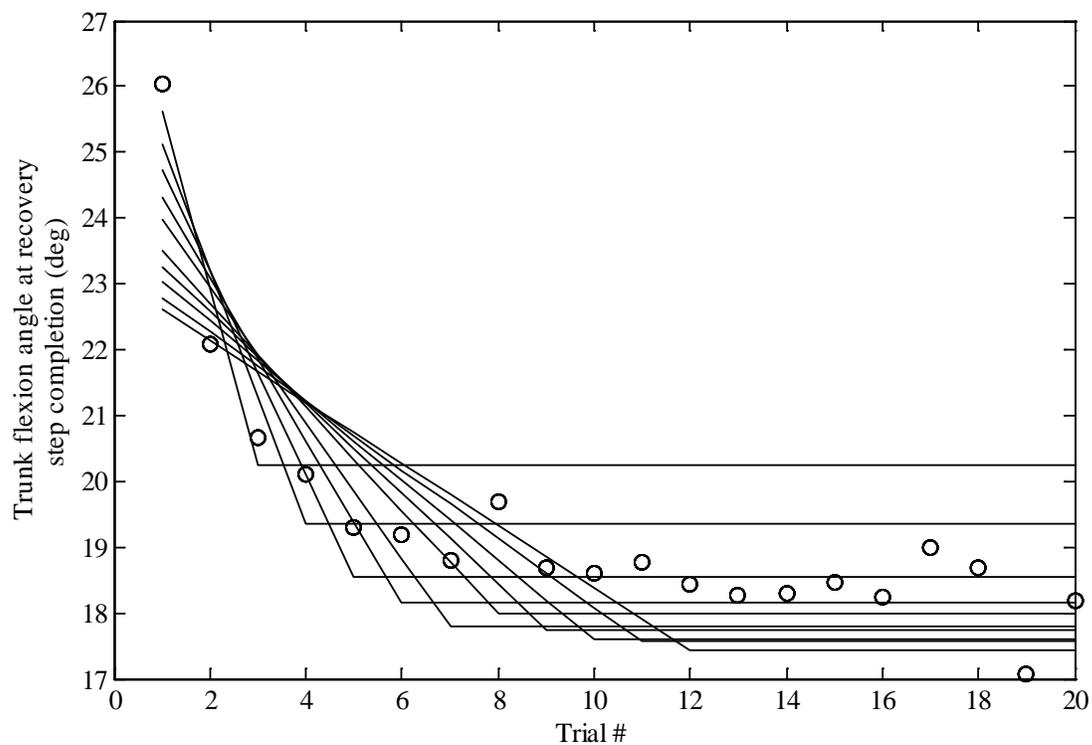


**Figure 11.** Flow chart depicting how many women completed each part of the study. Light grey: pre-training; middle grey: perturbation training; dark grey: post-training. *Italicized font* depicts reasons for dropout/missing data.

To test the second hypothesis that women with knee OA would require the same number of trials to acquire the kinematics associated with successful recovery, and upon skill acquisition, would display greater trial-to-trial variability of recovery kinematics, two separate analyses were carried out, described below.

To determine the number of trials necessary for skill acquisition, a method used by Hurt et al. (described below) (12). Using this method, the data was separated into two blocks according to where the dependent variables (trunk flexion angle at recovery step completion, trunk angular velocity at recovery step completion, and initial step length) plateaued after repeated exposures to the perturbations. To determine the trial at which the average value of the dependent variables plateaued, a piece-wise line-fitting procedure was used where two lines were fit to the performance curves. Performance curves were created using the average value of each dependent variable across subjects for each trial number. The first of the two lines fit to the data was related to the trial-to-trial changes in each dependent variable. This line was fit iteratively from trial 3 to trial 12. The second line represented the plateaued region and extended from the end of the first line, horizontally to the last trial (trial 20) (Figure 12). The line of best fit was selected based on fit with the highest accompanying r-squared value. The trial for which the line transitioned from a sloped to a horizontal line was considered the trial at which the recovery response plateaued and that trial number was noted for each dependent variable. Only women who had data for all 20 trials (n=17 OA and 20 control) were included in this analysis (see Figure 11, middle grey region). Those who did not have 20 trials were either drop-outs or those who had missing trials due to errors in equipment or investigator error. The second analysis addressed the trial-to-trial variability of each recovery kinematic. Variability of the kinematics associated with successful recovery step following skill acquisition was determined by first calculating the

within subject variability (using standard deviation) of the trials in the plateaued region of the performance curve. A group average was computed to determine the average within subject variability for each kinematic for the OA and the control group. Independent t-tests were used to determine differences in the within-subject variability between the OA and control group.



**Figure 12.** Example of the piece-wise line-fitting procedure utilized to determine the trial at which the values for the dependent variable plateaued following repeated perturbations. The fit that resulted in the highest r-squared was determined to be the line of best fit.

### 4.3 **Results**

The physical characteristics of the women who entered the study were similar between the OA and control groups. There were no significant differences in subject age, weight, or height between the two groups (Table X). However, women in the OA group had significantly higher pain scores, lower KOOS scores, slower 10-meter walk speeds, and slower 5-times sit-to-stand test (5xSST) times compared to the control group. Not all women completed all parts of the study (Figure 11). There were significant differences in KOOS score, 5xSST time, and 10 meter walk speed (both preferred and fast) between those who completed the study and those who dropped out. Thus, women who dropped out were characterized by poorer functional mobility, and higher pain and symptom scores compared to those that completed the study ( $p < 0.05$ ) (Table X).

TABLE X. SUBJECT CHARACTERISTICS (MEAN $\pm$ SD) FOR ALL SUBJECTS AND FOR SUBJECTS WHO DID AND DID NOT COMPLETE THE ENTIRE PROTOCOL.

	All subjects		Training	
	Knee OA (n=25)	Control (n=25)	Drop outs n=7 (6 OA)	Completed (n=41)
<b>Age (years)</b>	60.8 $\pm$ 6.9	60.4 $\pm$ 7.8	62.7 $\pm$ 7.2	60.1 $\pm$ 7.5
<b>Height (cm)</b>	163.8 $\pm$ 5.7	163.0 $\pm$ 6.2	164.2 $\pm$ 4.7	163.4 $\pm$ 6.1
<b>Weight (kg)</b>	82.6 $\pm$ 14.4	76.6 $\pm$ 18.9	83.5 $\pm$ 12.2	77.7 $\pm$ 17.0
<b>BMI (kg/m<sup>2</sup>)</b>	30.9 $\pm$ 5.9	28.7 $\pm$ 6.4	31.0 $\pm$ 5.2	29.1 $\pm$ 6.0
<b>VAS (mm)</b>	25.4 $\pm$ 22.4	4.2 $\pm$ 8.0*	25 $\pm$ 31.46	12.7 $\pm$ 16.8
<b>10MW speed (m/s)</b>	1.26 $\pm$ 0.20	1.46 $\pm$ 0.23*	1.18 $\pm$ 0.26	1.40 $\pm$ 0.22*
<b>10MW maximum speed (m/s)</b>	1.68 $\pm$ 0.28	2.00 $\pm$ 0.33*	1.52 $\pm$ 0.43	1.91 $\pm$ 0.30*
<b>5xSST</b>	14.8 $\pm$ 9.1	9.3 $\pm$ 2.5*	20.08 $\pm$ 16.90	10.62 $\pm$ 3.61*
<b>Total KOOS</b>	299.7 $\pm$ 98.2	465.0 $\pm$ 54.5*	237.0 $\pm$ 101.3	417.0 $\pm$ 89.5*

BMI=body mass index; 10MW=10 meter walk; 5xSST= five-time sit-to-stand

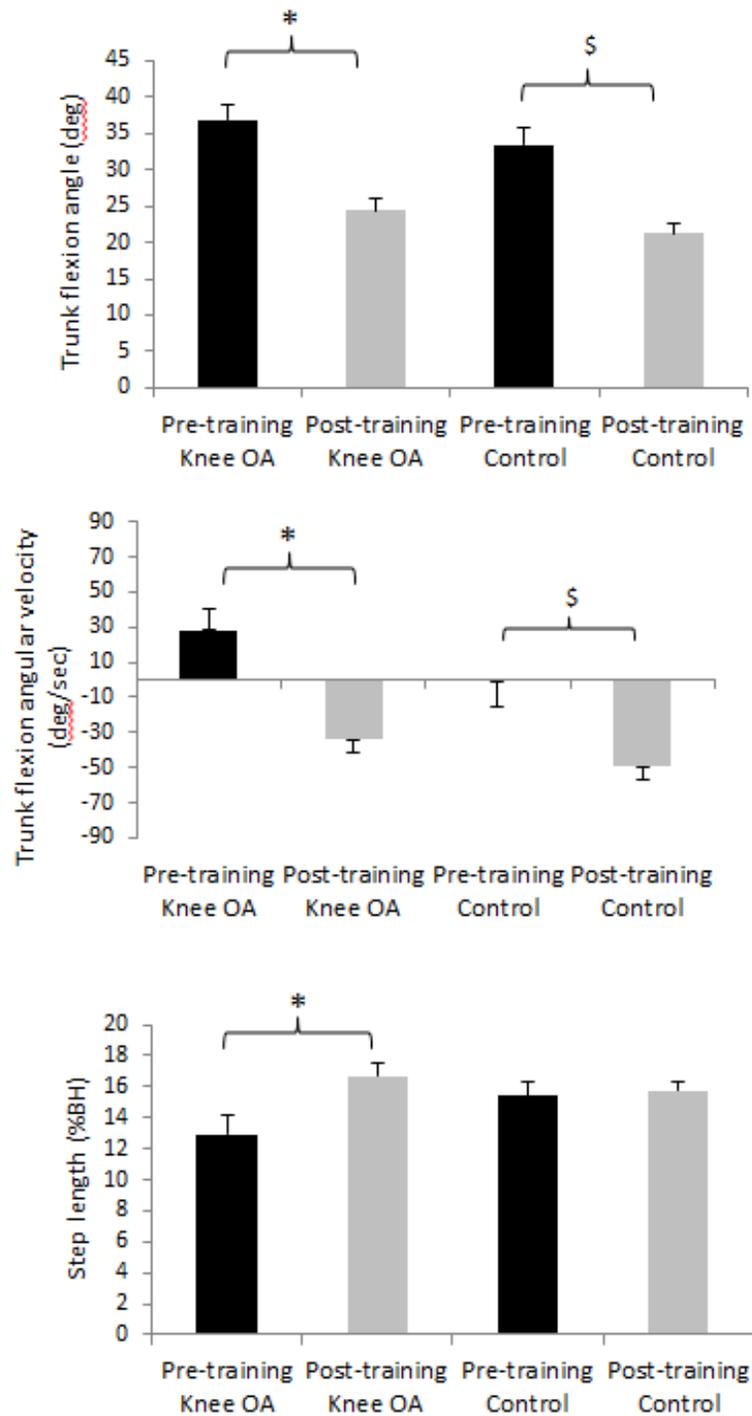
\*p<0.05 (between group differences for all subjects, and separately for those who did and did not complete training)

#### 4.3.1 Recovery step performance from pre- to post-training

Of the 23 women in the OA group that received the pre-training perturbation, seven fell (30.4%) compared to five of 25 (20%) in the control group. The between-group difference in the number of women who fell following the pre-training perturbation was not significant ( $X^2=0.860$ ,  $p=0.35$ )<sup>4</sup>. No women fell after the post-training perturbation (0/18 for the OA group; 0/24 for the control group).

<sup>4</sup> These results are the also reported in Chapter #3, pp. 67

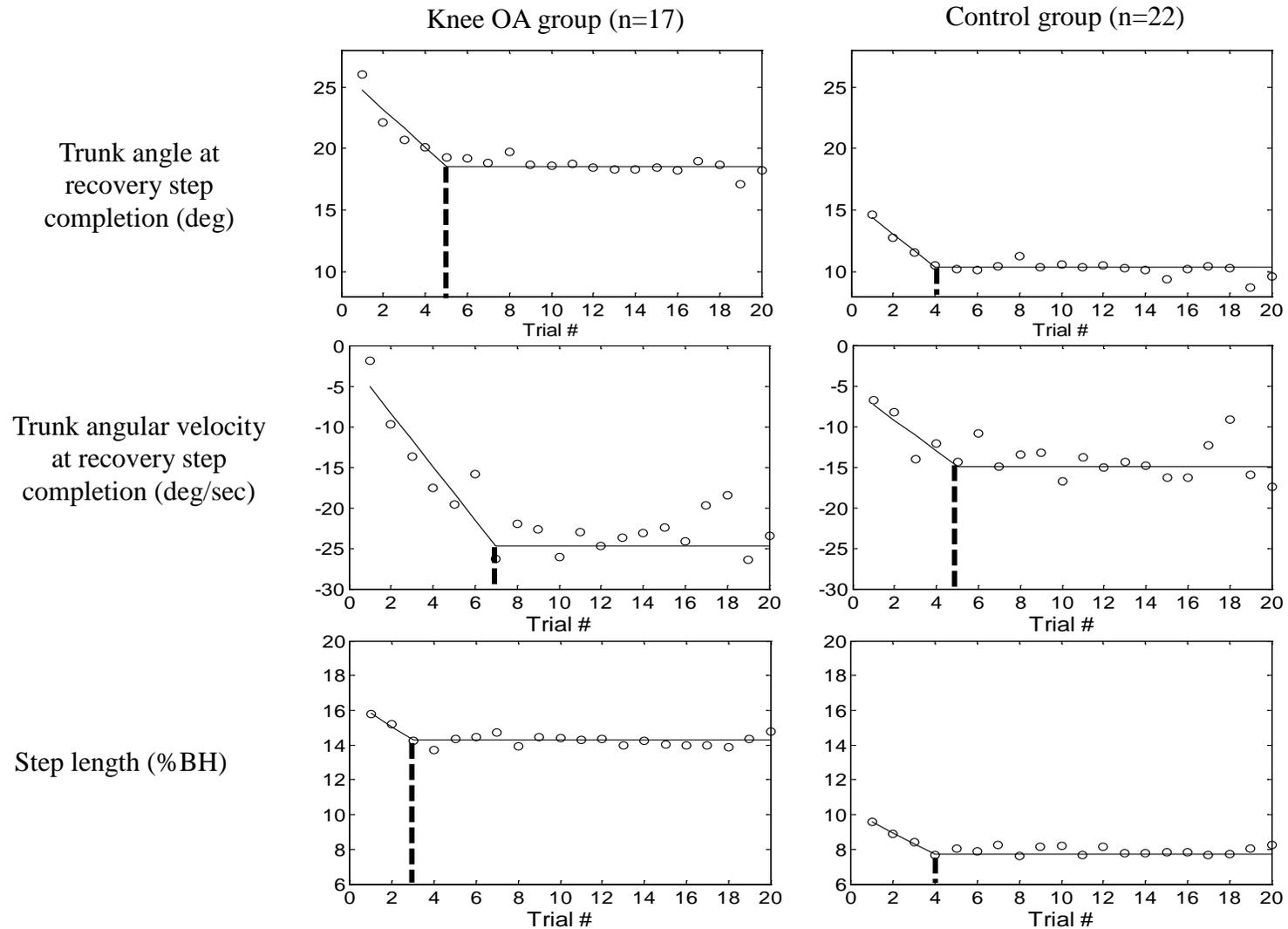
The trunk kinematics following the perturbation for both groups improved after the training (Figure 13). The women in the OA group exhibited a 35% reduction in trunk flexion at recovery step completion ( $23.8 \pm 7.2$  degrees vs.  $36.9 \pm 10.0$  degrees,  $p < 0.001$ ). Further, subjects went from having a trunk flexion velocity at step completion during the pre-training perturbation to a trunk extension velocity, denoted by a negative value, during the post-training perturbation ( $p < 0.001$ ). After training, the step length of the women in the OA group increased more than 20 percent (12.9%BH vs. 16.7%BH,  $p = 0.02$ ). In the control group, trunk flexion angle at recovery step completion decreased 37% percent ( $21.2 \pm 6.9$  vs.  $33.4 \pm 12.9$ ,  $p < 0.001$ ) and trunk extension velocity at recovery step completion improved becoming significantly more negative (i.e. greater trunk extension velocity) ( $p = 0.004$ ). Step length did not change after training by control group women ( $p = 0.78$ ).



**Figure 13.** Mean ( $\pm$ SEM) pre- and post-training kinematics in the OA and control group. Black bars represent the pre-training; grey bars represent post-training. Trunk variables taken at recovery step completion. \*significant differences between the pre- and post-training in the OA group ( $p < 0.05$ ). \$significant differences between the pre- and post-training in the control group ( $p < 0.05$ )

#### 4.3.2 **Skill acquisition and trial-to-trial variability in recovery kinematics**

The stepping response was modified in less than 8 trials in both groups as a result of one session of training (Figure 14). Values for trunk flexion angle and trunk angular velocity improved after the 5<sup>th</sup> and 7<sup>th</sup> trial, respectively in the OA group, and after the 4<sup>th</sup> and 5<sup>th</sup> trial, respectively, for the control group. Step length decreased and plateaued after the first 3 trials for the OA group and after the first 4 trials for the control group. The trial-to-trial variability in the plateaued region was not significantly different between the OA and control group ( $p=0.72, 0.24, 0.59$ , respectively) (Table XI).



**Figure 14.** The effect of training on recovery kinematics following repeated treadmill-delivered postural perturbations is shown for both the OA and control group. Performance curves were created for each recovery step kinematic by plotting the average between-subject value for each trial. Line of best fit for the data is shown. Changes in these variables occurred up to the transition point (where the sloped line becomes horizontal, evidenced by bold dotted line).

TABLE XI. RESULTS OF INDEPENDENT T-TESTS COMPARING THE VARIABILITY (MEAN $\pm$ SD) OF RECOVERY STEP KINEAMTICS AFTER SKILL ACQUISITION (WITHIN THE PLATEAUED REGION) BETWEEN THE OA AND CONTROL GROUP

	OA group (n=17)	Control group (n=22)	p-value
<b><i>Variability after skill acquisition</i></b>			
Trunk flexion/extension angle (deg)	2.86 $\pm$ 1.18	2.72 $\pm$ 1.26	0.718
Trunk angular velocity (deg/sec)	14.72 $\pm$ 4.62	17.37 $\pm$ 8.17	0.239
Step Length (%BH)	1.82 $\pm$ 0.68	1.93 $\pm$ 0.60	0.594

\*p<0.05

#### 4.4 **Discussion**

The primary purpose of this study was to determine whether task-specific perturbation training improves recovery step performance in people with knee OA. The results supported the hypothesis that women with OA can improve recovery kinematics needed for successful trip recovery, specifically by restoring control of the trunk and performing a longer initial recovery step, in one session of perturbation training. A secondary purpose of this study was to determine the rate and extent that women with knee OA were able to learn to perform a successful recovery following a large postural perturbation. The hypothesis that women with knee OA would require the same number of trials to acquire the kinematics associated with successful recovery, and upon skill acquisition, would display greater trial-to-trial variability of recovery kinematics was partially supported. Indeed, both groups acquired the kinematics associated with a successful

recovery response in less than 8 trials, determined as the number of trials before the value of each of the dependent variables (i.e. each recovery kinematic) plateaued. However, contrary to our hypothesis, once the skill was acquired there were no differences in variability of the dependent variables between the OA group and control group. This suggests that women with knee OA can improve their ability to perform recovery stepping responses to the same extent as otherwise healthy middle aged and older women.

Few studies have examined the effect of fall prevention interventions for individuals with OA. These studies have utilized Tai Chi (19, 20), walking programs (21), or water based balance programs (22). In general, these studies have had mixed results in reducing fall risk as measured by timed-up and go test, sit-to-stand test, gait speed, and Berg's balance scale). More importantly these studies did not monitor prospective fall rates following the intervention. Notably, these studies have lacked any specific training of the recovery stepping response, which is required following a large loss of dynamic stability (i.e. a trip or a slip). The current study supports the growing body of evidence that practicing the actual motor skill of performing a successful recovery stepping response to avoid a fall is an effective way to decrease fall risk (23). Indeed, training the recovery stepping response has reduced prospective trip-related falls in healthy middle-aged and older women (6), and has reduced, albeit, non-significantly, the number of prospective falls by frail older men and women (24) and older men (average age = 72 years) with Parkinson's disease (25). Accordingly, using this approach as a fall-prevention intervention may also be appropriate in those with knee OA in reducing the number of prospective falls.

#### **4.4.1 Recovery step performance from pre- to post-training**

The extent to which perturbation training can reduce trip-related fall risk depends on the extent to which the training can modify biomechanical variables associated with successful

recovery following a trip (2). Indeed, following one session of perturbation training during which women receive 20 identical perturbations, each requiring a forward-directed step to recovery dynamic stability, women with knee OA improved step length, trunk flexion angle, and trunk angular velocity by 28%, 34%, and 220% respectively. For those who recovered from the pre-training perturbation, trunk angular velocity was the only variable that was significantly impaired in the OA group compared to a control group, such that those in the OA group displayed a trunk flexion velocity at recovery step completion while the control group displayed a trunk extension velocity (data in chapter#3, pp. 70). Following the training session, women with knee OA were able to modify their trunk kinematics such that, similar to that observed in the control group, they displayed a trunk extension velocity (acting to reverse forward momentum and restore dynamic stability) at recovery step completion. This finding is not surprising as this variable has previously been shown to be amenable to task-specific perturbation training (2, 3), and is encouraging as it suggests that although people with knee OA have impaired kinematics related to control of the trunk, they can be improved to the level of people without knee OA following one session of training.

#### 4.4.2 **Skill acquisition and trial-to-trial variability**

Women in both groups were able to improve key kinematic variables associated with the recovery stepping response as a result of repeated exposure to the perturbations. Women needed no more than 7 trials before the kinematics associated with successful recovery attained a relatively constant value. As mentioned previously, obtaining a consistent level of performance from trial-to-trial suggests an improved level of skill acquisition (11). The number of trials needed before skill acquisition was consistent to results from healthy young adults following repeated laterally-directed perturbations (12). Following 30 repeated laterally-directed treadmill

perturbations, young adults acquired the skill of recovery, assessed by using the same piece-wise fitting method used in this study, within the first 10 trials. The current study was the first to assess skill acquisition of the recovery stepping response following forward-directed perturbations, and in middle aged and older women.

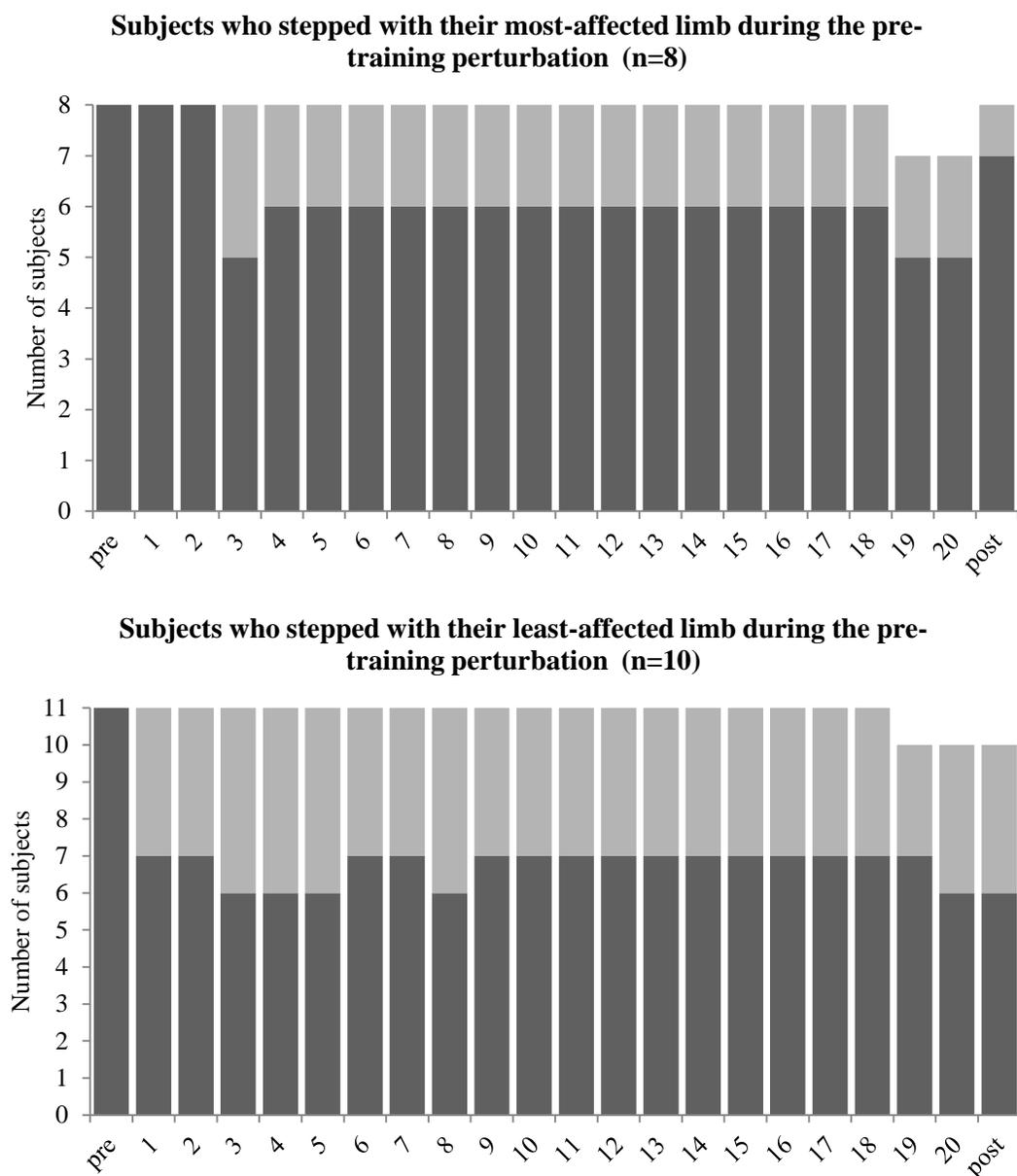
Despite a long recovery step being favorable for successful trip-recovery (4, 5), step length decreased during the training perturbations for both groups. These decreases in step length could reflect adaptation of an alternative recovery strategy, where the individual utilizes multiple short, rapidly executed steps. This could be a beneficial adaptation for women with knee OA, as shorter steps likely reduces the compressive forces acting across the knee joint, which consequently could reduce the possibility of pain during the loading phase of the recovery step. Future studies to address whether specifically training a strategy utilizing short, quick steps in women with OA would result in more favorable outcomes with respect to fall risk are warranted.

Following forward-directed perturbations which simulate trips, the kinematic variability occurring from trial-to-trial had not been directly assessed. As a motor skill is improved, performance is modified towards less variability (13). As mentioned previously, people with knee OA display increased spatial-temporal variability during gait, primarily in step length, which could reflect an inability to reproduce comparable movements from step to step (14). The authors did not speculate as to how knee OA could limit repeatability of movement patterns and future work could be done to identify these potential mechanisms. Contrary to our hypothesis, women with knee OA displayed no differences in the variability of their recovery responses compared to the control group. Consequently, if performance variability is a key indicator of

skill acquisition, then it can be concluded that women with knee OA can acquire the skill of recovery to the same extent as otherwise healthy controls.

#### 4.4.3 **Limb preferences**

A question that arose during the analysis portion of the study was whether women with knee OA had a preference of which foot they used as a recovery stepping foot. It could be hypothesized that women with knee OA would more frequently step with their least-affected limb following a perturbation as the initial weight-bearing phase of the recovery step can result in relatively high compressive and shear loads at the knee joint (26) which could evoke pain, or the anticipation of pain in women with knee OA. A post-hoc observation, however, did not seem to suggest that women with knee OA had a preference on which foot they stepped with when recovering from postural perturbations (Figure 15). In fact, when responding to the pre-training perturbation, 8 of the 19 (42%) women stepped with their most-affected limb compared to 11 of 19 (58%) who stepped with their least-affected limb. A surprising finding was that four women switched from stepping with their least-affected limb prior to the training trials, to their most-affected after completion of the training trials. It is possible that following training, some women with knee OA actually prefer to step with their most-affected limb. This would allow the least-affected limb to act as the support limb, which helps to counteract the forward angular momentum of the body and produce a large moment for push-off before the recovery limb hits the ground (27). Future work that asks individuals with knee OA respond to perturbations using both their most- and least-affected limb, and assesses performance for each, is needed before conclusions are made about limb preference.



**Figure 15.** Limb preferences throughout training session. (Top) For the women who stepped with their most-affected limb during the pre-training perturbation, the figure represents then number of women who stepped with their most-affected vs. in the subsequent training trials. Only one woman (1/8) switched to stepping with her least-affected limb during the post-training perturbation. (Bottom) The same figure is depicted only for women who stepped with their least-affected limb during the pre-training perturbation. Four women (4/11) switched to stepping with their most-affected during the post-training perturbation. Note: trials 19 and 20 for both graphs were missing one subject (missing data) and one subject in the bottom graph did not receive a post-training perturbation.

#### 4.4.4 **Limitations**

There were limitations to the present study that warrant mentioning. First, there were a large number of drop outs. Many of these women dropped out due to anxiety related to the unexpected nature of the disturbances and pain. Those who dropped out had lower functional mobility scores, and higher pain and symptom scores. It is possible that the women who dropped out may have remained in the study if smaller perturbations were used at the beginning of the training which allowed participants to become familiar with the treadmill and the requirements needed to successfully recover. The large number of dropouts suggests that for women with more severe disease, alternative strategies for assessing and training recovery steps may be warranted. Further, the possibility that the repeated nature of the perturbation may cause some subjects to preplan the recovery response cannot be ruled out. Indeed, a previous study has shown that as subjects become more familiar with a repeated postural perturbation, anticipatory responses are detected in later trials which are not observed in initial trials as subjects were able to preplan certain aspects of the recovery response (28). These anticipatory adjustments are generally assessed using forceplate (center of pressure) or electromyographic data, neither of which were utilized in the present study. However, there is no evidence that anticipatory adjustments can affect the recovery stepping response. Finally, only changes occurring over a single session of training were tested, providing no information on the retention or transfer of the skill. The study done by Pai et al., however, shows that a single session of perturbation training produces prospective decreases in all-cause falls (7) suggesting that one session may be sufficient to elicit long-term changes in the skill of performing successful recovery responses, and furthermore, can produce changes in the skill which are also transferable to the community.

#### 4.4.5 **Conclusion**

In summary, a single session of perturbation training significantly improved kinematics related to the recovery stepping response in women with knee OA. This skill was acquired in less than 8 trials, and to the same extent as otherwise healthy middle aged and older women. These findings give utility to the use of task-specific perturbation training to decrease fall risk by women with knee OA. Given that women with knee OA were able to improve kinematics associated with successful recovery to the same extent as women without OA, it is expected that the same task-specific perturbation training protocol (4 sessions of 30 perturbations of increasing magnitude) previously shown to prospectively reduce trip-related falls in middle aged and older adults by 50% (6), could also be effective in reducing prospective fall risk for people with knee OA.

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## 5 Conclusions

The purposes of this dissertation research, which focused on trip-related falls, were to identify the biomechanical risk factors that may be responsible for the increased fall risk of people with knee OA, and to establish if people with knee OA would benefit from an intervention that specifically targets the ability to perform recovery stepping responses. For each chapter, the specific purposes and hypotheses are repeated below:

### *Study 1 (Chapter #2)*

The purposes of this study were to document the occurrences of trip-related falls by people with knee OA compared to a control group and to characterize the relationship between MTC, MTC variability and trip-related falls by people with knee OA

The hypotheses were that (1) people with knee OA would report significantly more trip-related falls in the year preceding their participation in the study compared to the control group, and (2) that MTC would be significantly lower, and MTC variability would be significantly larger, in the OA group compared to the control group.

### *Study 2 (Chapter #3)*

The purpose of this study was to determine the extent to which knee OA negatively affects the recovery stepping response following a laboratory-induced trip and a large treadmill-delivered postural perturbation simulating a trip.

The hypotheses were that (1) women with knee OA would have a higher fall rate compared to a control group following both types of perturbations; (2) recovery kinematics following a laboratory-induced trip and a treadmill-delivered postural

perturbation would be impaired in an OA group compared to a control group; and (3) in women with OA, pain would be significantly associated with recovery kinematics.

*Study 3 (Chapter #4)*

The primary purpose of this study was to determine whether task-specific perturbation training improves recovery step performance in people with knee OA. A secondary purpose of this study was to determine the rate and extent that women with knee OA were able to learn to perform a successful recovery following a large postural perturbation.

The hypotheses were that a single session of perturbation training would improve the ability of people with knee OA to restore control of the trunk during the initial recovery step and to perform a sufficiently long initial recovery step following large treadmill-delivered postural perturbations, and, that women with knee OA would require the same number of trials to acquire the kinematics associated with successful recovery, and upon skill acquisition, would display greater trial-to-trial variability of recovery kinematics.

While many of the hypotheses were not fully supported, some key findings were attained that will drive future research working towards understanding the increased fall risk for people with arthritis. Published literature has consistently reported that people with OA are at a 2.5-times increased fall risk (1-4). Indeed, in the present sample, there was an increased number of retrospectively-reported falls in a group of women self-reporting knee OA group compared to a control group. In healthy older adults, trips, followed by slips, are the most common causes of falls (5). Prior to this dissertation, fall causes had not been reported for people with knee OA.

The present data shows that trips and slips were the predominant causes of self-reported falls in women with knee OA. Nearly two times (24% vs. 48%) as many women in the OA group reported having at least one trip-related fall in the last year compared to the control group (Chapter #2). This suggests that fall causes for women with knee OA may be similar to otherwise healthy older women. In fact, as the current work shows two-times as many women with knee OA sustaining trip related falls, women with knee OA could be at an increased risk for trip-related falls compared to women without OA.

A trip-related fall occurs following a sequence of events. First, during locomotion, an individual's swing foot is impeded by an object causing a stumble/trip (e.g. tripping on a curb or a crack in the sidewalk). Following this initial loss of dynamic stability, the individual is required to perform a compensatory measure, typically a recovery step, to restore dynamic stability and avoid a fall. Having an increase in the number of stumbles/trips, or having impaired recovery step performance would both increase the risk of a trip-related fall occurring by either increasing the number of occasions where a recovery response is necessitated, or by decreasing the likelihood that a recovery response would be successful to avoid a fall. The results from the first study (Chapter #2) show that although two times more women in the OA group reported having one or more trip-related fall(s) in the last year, there were no differences in any MTC measures suggesting that women with knee OA were no more likely to make contact with an unseen object as compared to the women without knee OA. Consequently, this would suggest that the increased trip-related fall risk may be due to inadequate recovery step performance.

Prior to the second study (Chapter #3) of this dissertation, there was no published literature related to the recovery stepping response for people with knee OA. Women with and without knee OA were subjected to two types of large postural perturbations (a laboratory-

induced trip and a treadmill-delivered perturbation), both requiring one or more successful forward-directed recovery steps to avoid a fall, and characterized their recovery abilities and underlying kinematics. Although there was not a higher rate of falls in the OA group following either type of perturbation, the results did report differences in recovery step kinematics between the two groups. Recovery step variables related to control of the trunk have previously been established as important variables for avoiding a trip-related fall (6-8). In particular, trunk angular velocity was significantly impaired in the OA group, such that the OA group was flexing at the trunk at recovery step completion while the control group had already begun to exhibit trunk extension velocity. The trunk extension velocity displayed in the control group reduces the forward- and downward directed angular momentum and contributes to restoring dynamic stability. Another important and interesting finding from this study (Chapter #3) was that 50% of fallers in the OA group failed to initiate a recovery stepping response while all women in the control group initiated a recovery step. The absence of a completed recovery step would result in the failure to reduce forward- and downward-directed angular momentum of the body, potentially contributing to larger ground forces at impact, which could affect the upper extremity and/or hip. Consequently, this may be a contributor to the increased fracture risk reported in those with knee OA (1, 9).

While pain is a primary symptom reported by people with knee OA, contrary to our hypothesis in Chapter #3, pain was not significantly associated with any recovery step kinematics. This could imply that self-reported/perceived knee pain does not influence important biomechanical factors associated with a recovery step following large perturbations. This could also imply that individuals with knee OA prioritize postural responses over attention to perceived pain. This finding also suggests that when assessing fall risk of people with knee OA, those with

lower pain scores should not necessarily be considered at lower fall risk. These findings and implications, however, should be interpreted with caution as the current sample of women with knee OA had low pain scores (the average VAS score was 25 mm, on a scale of 0-100 with 100 being highest pain). Future work is needed to clarify the influence of pain using a sample with a larger range of pain scores to determine if women experiencing high levels of pain related to their knee OA may also prioritize recovery, or whether those with high pain should be considered at higher fall risk than those with low pain.

Chapter #3 also contributed an important and novel finding to the literature related to fall-prevention interventions. Past work on healthy middle aged and older adults has shown repeatedly that the ability to limit trunk motion following both treadmill-delivered and laboratory-induced trips discriminates fallers from non-fallers. The present results show that the biomechanical causes for falls by people with knee OA are consistent with the results from healthy controls. Indeed, similar to that seen in otherwise healthy older adults, fallers in the OA group had a more flexed trunk at recovery step completion, a higher trunk flexion velocity, and a shorter recovery step length following both laboratory-induced trips and treadmill-delivered perturbations compared to non-fallers in the OA group (6, 7). This finding is important as these variables have been shown to be modifiable using task-specific perturbation training (10). As the biomechanical causes for trip-related falls may be similar for those with and without knee OA, trip-specific perturbation training should also be effective to reduce fall risk in women with knee OA.

The final study of this dissertation was the first to utilize a trip-specific perturbation training protocol in a group of women with knee OA (Chapter #4). Indeed, women with knee OA were able to improve key recovery kinematics in as little as one session of trip-specific

perturbation training. While 7/23 OA women and 5/25 control women fell after the initial pre-training perturbation, none fell after delivery of the same disturbance subsequent to receiving 20 training perturbations. During this short training protocol, the motor skill of successful recovery was acquired in less than 10 trials for both groups, as measured by determining the trial at which the value for each recovery kinematic plateaued. Further, trial-to-trial variability in recovery step kinematics upon skill acquisition between the two groups was similar suggesting that middle aged and older women with knee OA can improve recovery kinematics with few exposures, and to the same extent, as the control subjects. These results provide rationale for the use of trip-specific perturbation training to decrease trip-related fall risk by people with knee OA. Given that people with knee OA are able to acquire the kinematics associated with successful recovery with a similar number of trials and to the same extent as healthy controls, it is expected that the 4 sessions of training previously shown to reduce trip-related fall rates prospectively by healthy middle aged and older women by 50% (11), could also be sufficient for people with OA. The extent to which this is true should be tested prospectively.

This dissertation had several limitations which should be addressed. First, the biomechanical mechanisms leading to trip-related falls were only considered. Thus, the results cannot be extended to other types of falls which commonly occur in the community (i.e. slips, knee buckling, etc.). Another limitation was that without the use of radiographs/X-rays, it could not be confirmed that women with knee OA actually had degenerative changes occurring at the joint although they answered “yes” to having been told by a doctor to have knee OA. Similarly, it could not be confirmed that women in the control group did not have OA at the knee although they answered no to questions about pain and whether they had been diagnosed. In the current study, women in the OA group reported a VAS score of  $25.4 \pm 22.4$ , considering these women

with mild-severity OA. Future work should consider women with moderate and/or severe OA to determine if these results are generalizable to a more symptomatic sample who may benefit more-so from the current results. Finally, the current work was underpowered to detect differences in fall-rates as significant. This was anticipated in the design of the study as large sample sizes are required to see significant differences in fall-rates, and consequently, sample size was chosen such that it was powered to detect differences in recovery step kinematics between groups. Despite the limitations of this dissertation, this work is novel as it is the first to study the recovery stepping response in a population which affects nearly 40% of Americans over the age of 60 (12). The positive findings from this preliminary work outline the potential for future work with a larger sample sizes with a larger range of OA severity.

The results of the three studies making up this dissertation are the first attempt to understanding, and addressing, the biomechanical mechanisms behind the increased fall risk by people with OA. It has been well established in the past literature that people with OA, particularly knee OA, are at a higher risk of falls compared to their age-matched counterparts. The results of this dissertation suggest that women with knee OA experience trip-related falls in the community to the same extent as control subjects. This increased risk is likely due to impaired recovery step kinematics – particularly of those related to control of the trunk. Further, one session of trip-specific perturbation training improved these key recovery step kinematics in women with knee OA to the same extent as healthy control subjects. In summary, this dissertation contributes to the existing fall literature as it extends work that has been done in otherwise healthy middle aged and older women to those with knee OA who are at a particularly high fall risk. This work also supports the utility of implementing trip-specific fall prevention interventions, which have been estimated to have the potential to reduce the number of falls by

over 1.1 million per year and annual medical care costs by over US\$580 million (13), to high fall risk populations, particularly those with knee OA.

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10. Grabiner MD, Bareither ML, Gatts S, Marone J, Troy KL: Task-specific training reduces trip-related fall risk in women. Med Sci Sports Exerc 44(12): 2410-2414, 2012
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13. Grabiner MD, Crenshaw JR, Hurt CP, Rosenblatt NJ, Troy KL: Exercise-based fall prevention: Can you be a bit more specific? Exerc Sport Sci Rev 42(4): 161-168, 2014.

## APPENDIX I

### UNIVERSITY OF ILLINOIS AT CHICAGO

Office for the Protection of Research Subjects (OPRS)  
Office of the Vice Chancellor for Research (MC 672)  
203 Administrative Office Building  
1737 West Polk Street  
Chicago, Illinois 60612-7227

#### Approval Notice

#### Initial Review – Expedited Review

May 11, 2012

Mackenzie Hoops, MS  
Department of Kinesiology and Nutrition  
1919 W, Taylor Street  
Room 950 AHSB, M/C 994  
Chicago, IL 60612  
Phone: (312) 413-9432 / Fax: (312) 996-3532

**RE: Protocol # 2012-0425**

**“Trip-related Falls and Knee Osteoarthritis: An issue of frequent tripping or impaired recovery response?”**

Dear Ms. Hoops:

Members of Institutional Review Board (IRB) #1 reviewed and approved your research protocol under expedited review procedures [45 CFR 46.110(b)(1)] on May 10, 2012. You may now begin your research.

Please note the following information about your approved research protocol:

**As previously noted during the initial review, until Rush University Medical Center (RUMC) IRB approval is submitted through an amendment and approved by the UIC IRB, identifiable information may not be shared with your RUMC investigators. Current approved activities are limited to activities that do not engage RUMC in your research -- recruitment and release of patient health information through the subjects' authorization via the informed consent/authorization document.**

**Protocol Approval Period:** May 10, 2012 - May 9, 2013

**Approved Subject Enrollment #:** 60 Total

**Additional Determinations for Research Involving Minors:** These determinations have not been made for this study since it has not been approved for enrollment of minors.

**Performance Sites:** UIC, *\*Rush University Medical Center*

**Sponsor:** None

**Research Protocol(s):**

- a) Trip-Related Falls and Knee Osteoarthritis: An Issue of Frequent Tripping or Impaired Recovery Response?- Research Protocol, Version 1.1, 5/10/2012

**Recruitment Material(s):**

- a) Internet Advertisement: Knee Osteoarthritis and Falls Study, Version 1.1, 5/10/2012
- b) Flyer: "Research Subjects with Knee Osteoarthritis Needed" version 1.1, 5/10/2012
- c) Flyer: "Research Subjects Needed 45 Years or Older" Version 1.1, 5/10/2012
- d) Recruitment Script: "Some researchers at UIC..." (to be used by RUMC Clinicians), Version 1.1, 5/10/2012

**Informed Consent/ HIPAA Authorization (s):**

- a) Alteration of Informed Consent, Telephone Script: Knee Osteoarthritis and Falls Study, Version 1.0, 5/8/2012
- b) Waiver of Documentation of Signed Informed Consent granted under [45 CFR 46.117 (c)] for recruitment and telephone screening
- c) Combined Consent/Authorization: Knee Osteoarthritis and Falls Study: Control Subjects, Version 1.0, 5/08/2012
- d) Combined Consent/Authorization: Knee Osteoarthritis and Falls Study: Patient Subjects, Version 1.0, 5/08/2012

Your research meets the criteria for expedited review as defined in 45 CFR 46.110(b)(1) under the following specific category: 4, 5, 6

**(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving X-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)**

**Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.,**

**(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis),.**

**(6) Collection of data from voice, video, digital, or image recordings made for research purposes.**

Please note the Review History of this submission:

Receipt Date	Submission Type	Review Process	Review Date	Review Action
05/09/2012	Initial Review	Expedited	05/10/2012	Approved

Please remember to:

**→ Use only the IRB-approved and stamped consent document(s) enclosed with this letter when enrolling new subjects.**

**→ Use your research protocol number (2012-0425) on any documents or correspondence with the IRB concerning your research protocol.**

**→ Review and comply with all requirements of the, "UIC Investigator Responsibilities, Protection of Human Research Subjects"**

**Please note that the UIC IRB has the right to ask further questions, seek additional information, or monitor the conduct of your research and the consent process.**

**Please be aware that if the scope of work in the grant/project changes, the protocol must be amended and approved by the UIC IRB before the initiation of the change.**

We wish you the best as you conduct your research. If you have any questions or need further help, please contact the OPRS office at (312) 996-1711 or me at (312) 355-1404. Please send any correspondence about this protocol to OPRS at 203 AOB, M/C 672.

Sincerely,

Sheilah R. Graham, BS

IRB Coordinator, IRB # 1

Office for the Protection of Research Subjects

Enclosure(s):

- 1. UIC Investigator Responsibilities, Protection of Human Research Subjects**
- 2. Informed Consent Document/HIPAA Authorization (s):**
  - a) Combined Consent/Authorization: Knee Osteoarthritis and Falls Study: Control Subjects, Version 1.0, 5/08/2012
  - b) Combined Consent/Authorization: Knee Osteoarthritis and Falls Study: Patient Subjects, Version 1.0, 5/08/2012
  - c) Alteration of Informed Consent, Telephone Script: Knee Osteoarthritis and Falls Study, Version 1.0, 5/8/2012
- 3. Recruiting Material(s):**
  - a) Internet Advertisement: Knee Osteoarthritis and Falls Study, Version 1.1, 5/10/2012
  - b) Flyer: "Research Subjects with Knee Osteoarthritis Needed" version 1.1, 5/10/2012
  - c) Flyer: "Research Subjects Needed 45 Years or Older" Version 1.1, 5/10/2012
  - d) Recruitment Script: "Some researchers at UIC..." (to be used by RUMC Clinicians), Version 1.1, 5/10/2012
- 4. Data Security Enclosure**

cc: Mark D. Grabiner, Faculty Sponsor, Kinesiology and Nutrition, M/C 994  
Charles B. Walter, Department of Kinesiology and Nutrition, M/C 517

## APPENDIX II

### UNIVERSITY OF ILLINOIS AT CHICAGO

Office for the Protection of Research Subjects (OPRS)  
Office of the Vice Chancellor for Research (MC 672)  
203 Administrative Office Building  
1737 West Polk Street  
Chicago, Illinois 60612-7227

#### Approval Notice

#### Continuing Review (Response To Modifications)

April 26, 2013

Mackenzie Hoops

Department of Kinesiology and Nutrition

1919 W, Taylor Street

Room 650 AHSB, M/C 994

Chicago, IL 60612

Phone: (312) 413-9432 / Fax: (312) 996-3532

**RE: Protocol # 2012-0425**

**“Trip-related Falls and Knee Osteoarthritis: An issue of frequent tripping or impaired recovery response?”**

Dear Ms. Hoops:

Your Continuing Review (Response To Modifications) was reviewed and approved by the Expedited review process on April 25, 2013. You may now continue your research.

Please note the following information about your approved research protocol:

**Protocol Approval Period:**

May 9, 2013 - May 9, 2014

**Approved Subject Enrollment #:** 60 (13 enrolled to date)

**Additional Determinations for Research Involving Minors:** These determinations have not been made for this study since it has not been approved for enrollment of minors.

**Performance Sites:** UIC, Rush University Medical Center

**Sponsor:** None

**Research Protocol(s):**

- b) Trip-Related Falls and Knee Osteoarthritis: An Issue of Frequent Tripping or Impaired Recovery Response?- Research Protocol, Version 3.1, 2/4/2013

**Recruitment Material(s):**

- e) Internet Advertisement: Knee Osteoarthritis and Falls Study, Version 1.1, 5/10/2012
- f) Flyer: "Research Subjects with Knee Osteoarthritis Needed" version 1.1, 5/10/2012
- g) Flyer: "Research Subjects Needed 45 Years or Older" Version 1.1, 5/10/2012
- h) Recruitment Script: "Some researchers at UIC.." (to be used by RUMC Clinicians), Version 1.1, 5/10/2012
- i) Flyer: "Research Subjects with Knee Osteoarthritis Needed" Adults 45 years of age or older, Version 1.1, 11/06/2012

**Informed Consent/HIPAA Authorization(s):**

- e) Alteration of Informed Consent, Telephone Script: Knee Osteoarthritis and Falls Study, Version 1.0, 5/8/2012
- f) Waiver of Documentation of Signed Informed Consent granted under [45 CFR 46.117 (c)] for recruitment and telephone screening
- g) Combined Consent/Authorization: Knee Osteoarthritis and Falls Study: Control Subjects, Version 2.2, 3/12/2013
- h) Combined Consent/Authorization: Knee Osteoarthritis and Falls Study: Patient Subjects, Version 2.2, 3/12/2013

Your research meets the criteria for expedited review as defined in 45 CFR 46.110(b)(1) under the following specific categories:

**(4)** Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving X-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.),

**(5)** Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis),.

(6) Collection of data from voice, video, digital, or image recordings made for research purposes.

**Please note the Review History of this submission:**

Receipt Date	Submission Type	Review Process	Review Date	Review Action
04/17/2013	Continuing Review	Expedited	04/22/2013	Modifications Required
04/24/2013	Response To Modifications	Expedited	04/25/2013	Approved

Please remember to:

→ Use your **research protocol number** (2012-0425) on any documents or correspondence with the IRB concerning your research protocol.

→ Review and comply with all requirements on the enclosure,

**"UIC Investigator Responsibilities, Protection of Human Research Subjects"**

*(<http://tiger.uic.edu/depts/ovcr/research/protocolreview/irb/policies/0924.pdf>)*

**Please note that the UIC IRB has the prerogative and authority to ask further questions, seek additional information, require further modifications, or monitor the conduct of your research and the consent process.**

**Please be aware that if the scope of work in the grant/project changes, the protocol must be amended and approved by the UIC IRB before the initiation of the change.**

We wish you the best as you conduct your research. If you have any questions or need further help, please contact OPRS at (312) 996-1711 or me at (312) 996-0865. Please send any correspondence about this protocol to OPRS at 203 AOB, M/C 672.

Sincerely,

Tricia Hermanek, BS

IRB Coordinator, IRB # 1

## Office for the Protection of Research Subjects

Enclosure(s):

**5. Informed Consent Document/HIPAA Authorization(s):**

- d) Combined Consent/Authorization: Knee Osteoarthritis and Falls Study: Control Subjects, Version 2.2, 3/12/2013
- e) Combined Consent/Authorization: Knee Osteoarthritis and Falls Study: Patient Subjects, Version 2.2, 3/12/2013
- f) Alteration of Informed Consent, Telephone Script: Knee Osteoarthritis and Falls Study, Version 1.0, 5/8/2012

**6. Recruiting Material(s):**

- e) Internet Advertisement: Knee Osteoarthritis and Falls Study, Version 1.1, 5/10/2012
- f) Flyer: "Research Subjects with Knee Osteoarthritis Needed" version 1.1, 5/10/2012
- g) Flyer: "Research Subjects Needed 45 Years or Older" Version 1.1, 5/10/2012
- h) Recruitment Script: "Some researchers at UIC.." (to be used by RUMC Clinicians), Version 1.1, 5/10/2012
- i) Flyer: "Research Subjects with Knee Osteoarthritis Needed" Adults 45 years of age or older, Version 1.1, 11/06/2012

cc: Charles B. Walter, Department of Kinesiology and Nutrition, M/C 517  
Mark D. Grabiner, Faculty Sponsor, M/C 994

**APPENDIX III**

UNIVERSITY OF ILLINOIS  
AT CHICAGO

Office for the Protection of Research Subjects (OPRS)  
Office of the Vice Chancellor for Research (MC 672)  
203 Administrative Office Building  
1737 West Polk Street  
Chicago, Illinois 60612-7227

**Approval Notice**  
**Continuing Review**

April 22, 2014

Mackenzie L. Pater, MS  
Department of Kinesiology and Nutrition  
1919 W, Taylor St., Rm 650, AHSB, M/C 994  
Chicago, IL 60612  
Phone: (312) 413-9432 / Fax: (312) 996-0319

**RE: Protocol # 2012-0425**

**“Trip-related Falls and Knee Osteoarthritis: An issue of frequent tripping or impaired recovery response?”**

Dear Ms. Pater:

Your Continuing Review was reviewed and approved by Members of IRB #1 by the Expedited review process on April 18, 2014. You may now continue your research.

Please note the following information about your approved research protocol:

<b><u>Protocol Approval Period:</u></b>	May 9, 2014 - May 9, 2015
<b><u>Approved Subject Enrollment #:</u></b>	80 (21 enrolled to date)

**Additional Determinations for Research Involving Minors:** These determinations have not been made for this study since it has not been approved for enrollment of minors.

**Performance Sites:** UIC, Rush University Medical Center

**Sponsor:** National Institutes of Health (NIH)

**PAF#:** 2013-02904

**Grant/Contract No:** 11278230

**Grant/Contract Title:** Ruth L. Krischstein National Research Service Awards

**Research Protocol(s):**

- c) Trip-Related Falls and Knee Osteoarthritis: An Issue of Frequent Tripping or Impaired Recovery Response?- Research Protocol, Version 7.2, 3/03/2014

**Recruitment Material(s):**

- j) Flyer: "Seeking Research Subjects living with Knee Osteoarthritis" version 2.0, 2/20/2014
- k) Flyer: "Seeking Research Subjects 50 Years or Older" Version 2.0, 2/20/2014
- l) Recruitment Script: "Some researchers at UIC.." (to be used by RUMC Clinicians), Version 2.1, 3/03/2014
- m) Internet Advertisement: Knee Osteoarthritis and Falls Study, Version 2.1, 3/03/2014
- n) Flyer: "Seeking Women with and without Knee Osteoarthritis for a research study" Women 50 years of age or older, Version 2.0, 2/20/2014
- o) Knee Osteoarthritis and Falls Study, Telephone Script, Version 2.1, 3/03/2014
- p) Letter/email to health professional/clinician, Version 1.1, 3/03/2014

**Informed Consent(s):**

- i) Alteration of Informed Consent, Telephone Script: Knee Osteoarthritis and Falls Study, Version 1.0, 5/8/2012
- j) Waiver of Documentation of Signed Informed Consent granted under [45 CFR 46.117 (c)] for recruitment and telephone screening
- k) Combined Consent/Authorization: Knee Osteoarthritis and Falls Study: Control Subjects, Version 6.2, 3/03/2014
- l) Combined Consent/Authorization: Knee Osteoarthritis and Falls Study: Patient Subjects, Version 6.2, 3/03/2014

Your research continues to meet the criteria for expedited review as defined in 45 CFR 46.110(b)(1) under the following specific categories:

**(4)** Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving X-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

- (5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis),.
- (6) Collection of data from voice, video, digital, or image recordings made for research purposes.

**Please note the Review History of this submission:**

Receipt Date	Submission Type	Review Process	Review Date	Review Action
04/14/2014	Continuing Review	Expedited	04/18/2014	Approved

Please remember to:

→ Use your **research protocol number** (2012-0425) on any documents or correspondence with the IRB concerning your research protocol.

→ Review and comply with all requirements on the enclosure,

**"UIC Investigator Responsibilities, Protection of Human Research Subjects"**

*(<http://tiger.uic.edu/depts/ovcr/research/protocolreview/irb/policies/0924.pdf>)*

**Please note that the UIC IRB has the prerogative and authority to ask further questions, seek additional information, require further modifications, or monitor the conduct of your research and the consent process.**

**Please be aware that if the scope of work in the grant/project changes, the protocol must be amended and approved by the UIC IRB before the initiation of the change.**

We wish you the best as you conduct your research. If you have any questions or need further help, please contact OPRS at (312) 996-1711 or me at (312) 355-2939. Please send any correspondence about this protocol to OPRS at 203 AOB, M/C 672.

Sincerely,

Jewell Hamilton, MSW

IRB Coordinator, IRB # 1

Office for the Protection of Research Subjects

Enclosure(s):

**7. Informed Consent Document(s):**

- g) Combined Consent/Authorization: Knee Osteoarthritis and Falls Study: Control Subjects, Version 6.2, 3/03/2014
- h) Combined Consent/Authorization: Knee Osteoarthritis and Falls Study: Patient Subjects, Version 6.2, 3/03/2014

**8. Recruiting Material(s):**

- j) Flyer: "Seeking Research Subjects living with Knee Osteoarthritis" version 2.0, 2/20/2014
- k) Flyer: "Seeking Research Subjects 50 Years or Older" Version 2.0, 2/20/2014
- l) Recruitment Script: "Some researchers at UIC.." (to be used by RUMC Clinicians), Version 2.1, 3/03/2014
- m) Internet Advertisement: Knee Osteoarthritis and Falls Study, Version 2.1, 3/03/2014
- n) Flyer: "Seeking Women with and without Knee Osteoarthritis for a research study" Women 50 years of age or older, Version 2.0, 2/20/2014
- o) Knee Osteoarthritis and Falls Study, Telephone Script, Version 2.1, 3/03/2014
- p) Letter/email to health professional/clinician, Version 1.1, 3/03/2014

cc: Charles B. Walter, Department of Kinesiology and Nutrition, M/C 517  
Mark D. Grabiner, Faculty Sponsor, Kinesiology and Nutrition, M/C 994  
OVCR Administration, M/C 672

## CURRICULUM VITA

# Mackenzie L. Pater, MS

Clinical Biomechanics and Rehabilitation Laboratory  
Department of Kinesiology and Nutrition  
University of Illinois - Chicago  
mhoops2@uic.edu  
lab phone: 312-413-9432

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### Education

- Graduate*  
2011-present      **University of Illinois at Chicago**, Ph.D. (Kinesiology)  
Chicago, IL  
Advisor: Dr. Mark D. Grabiner  
GPA: 3.9  
Dissertation topic: *Modifiable Fall Risk Factors in People with Knee Osteoarthritis*  
Awards: NIH NRSA F31 Fellowship
- Graduate*  
2009-2011      **Wake Forest University**, M.S. (Health and Exercise Science)  
Winston-Salem, NC  
Advisor: Dr. Stephen P. Messier  
GPA: 3.808  
Thesis: *The Influence of Obesity and Alignment on Knee Joint Loads during Osteoarthritic Gait*
- Undergraduate*  
2005-2009      **University of Dayton**, B.S. (Pre-Physical Therapy)  
Dayton, OH  
Advisor: Dr. Paul Vanderburgh  
GPA: 3.49 (overall); 3.79 (major)  
Undergraduate Thesis: *Age, Sex, and Finish Time as Determinants of Pacing in the Marathon*
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### Research Experience

**2011-present    UIC Clinical Biomechanics Research Laboratory**

*NIH Pre-doctoral fellow, Research Assistant*

**Projects:** fall risk factors by individuals living with lower extremity osteoarthritis; recovery stepping performance in stroke victims; influence of attention/distraction on recovery stepping performance; feed-forward responses to slippery surfaces

**Skills:** data collection using motion capture systems, force plates, instrumented treadmills, EMG systems; strength testing using BioDex; custom coding in Matlab for data processing; IRB communications; knowledge of recovery step kinematics in response to trips and slips; protocol development; monitoring/supervising undergraduate research assistants

**2009-2011 J.B. Snow Biomechanics Laboratory; Wake Forest University**

*Research Assistant, Biomechanics Lab Technician*

**Projects:** effect of weight loss through diet and exercise on joint loads and inflammatory biomarkers in individuals living with knee osteoarthritis; causes of overuse injuries in runners; reliability testing for anthropometric and strength testing

**Skills:** lab management; data collection using motion capture system; rearfoot motion processing using KinTrak; knowledge with running and walking mechanics; strength testing using isokinetic dynamometer (KinCom); anthropometric measurements; development of manual of operations

**2008-2009 United States Army Research Institute for Environmental Medicine (USARIEM), Natick, MA**

*Summer Biomechanics Lab Intern*

**Projects:** influence of soldier load carriage on lower extremity injury; knee injury prevention for female college athletes, forced cadence walking/marching

**Skills:** data collection using 3D and 2D motion capture systems, forceplates, dual force-plate treadmill; EMG; ParvoMedics metabolic cart; protocol development; literature searches; laboratory tours

**2009 Department of Health and Sports Sciences; University of Dayton**

*Undergraduate Research Assistant*

**Project:** determine the influences of age, sex, and run time on marathon pacing

**Skills:** data management; data mining; data analysis; poster presentation

### **Professional/Teaching Experience**

#### **2011-2013      University of Illinois at Chicago Department of Kinesiology and Nutrition**

*Graduate Instructor:* Fundamentals of Motion Capture for Movement Analysis

An new course for upper level undergraduate Kinesiology students focusing on the fundamentals of collecting data of human movement. Includes motion capture, force plate data, and EMG analysis as well as research methods and professional research presentations.

**Responsibilities:** Course development, course manual development, lecture delivery and development, assistance to students on data collection methods, as well as interpreting results and formulating a testable research hypothesis and a professional presentation to present their findings.

*Teaching Assistant:* Biomechanics of the Neuromusculoskeletal System; Aging and the *Neuromusculoskeletal System*

**Responsibilities:** weekly office hours; tutoring; grade homeworks/exams

*Guest Lecturer:* Human Anatomy and Physiology; Biomechanics of the Neuromusculoskeletal System; Aging and the *Neuromusculoskeletal System*

#### **2010-2011      Wake Forest University Department of Health and Exercise Sciences**

*Teaching Assistant:* Graduate and Undergraduate Biomechanics Lab

**Responsibilities:** Assist with Graduate Biomechanics Lab on isokinetic testing, 3D motion analysis with video and force platform systems, and anthropometric measures. Instructing and consulting Undergraduates through a Motion Capture workshop with instruction on 2-dimensional motion capture and digitizing.

#### **2009-2011      Wake Forest Healthy Exercise and Lifestyles ProgramS (HELPS)**

*Supervisor/Exercise Leader*

**Responsibilities:** instruct patients with exercise and rehabilitation equipment; provide modalities such as resting and exercise EKG; greet patients; maintain clean facility; graded exercise testing

**2007-2008**      **Miami Valley Hospital, Dayton, OH**

*Physiotherapy Volunteer*

**Responsibilities:** Observed physical and occupational therapists; interacted with patients

**2006**              **University of Dayton**

*Adapted Physical Education*

**Responsibilities:** Assisted young girls (3<sup>rd</sup> - 4<sup>th</sup> grade) with special needs to improve physical fitness working to improve flexibility, strength, and endurance primarily; worked on developing psychosocial relationships

## **Presentations and Manuscripts**

### **Publications**

- 1) March DS, Vanderburgh PM, Titlebaum PJ, **Hoops ML**. Age, Sex, And Finish Time as Determinants of Pacing in the Marathon. *Journal of Strength and Conditioning Research*, 2010; 25(2): 286-91.
- 2) **Hoops ML**, Rosenblatt NJ, Hurt CP, Crenshaw J, Grabiner MD. Does lower extremity osteoarthritis exacerbate risk factors for falls in older adults? *Women's Health*. 2012; 8(6): 685-698.
- 3) Messier SP, **Pater ML**, Legault C, Loeser RF, Hunter DJ, Holt R, DeVita P. Influence of Alignment and Obesity on Knee Joint Loading in Osteoarthritic Gait. *Osteoarthritis and Cartilage*, 2014(22): 912-917.
- 4) **Pater ML**, Rosenblatt NJ, Grabiner MD. Expectation of an upcoming large postural perturbation influences the recovery stepping response and outcome. *Gait and Posture*, In press.
- 5) **Pater ML**, Rosenblatt NJ, Grabiner MD. Knee osteoarthritis negatively affects the recovery step following large forward-directed postural disturbance (In preparation).

### **Invited Presentations**

- 1) **Hoops ML**. Soldier Load Carriage: More harm than benefit? Graduate Biomechanics Symposium, Wake Forest University, November 2009.
- 2) **Hoops ML**, Grabiner MD. Risk factors for falls in patients with lower extremity OA - what distinguishes these from age-related risk factors? Rheumatology Research Conference, Rush University Medical Center, Chicago, IL. January 2011.

- 3) Grabiner MD, **Pater ML**, Rosenblatt NJ, Wilson KA. Evidence-based construction of a task-specific fall-prevention intervention. World Congress of Biomechanics, July 2014.
- 4) **Pater ML**. Associating knee osteoarthritis with fall risk. Applied Health Science Cells to Community Research Day, University of Illinois at Chicago, Chicago IL, September 2014.

### Poster Presentations

- 1) **Hoops ML**, Vanderburgh PM, Laubach LL, Titlebaum PJ, March DS. Age, Sex, and Finish Time as Determinants of Pacing in the Marathon. Standard Symposium, University of Dayton, April 2009.
  - 2) **Hoops ML**, Vanderburgh PM, Laubach LL, Titlebaum PJ, March DS. Age, Sex, and Finish Time as Determinants of Pacing in the Marathon. 56th Annual meeting of the American College of Sports Medicine, Seattle, WA, May 2009.
  - 3) Schacht E, **Hoops ML**, Munsey M, Newman J, Messier SP. Test-retest reliability of measurements of quadriceps angle and hip abduction strength. Meeting of the Minds, Wake Forest University, March 2011.
  - 4) Messier SP, **Hoops ML**, Lagault C, Loeser RF, Hunter DH, DeVita P. The Interaction of Malalignment and Obesity in Knee Osteoarthritis: Does it Exacerbate Knee Joint Loading? World Congress on Osteoarthritis, San Diego, CA, September 2011.
  - 5) **Hoops ML**, Rosenblatt NJ, Skořichet A, Grabiner MD. Knee Moments During a Compensatory Step: Implications for knee joint loading in patients with knee osteoarthritis. American Society of Biomechanics Annual Meeting, Gainesville, FL, September 2012.
  - 6) Schmit, C, Grabiner MD, Rosenblatt NJ, **Hoops ML**, Searer D. Learning to Perform a Precision Backward-directed Step. Student Research Forum, University of Illinois at Chicago, April 2013.
  - 7) Szukala R, Wadaw AJ, Brimm N, Skořichet AD, Rosenblatt NJ, **Hoops ML**, Grabiner MD. Step Width Variability during Treadmill Locomotion. Student Research Forum, University of Illinois at Chicago, April 2013.
  - 8) **Pater ML**, Rosenblatt NJ, Grabiner MD. An attention diverting task negatively affects recovery step kinematics and fall incidence. American Society of Biomechanics Annual Meeting, Omaha, NE, September 2013.
  - 9) Rosenblatt NJ, Bauer A, Rotter D, **Pater ML**, Grabiner MD. Active Dorsiflexing Prostheses May Reduce Trip-Related Fall Risk. American Society of Biomechanics Annual Meeting, Omaha, NE, September 2013.
  - 10) Grabiner MD, **Pater ML**, Rosenblatt NJ. A brief history of evidence-based design of fall-risk assessment and fall-prevention intervention in the CBR laboratory. Applied Health Science Research Day, University of Illinois at Chicago, November 2014.
  - 11) Brinlee A, **Pater ML**, Rosenblatt NJ, Sridher A. Mediolateral gait kinematics of young adults walking over a known slippery surface. University of Illinois at Chicago Honors College Research Symposium, November 2014.
  - 12) **Pater ML**, Rosenblatt NJ, Grabiner MD. Knee osteoarthritis affects the recovery stepping response following a large postural perturbation. Orthopedic Research Society Annual Meeting, Las Vegas, NV, March 2015 (Accepted).
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**Funded Grants**

**2013-2015**                    **Pater ML** (PI). *Associating knee osteoarthritis with fall risk: implications for interventions*. Ruth L. Kirschstein pre-doctoral fellowship (F31), National Institute of Health

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**Certifications**

**2007**                    CPR and AED, American Heart Association  
**2013**                    HIPAA

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**Professional Memberships/Conference Attendance**

**2005-2010**                    American College of Sports Medicine  
**2012-Present**                    American Society of Biomechanics  
**2012-Present**                    Osteoarthritis Research Society International  
**2013-Present**                    Orthopedic Research Society

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**Journal Reviewing**

**2012-Present**                    Gait and Posture  
**2013-Present**                    Journal of Multidisciplinary Healthcare  
**2013-Present**                    Medicine & Science in Sports and Exercise  
**2015-Present**                    PLOS ONE

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**Laboratory Instrumentation and Software**

3D Motion Analysis Systems (Cortex, Qualysis, Orthotrak, KinTrak)  
 Dartfish Motion Analysis (2D)  
 Simbex ActiveStep (operation and disturbance profile development)  
 Isokinetic Dynamometers (Biodex, KinCom)  
 Noraxon telemetered electromyography system  
 AMTI force platform  
 Force plate instrumented treadmill  
 MATLAB software  
 SPSS statistical software software  
 SAS statistics software  
 Microsoft Office software