

Understanding the Importance of Fear of Movement on Physical Activity and Physical Function
in
People with Knee Osteoarthritis

by

Huaning Liu

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Author's Declaration:

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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ABSTRACT:

Pain is the main reason why people with knee osteoarthritis (KOA) consult a healthcare provider (Jackson et al., 2020). The benefits of physical activity (PA) for KOA symptoms, including pain, are clear (Verhagen et al., 2019). However, people with KOA face numerous barriers to exercise. For example, fear of movement (FOM) is highly prevalent in KOA (58% to 86%) (Aykut Selçuk & Karakorum, 2020; Gunn et al., 2017; Tan et al., 2022) and is associated with lower levels of PA. It is likely that FOM affects the relationships between pain intensity and PA, but it is currently unclear if FOM is a covariate, a mediator, or a moderator in this relationship.

The purpose of this study was to investigate how FOM affects the relationship between pain intensity or pain sensitization with the weekly level of PA in a sample of KOA. Additionally, this study investigated how FOM affects the relationships between pain intensity, physical function, and muscle impairments (including walking speed and quadriceps muscle power) in a sample of KOA.

Participants who met the clinical criteria for KOA set forth by the American College of Rheumatology were included. PA was measured using a commercial 3-axis accelerometer (wGT3X-BT, Actigraph, USA). Pain intensity was measured via a validated, self-report questionnaire, the pain subscale of the Knee Injury and Osteoarthritis Outcome Score (KOOS-Pain). Pressure-pain threshold was determined using an algometer (FPX 25, Wagner, USA). FOM was self-reported by participants on the Brief Fear of Movement Scale (BFMS). Walking speed was measured from the 6-minute walk test. Quadriceps muscle power was obtained with a commercial dynamometer (System 4, Biodex, USA). Multiple linear regression was used to test the relationships between PA and pain (pain intensity and pain sensitization in separate

analyses), after adjusting for age and body mass index (BMI). Then, the regression model was repeated, adding FOM and its interactions with the covariates.

Thirty-one participants completed this study. After adjusting for the covariates (age and BMI), pain was not associated with PA levels (pain intensity: $R^2 = 0.199$, $p = 0.107$; pain sensitization: $R^2 = 0.233$, $p = 0.072$). After adding the moderator variable FOM and its interactions, our results showed a significant moderation effect of the BMI x FOM interaction (pain intensity: $p = 0.003$; pain sensitization: $p = 0.002$) in explaining variance in PA. The covariates, pain, and FOM (moderator) explained variance in PA in people with KOA (pain intensity: $R^2 = 0.525$, $p = 0.009$; pain sensitization: $R^2 = 0.567$, $p = 0.005$). FOM did not significantly moderate the relationship between pain intensity with either walking speed nor quadriceps muscle power ($p > 0.05$).

Our results have important clinical implications. Our results suggest that those with higher levels of FOM combined with higher levels of BMI are less physically active compared to their counterparts. Rehabilitation clinicians should provide education on the benefits of PA and exercise in all people with KOA, but especially to those with higher BMI and higher FOM levels. Additionally, clinicians should use simple self-report tools such as the BFMS to screen for the level of FOM and provide additional education on safety of PA in KOA.

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LIST OF ABBREVIATIONS:

6MWT	6-minute walk test
ACR	American College of Rheumatology
ADLs	Activities of daily living
ATS	American thoracic society
BFMS	Brief Fear of Movement scale
CNS	Central nervous system
DV	Dependent variable
FOM	Fear of movement
IASP	International Association for the Study of Pain
ICC	Intraclass correlation coefficient
IV	Independent variable
kg	Kilogram
KOA	Knee osteoarthritis
KOOS	Knee Injury and Osteoarthritis Outcome Score
kPa	Kilopascal
lb or lbs	Pounds
m	Meters
MR	Multiple regression model
MSRS	Movement Specific Reinvestment Scale
NeP	Neuropathic pain
Nm	Newton-meter
NPRS	Numeric Pain Rating Scale
OA	Osteoarthritis
OARSI	Osteoarthritis Society Research International
PA	Physical activity
PNS	Peripheral nervous system
PPT	Pressure-pain threshold
PT or PTs	Physiotherapist(s)
QST	Quantitative sensory testing
s	Seconds
SD	Standard deviation
SR-MA	Systematic review with meta-analysis
STAI	State Trait Anxiety Inventory
STAI-S or STAI-T	State Trait Anxiety Inventory - State Section or Trait Section
TSK	Tampa Scale for Kinesiophobia
W	Watt

1. INTRODUCTION:

According to the Osteoarthritis Society Research International (OARSI), osteoarthritis (OA) is a condition that can affect any movable joint in the body (OARSI, 2015). OA causes micro and/or macro trauma to a joint, which leads to degeneration of the cells and the tissues of that joint. At first, the trauma causes changes in the tissue metabolism at a molecular level. As the condition progresses, physiological changes at the joint also occur (OARSI, 2015). Globally, in people with OA, 60.6%, 23.7%, and 5.5% have knee, hand, and hip OA (Long et al., 2022).

OA is a major public health issue, affecting 240 to 500 million people worldwide (Aoyagi et al., 2022; Katz et al., 2021). In Canada, in people over 65 years old, 48.7% have a diagnosis of KOA (Statistics Canada, 2015). Costs associated with KOA management in Canada are expected to rise from \$2.9 billion in 2010 to \$7.6 billion in 2031 (Sharif et al., 2015).

Knee OA (KOA) often presents with inflammation of the synovial membrane of the knee, narrowing of joint spaces, osteophyte formation, and damage to the cartilage, bone marrow, and menisci of the knee (Katz et al., 2021). Inflammation in OA is mainly due to the activities of macrophages (Katz et al., 2021), which are blood cells that are activated in response to inflammatory signals in the body (Chen et al., 2020). Macrophages release proinflammatory cytokines, which increases the inflammatory process (Zhang & An, 2007). Proinflammatory cytokines, such as interleukin 6, monocyte chemoattractant protein-1, vascular endothelial growth factor, and mitogen-inducible gene-6, are present in the synovial fluid of the joint affected by OA (Katz et al., 2021). These cytokines compromise joint tissue and inhibit the remodeling of the joint affected by OA. The persistent activity of the macrophages and the

presence of proinflammatory cytokines within the synovium of the knee maintain a chronically inflamed state in the knee, similar to a chronic wound condition (Katz et al., 2021).

Physiological changes of joint tissues in KOA can cause a variety of symptoms, such as pain (Heidari, 2011), morning stiffness (Heidari, 2011), knee joint range of motion limitation (Heidari, 2011) and feeling that the knee is instable or is giving away (Gustafson et al., 2015). These symptoms can significantly lower a person's ability to perform activities of daily living (ADLs), including self-care tasks, personal hygiene tasks, and mobility tasks (Clynes et al., 2019). Of all of the symptoms and challenges with ADLs that a person with KOA must face, pain in KOA is the primary reason why people take action to obtain medical treatment (Jackson et al., 2020). A large study (n = 2170) from Europe and America showed that 50.9% of participants with hip OA and/or KOA rate their pain as moderate/severe (Jackson et al., 2020). People with KOA with moderate/severe pain are more likely to report needing help with ADLs, using a walking aid, joint stiffness, history of falls, opioid usage, increased absenteeism, and more work-related impairments (Jackson et al., 2020). Additionally, in older adults with OA, pain is a significant predictor of reduced physical activity (PA) (Davison et al., 2016).

It was long thought that in KOA, those with higher reported pain intensity are more likely to perform lower levels of PA, however, various studies reported conflicting results for this relationship. Burrows and colleagues (2020) completed a systematic review and meta-analysis (SR-MA) on this topic and the authors concluded that there seems to be a relationship between participation in moderate to vigorous PA and pain intensity in KOA, but that relationship does not seem to be true when examining total level of PA in KOA (Burrows et al., 2020). This inconsistency in findings between different studies suggests that there might be other factors that influence the relationship between reported pain levels and levels of PA in people with KOA.

Fear of movement (FOM), or kinesiophobia, is defined as an extreme and unfounded fear related to movement that occurs after experiencing a painful injury (Luque-Suarez, Martinez-Calderon & Falla, 2019). People with FOM believe that PA and movement will cause injury (Lundberg et al., 2006). In KOA, the prevalence of FOM ranges from 58% to 86% (Aykut Selçuk & Karakorum, 2020; Gunn et al., 2017; Tan et al., 2022) and people with higher FOM levels perform lower levels of PA (Aykut Selçuk & Karakorum, 2020). Although it is clear that FOM is highly prevalent in KOA, currently, it is not known if FOM is independently associated with PA levels in people with KOA or if FOM is a mediator or moderator variable. The primary objective of this study is to determine if FOM moderates the relationship between pain and PA levels. Secondary objectives are to determine if FOM moderates the relationship between pain intensity physical performance, such as walking speed and quadriceps muscle power.

2. PHYSICAL FUNCTION IN KOA:

2.1. Defining Physical Function versus Physical Activity:

Physical function is defined as a person's ability to live autonomously (Garber et al., 2010) and to “move around” in society (Dobson et al., 2013). Within the broad term of physical function, PA is defined as any movement generated by the muscles in the body that necessitate the use of energy (WHO, 2022). PA is an umbrella term that includes any movement performed with specific training goals and without training goals (e.g., cooking food) (WHO, 2022). Exercise is a form of PA that is usually structured and performed repetitively with a specific training goal (Dasso, 2019). PA and exercise both significantly improve symptoms and pain related to KOA (Verhagen et al., 2019).

In KOA, the ability to perform PA is determined by a variety of variables that interact in complex ways. Examples of physical factors that influence PA include pain intensity and fatigue. Examples of psychological factors include levels of motivation or believing that PA is dangerous for KOA. Examples of environmental factors include costs related to participating in PA or poor weather that prevents participation in PA (Kanavaki et al., 2017).

2.2. Muscle Impairments, Strength, and Power in KOA:

Impairment is defined as a loss of normal body function (WHO, 2002). In KOA, examples of impairments include reduced knee range of motion (Taylor et al., 2014) and reduced muscle strength (Alnahdi, Zeni & Snyder-Mackler, 2012). The term “muscle impairment” is

often used in the literature to discuss the loss of muscle strength in KOA (Alnahdi, Zeni & Snyder-Mackler, 2012).

Muscle strength is the capacity of a muscle to develop force against a resistance (Evans, 2019). In KOA, the strength of the quadriceps muscle is often impaired when compared to healthy controls (Alnahdi, Zeni & Snyder-Mackler, 2012; Myers, 2020). Quadriceps muscle strength is an important indicator of overall function and well-being in KOA. Weakness of the quadriceps is associated with higher pain intensity (Muraki et al., 2015; Myers, 2020; O'Reilly et al., 1998), disability (O'Reilly et al., 1998), slower gait speed (Machado et al., 2022), poorer overall mobility (Myers, 2020), balance (Myers, 2020), and physical function, such as walking abilities, going up and down the stairs, and getting up and down from the floor (Alnahdi, Zeni & Snyder-Mackler, 2012).

Muscle power is defined as the amount of force generated at a certain velocity (speed) by a muscle contraction (Accettura et al., 2015; Reid & Fielding, 2012; Sapega & Drillings, 1983). Muscle strength and muscle power both decline with age, but power declines more rapidly than strength with aging (Skelton et al, 1994). In KOA, quadriceps muscle power is related to better walking and stair climbing abilities (Accettura et al., 2015), and self-perceived quality of life (Reid et al., 2015).

2.3. Physical Function Tests in Knee Osteoarthritis:

There are many ways to measure a person's physical function. For instance, walking tests, which are categorized as performance-based tests, can be used to quantify a person's level of physical function (Dobson et al., 2013). Walking tests can assess walking speed, walking abilities over long distances, and aerobic capacity (Dobson et al., 2013).

It is well accepted that walking speed is a very powerful indicator of overall health status (Master et al., 2021). Slow walking speed is related to higher disability, morbidity, falls, lower quality of life, hospitalization, and functional dependence (Alenazi et al., 2021). Further, slow walking speed is associated with a 51% increase in all-cause mortality (Master et al., 2021). Walking speed is significantly impaired in people with KOA (Ornetti et al., 2010).

3. UNDERSTANDING PAIN:

The International Association for the Study of Pain (IASP) defines pain as “an unpleasant sensory and emotional experience”, associated with or without tissue damage. IASP specifies that pain is a learned and personal experience and that pain is influenced by biopsychosocial input (IASP, 2021). Pain experts developed three categories to classify pain: nociceptive, neuropathic, and nociplastic pain (Fitzcharles et al., 2021). A person can experience a combination of these pain types, including all three types of pain at the same time (Fitzcharles et al., 2021).

3.1. IASP’s Terminology related to Nociceptive Pain:

Although often used interchangeably, IASP (2021) provides different definitions for noxious stimulus, nociceptive stimulus, nociceptors, nociception, nociceptive neurons, and nociceptive pain:

- **Noxious stimulus:** a stimulus that can damage the integrity of bodily tissue.
- **Nociceptive stimulus:** a stimulus, transmitted by nociceptors, that can cause or has the potential to cause tissue damage.
 - A nociceptive stimulus, unlike a noxious stimulus, activates the nociceptors but does not have to be noxious, meaning that it is not necessary for the nociceptive stimulus to have the potential to damage the integrity of bodily tissue.
- **Nociceptors:** a receptor in the peripheral nervous system (PNS) that encodes for noxious stimulus at a specific threshold.
- **Nociception:** the neural mechanism for transmitting a noxious stimulus.

- **Nociceptive neurons:** a neuron located in the central nervous system (CNS) or the PNS that can detect a noxious stimulus and transmit this signal.
- **Nociceptive pain:** sensation of pain due to activation of nociceptors from an actual or potential harm to non-neural bodily tissue.

3.2. Nociceptive Pain:

Dubin and Patapoutian (2010) explain that nociceptors are usually quiet but will generate an action potential in an all-or-nothing fashion if they are stimulated. Once stimulated, the action potential will travel through myelinated small fibres ($A\beta$ and $A\delta$ fibres) or unmyelinated C fibres to reach the dorsal horn of the spinal cord. Interneurons in the dorsal horn of the spinal cord can either reduce or increase the nociceptive signals from the periphery. The signals then travel to different areas of the brain. Whether or not pain will be perceived and the intensity of pain felt is dependent on the activity of excitatory and inhibitory interneurons at the dorsal horn of the spinal cord level and the facilitatory and inhibitory pathways in the brain when the brain processes nociceptive information (Dubin & Patapoutian, 2010).

3.3. Neuropathic Pain:

Neuropathic pain (NeP) is divided into central and peripheral NeP. The term NeP describes the sensation of pain due to an abnormally functioning nervous system (IASP, 2021). Central NeP occurs when there is injury or damage to the CNS, which includes the brain and the spinal cord. Peripheral NeP occurs when there is injury or damage to the PNS (IASP, 2021) and injury or damage to the unmyelinated C fibers and the myelinated $A\beta$ and $A\delta$ sensory fibres

located in the PNS (Colloca et al., 2017). Examples of conditions that involve central NeP include stroke, transverse myelitis, and Parkinson's disease. Examples of conditions that involve peripheral NeP include diabetes neuropathy, viral infections, or Guillain-Barre syndrome. At the peripheral level, due to injury or damage to the PNS, the activities of the sensory nerves are affected. Additionally, there is an amplification of ascending sensory signals and a decreased inhibition of descending signals at the spinal cord level. The lack of balance between the afferent and efferent neuronal activity related to sensation contributes to the maintenance, or persistence, of NeP. The increased afferent signal to higher levels of the brain can also contribute to the development of central sensitization (Colloca et al., 2017).

3.4. Nociplastic Pain:

Nociplastic pain is defined as pain due to an abnormal mechanism in nociception, which leads to nociceptors in the PNS to be activated. In nociplastic pain, there is no noticeable indication of tissue damage nor indication of insult to the CNS or PNS (IASP, 2021). Research is ongoing to understand the pathophysiology of nociplastic pain. In nociplastic pain, just as in NeP, there is an amplification of afferent pain signals and decreased inhibition of efferent pain signals. Common categories of nociplastic pain include chronic widespread pain, complex regional pain syndrome, chronic primary headaches and orofacial pain, chronic primary visceral pain, and chronic primary musculoskeletal pain (Fitzcharles et al., 2021).

3.5. Pain Intensity and Radiographic Imaging in KOA:

According to the American College of Rheumatology (ACR), KOA can be diagnosed using blood work, radiographic imaging, and/or with clinical symptoms (Altman et al., 1986). A study with data from different continents ($n = 3021$) showed that greater severity of KOA on imaging is associated with more repeated bouts of knee pain (Wang et al., 2018).

Interestingly, the amount of knee joint degeneration on imaging does not always match the reported pain intensity. One systematic review concluded that in people with radiographic findings of KOA, 15-76% will experience knee pain (Bedson & Croft, 2008). A person with mild KOA pain intensity can have strong evidence of KOA on imaging (Altuwairqi et al., 2023) and a person with mild evidence of KOA on imaging can report severe KOA pain intensity (Finan et al., 2013). The lack of correlation between reported pain intensity and radiographic evidence of KOA is likely due to, at least in part, the presence of pain sensitization.

3.6. Understanding Pain Sensitization:

To understand pain sensitization in KOA, it is important to first understand the difference between habituation and sensitization. Ursin (2014) explains that when humans face a novel and unfamiliar stimulus, they will respond by stopping their current activity and then immediately enter a state of heightened arousal to find the stimulus origin. If the same stimulus re-emerges, the response to this specific stimulus gradually decreases over time. This behavior is known as habituation. Sensitization is the opposite of habituation, where repetitive presentation of the same stimulus increases the response over time. Sensitization occurs when there is repetitive activation

of neural circuits, resulting in their improved efficiency to transmit information due to synaptic changes. As a consequence, the response to the same stimulus is heightened (Ursin, 2014).

In pain science, the term “sensitization” is used to describe the neurophysiological phenomenon of a state of heightened sensitivity of the nociceptive neurons (activation below their typical threshold) and a potential increase in the total area of the receptive fields of the nociceptive neurons (IASP, 2021). Pain sensitization occurs when habituation to painful stimulus does not occur (Ursin, 2014). IASP (2021) states that peripheral sensitization occurs when nociceptive neurons in the PNS generate an action potential below their normal threshold of activation. Central sensitization is when this occurs in the CNS, such as when neurons in the CNS (such as the dorsal horn of the spinal cord) that usually only respond to noxious input will be activated with a normally non-noxious stimulus (IASP, 2021; Imamura et al., 2008).

It is important to note the distinction between the three categories of pain and pain sensitization. Nociceptive (non-neural tissue origin of pain sensation), NeP (abnormality in the nervous system causing pain), and nociplastic (unclear cause) pain describe the origin of the painful sensation. Pain sensitization describes the heightened sensitivity of the nociceptive neurons and their response to a stimulus below their normal threshold of activation (regardless of whether the stimulus is noxious or not).

4. PAIN SENSITIZATION IN KOA:

4.1. Measurements of Pain Sensitization:

There are various ways to test for pain sensitization in humans (Rankin et al., 2022). In KOA specifically, it is possible to assess symptoms of sensitization using validated self-report questionnaires, such as the Central Sensitization Inventory and the modified painDETECT (Gervais-Hupé et al., 2018). It can also be measured objectively using quantitative sensory testing (QST), which is a method used to quantify sensation (Weaver et al., 2022) and to determine if there is a heightened or diminished sensory response using various thermal and mechanical stimuli (Rolke et al., 2006).

Pressure-pain threshold, sometimes written as pain-pressure threshold (PPT), is part of QST testing and is commonly used to establish the presence of pain sensitization in KOA (Rolke et al., 2006; Rankin et al., 2022; Weaver et al., 2022). PPT testing allows the researcher to quantify a threshold for mechanical pain detection using an algometer (Stausholm et al., 2023). An algometer is a tool that can quantify the amount of pressure applied per surface area on the skin of a person. The person is instructed to tell the researcher when pressure applied on the skin first turns into pain. The researcher can compare different pressure-pain tolerance profile between individuals (Rankin et al., 2022; Stausholm et al., 2023). Currently, there are no published values for PPT that are considered normal at the knee, but one study ($n = 280$) suggests that the average PPT value for knee pain is 324 kPa (Sylwander et al., 2021). Another study suggests that a cut-off value of 241.5kPa could be used to separate responders from non-responders for physiotherapy rehabilitation exercises (Hattori et al., 2022b).

4.2. Pain Intensity and Pain Sensitization in KOA:

Pain intensity, pain sensitization, and PPT values are related in KOA. There is an inverse relationship between the likelihood of pain sensitization and PPT values (Carlesso et al., 2022). Those with pain sensitization are more likely to report higher pain intensity (Previtali et al., 2022). A recent SR-MA (53 studies, $n = 7117$) shows that the prevalence of pain sensitization in KOA is as high as 20% (95% CI = 16-26%) (Previtali et al., 2022). Two SR-MAs and three other studies show that in KOA, those who report severe KOA symptoms are also more likely to have lower PPT values compared to those with milder symptoms (Aoyagi et al., 2022; Bevilacqua-Grossi et al., 2019; De Oliveira Silva et al., 2019; Fingleton et al., 2015; Goode et al., 2014). Finally, lower PPT value is associated with higher pain hypervigilance, which is defined as augmented sensory state to search for pain on the body repetitively (Herbert et al., 2014).

PPT values may be useful for predicting the likelihood of improving KOA symptoms with exercise. Lower PPT values predicted (odds ratio = 0.48) non-responsiveness to physiotherapist-prescribed exercises (knee strengthening, aerobics, and range of motion exercises), after adjusting for age, sex, depression levels, and adherence to treatment (O'Leary et al., 2018). Another study from Japan ($n = 101$) showed similar results: people with KOA who reported greater pain intensity and showed lower PPT values did not see their pain significantly improve (only a 0.4 change on the numeric rating scale) after a 12-week physiotherapy exercise program for KOA (Hattori et al., 2022a).

A SR-MA shows that local PPT values did not change after an exercise program (ranging from 5-12 weeks of resistance and/or aerobic training) for KOA (Hall et al., 2020). A more recent study concluded similar results for gait training. Local PPT values at the knee did not change

after a 6-week, 3/week, 30min/day of supervised walking program (Klinedinst et al., 2023). These results agree with another study by Satake and colleagues (2021) who found that pain intensity during ambulation correlated with body mass index and OA severity on imaging, suggesting a mechanical origin of pain. However, PPT values inversely correlated with pain intensity at rest ($r = -0.23$; $p = 0.02$) and had no correlation ($r = -0.02$, $p = 0.87$) with pain intensity during ambulation, suggesting that source of pain during ambulation is likely not only due to mechanical stimulations at the knee (Satake et al., 2021). Aerobic, local resistance exercises, and gait training exercises likely targets the local mechanical impairments in KOA that leads to pain but does not address the non-mechanical sources of pain.

These findings that pain sensitization is unchanged by exercise are concerning, as pain sensitization is present in 20% of people with KOA and it is associated with higher pain. Current guidelines strongly recommend exercise as an effective treatment for KOA (Kolasinski et al., 2020; Verhagen et al., 2019) but it failed to increase PPT values at the knee. Researchers also found that there is no added benefit for improving PPT scores when educational videos are added to exercise therapy in KOA (Ozturk et al., 2021). Thus, more research is needed on the management of pain sensitization, what factors contribute to sensitization, and how to develop tailored treatment program for people with KOA and sensitization.

4.3. Pain and Physical Function in KOA:

Pain sensitization affects ambulation abilities and other weight bearing activities in people with KOA. For pain sensitization, three studies found that lower PPT values are associated with shorter distances walked on the 6MWT and slower gait speed (Aoyagi et al.,

2022; Corrigan et al., 2023; Jaber et al., 2022). A large study (n = 2749; 5479 knees) found that lower PPT values are associated with greater pain intensity during standing and completing stairs (Aoyagi et al., 2022).

The presence of pain sensitization is related to greater stiffness, altered lower extremity muscle co-contraction during static and dynamic tasks, and lower extremity muscle weakness. When assessed by the Metitur Good Balance System, people with KOA and pain sensitization seems to have to greater postural stiffness when standing on a foam surface (Hirata et al., 2019). As for muscle co-contraction (assessed with electromyography), one study (n = 1633) found that those with KOA and pain sensitization are more likely to co-contract their medial hamstrings during maximal isokinetic effort (quadriceps) on a dynamometer compared to people with KOA but less sensitization (Stefanik et al., 2020). Similarly, another study (n = 90) found that those with KOA and pain sensitization are more likely to co-contract their lateral hamstrings and their vastus lateralis during while walking fast (Lee et al., 2023). Finally, one study found that people with KOA with lower PPT values have lower maximal quadriceps muscle strength compared to people with KOA with higher local PPT values (Corrigan et al., 2023).

4.4. Physical Activity and Reported Pain Intensity in KOA:

People with KOA are recommended to be as physically active as possible (Kraus et al., 2019). Older adults are recommended to perform at least 150 minutes of moderate to vigorous intensity exercise per week, in periods of at least 10 minutes each (Rausch Osthoff et al., 2018). Accumulating at least 45 minutes of moderate to vigorous intensity exercise per week reduces symptoms of KOA (Kraus et al., 2019). However, a SR-MA that included studies published from different continents showed that only 13% of people with KOA completed the recommended

amount of PA for older adults. The average amount of moderate to vigorous PA completed is 50 minutes/week (Wallis et al., 2013). The vast majority of people with KOA (62%) self-report either being inactive or only completing mild intensity PA (Goff et al., 2024). In contrast, a study in England ($n > 92000$) showed that in people over 65 years old, about 25% perform the recommended amount of PA (McPhee et al., 2016).

There is conflicting evidence on whether if there is an association between pain intensity and PA levels. For example, among many others, two studies suggest that there is no relationship between pain intensity and PA levels (Brisson, Gatti & Maly, 2020; Shim et al., 2018); while among many, two other studies suggest the opposite (Aldosari et al., 2022; Balogun, 2020). Burrows and colleagues (2020) completed a SR-MA on this topic concluded that there is a too large heterogeneity ($I^2 = 91\%$) in the included studies to compose firm conclusions about the association between PA and pain. There seems to be an inverse relationship between participation in moderate to vigorous PA levels and pain intensity in people with KOA. However, when purely examining the total PA levels, the 95% confidence interval include zero (Burrows et al., 2020). Nonetheless, clearer associations are shown between pain intensity levels and muscle strength, muscle power, and aerobic capacity (Burrows et al., 2020).

Studies have examined the reasons why people with KOA perform less than the recommended amount of PA. Kanavaki and colleagues (2017) developed three categories of barriers and facilitators to PA in KOA: physical health factors, intrapersonal/psychological factors, and social environment factors. These authors report that physical health related barriers to PA in hip OA and/or KOA include overall pain intensity, age, obesity, advanced OA disease progression, fatigue, stiffness, physical capacity, and reduced fitness. Intrapersonal, psychological, and social environmental barriers to PA include lack of knowledge the condition,

fear that PA could worsen OA, low motivation, low support from health care professionals, busy schedule, feeling depressed, and stress (Kanavaki et al., 2017).

5. FEAR OF MOVEMENT IN KOA:

5.1. Fear and Fear of Movement:

Fear is defined as a conscious emotion triggered by a set of actual or perceived threatening or dangerous stimuli that is occurring imminently (Adolphs, 2013; Penninx et al., 2021). Fear is context-dependent (Adolphs, 2013).

Fear of movement (FOM), or kinesiophobia, is defined as an extreme and unfounded fear related to movement that occurs after experiencing a painful injury (Luque-Suarez, Martinez-Calderon & Falla, 2019). People with FOM believe that PA and movement will cause injury (Lundberg et al., 2006). From this perspective, it is unsurprising that FOM correlates with a greater risk of reduced quality of life, greater disability, and greater pain intensity in people with chronic musculoskeletal pain (Luque-Suarez, Martinez-Calderon & Falla, 2019). A study completed in Europe (n = 140) showed that 54% of people seeking physiotherapy treatment for musculoskeletal conditions present with FOM (Lundberg et al., 2006). Similarly, the prevalence of FOM in KOA ranges from 58% to 86% (Aykut Selçuk & Karakorum, 2020; Gunn et al., 2017; Tan et al., 2022). Due to the high prevalence of FOM in KOA, current research shows that FOM likely is a substantive contributor to elevated pain intensity, lower PA levels, and physical function in people living with KOA.

5.2. FOM, Pain Intensity, and Mental Health in KOA:

Higher FOM in KOA correlates with pain intensity and mental health. Specifically, higher FOM scores on self-reported questionnaires correlate with higher pain intensity at rest and

with activity ($r = 0.291$ to 0.728) (Alaca, 2019; Alshahrani et al., 2022; Aydemir, Huang & Foucher, 2022; Greenwood et al., 2023; Gunn et al., 2017; Odole et al., 2019). The large variation in correlation is likely due, at least in part, to the authors from the different studies using different questionnaires to assess pain intensity in KOA. Higher FOM also correlates with poorer mental health assessed by self-report questionnaires (Short Form 12 and 36) (Aykut Selçuk & Karakorum, 2020; Helminen et al., 2020) and higher depressive symptoms assessed by self-reported questionnaires (Patient Health Questionnaire depression scale, 8-items version) (Gunn et al., 2017).

5.3. Fear of Movement and Physical Activity in KOA:

Higher FOM in KOA is associated with lower PA levels when measured subjectively and objectively. Using self-reported questionnaires, in people with KOA and high FOM scores, 68.4%, 27.7%, and 3.9% had low, moderate, and high PA levels. In contrast, in people with low FOM scores, 46.2%, 23.1%, and 30.7% had low, moderate, and high PA levels (Aykut Selçuk & Karakorum, 2020). Three other studies concluded similar results between PA levels and FOM levels (Aydemir, Huang & Foucher, 2022; Goff et al., 2024; Kiliç et al., 2018). When PA is measured objectively by accelerometry, every one-point increase on a 6-item self-report FOM questionnaire was associated with 117 fewer steps per day ($p = 0.036$; $R^2_{\text{adjusted}} = 0.35$) in a sample of KOA, after adjusting for age, sex, body mass index, pain, level of education, and employment status (Uritani et al., 2020). This pattern suggests a dose-response relationship where greater FOM is associated with lower PA.

5.4. Fear of Movement and Muscle Impairments in KOA:

Higher FOM in KOA correlates with knee muscle impairments. Higher FOM scores on self-reported questionnaires correlates with lower with knee flexion strength ($r = -0.529$) (Aydemir, Huang & Foucher, 2022) and knee extension strength ($r = -0.437$) measured using a commercial dynamometer (Aydemir, Huang & Foucher, 2022; Myers, 2020). The association between knee flexion strength and self-report PA scores and knee extension strength and self-report PA scores were significantly mediated by FOM scores on questionnaires, but not by pain. Hence, the authors suggests that FOM, not pain, can significantly impact PA participation in people with KOA (Aydemir, Huang & Foucher, 2022).

5.5. FOM and Physical Function in KOA:

Higher FOM in KOA correlates with some physical function tests. Higher FOM scores on self-reported questionnaires correlates with poorer physical self-reported function ($r = 0.386$ to 0.544) (Aykut Selçuk & Karakorum, 2020; Gunn et al., 2017; Helminen et al., 2020; Odole et al., 2019) and with increased self-rated difficulty to descend stairs ($r = 0.53$) (Stensdotter, Vårbakken & Roeleveld, 2023). Higher self-reported FOM correlate with longer total time to complete the five times sit-to-stand tests ($r = 0.49$) (Alshahrani et al., 2022) and with lower reach scores on the multi-directional functional reach test ($r = -0.353$ to -0.476) (Sanchez-Heran et al., 2016). While these studies seem to indicate that both self-report and performance scores of physical functions are lower in those with a higher self-report FOM, there are some variations. For example, FOM scores had no correlation with the unilateral stand test (Gunn et al., 2017) nor gait speed measured by the 6MWT (Machado et al., 2022).

6. GAPS IN THE LITERATURE:

PA engagement in people living with KOA is, generally, below the recommended amount. Pain sensitization is present in 20% of people with KOA and it is associated with higher reported pain intensity. FOM is present in more than 50% of people with KOA and is associated with lower PA and higher pain intensity. It is likely that FOM affects the relationships between pain intensity and PA, but it is currently unclear if FOM is a covariate, a mediator, or a moderator in this relationship.

Despite advancements in the research about FOM in KOA, major gaps in knowledge remain, including the following:

- I. No research has studied if the level of FOM moderates the association between PA and pain intensity in people with KOA. Higher FOM level correlates with higher pain intensity and lower PA. Due to the high prevalence of FOM in KOA, FOM is likely a critical factor that influences the relationship between reported pain intensity and PA levels.
- II. It is not known if there is a relationship between pain sensitization and PA and if it does exist, whether the relationship between pain sensitization and PA is moderated by FOM in people with KOA. Nearly 20% of people with KOA have pain sensitization. Those with pain sensitization are more likely to have lower PPT values and report higher pain levels.

III. There is currently no research that examined if FOM moderates the impact of pain intensity on knee power or walking speed in people with KOA. People with KOA have weaker quadriceps muscles. People with KOA with higher PPT values perform better on the 6MWT. FOM is a mediator of knee strength (flexion and extension) and PA, but it remains unclear if FOM moderates the impact of knee power, a variable distinct and more sensitive to change than strength, on PA.

7. PURPOSE:

The primary purpose of this study is to investigate how FOM affects the relationship between pain (pain intensity and pain sensitization) with PA in a sample of KOA. Additionally, this study will investigate how FOM affects the relationships between pain intensity with physical function and muscle impairments (including walking speed and quadriceps muscle power) in a sample of KOA.

7.1. Defining Statistical Terminology:

7.1.1. Predictor(s) and Outcome:

In linear regression analysis, Field (2009) explains that a predictor variable is the independent variable (IV) and is used to predict an outcome, which is the dependent variable (DV). If the model has one predictor, it is called a simple linear regression model; if the model has two or more predictors, it is called a multiple linear regression model (Field, 2009).

Field (2009) mentions that the mathematical equation for regression model should be written as shown below, where:

β_0 = y-intercept (0,Y),

β_1, β_2 = regression coefficient for IV_1 and IV_2 ,

x_1, x_2 = the IVs (predictors),

ε = error.

$$outcome = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \cdots + \varepsilon$$

7.1.2. Covariates:

Field (2009) explains that a covariate is a variable that is related to the DV and can influence the value of the DV, regardless of the selected IVs of the study. Covariates should be accounted for in the regression model to improve the accuracy of the model (Field, 2009).

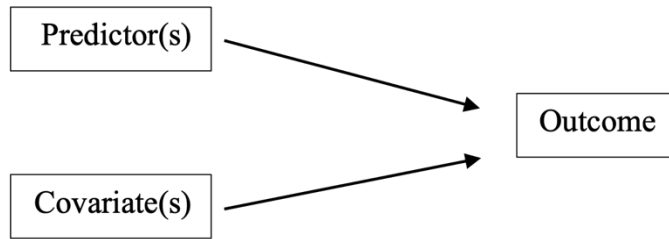


Figure 1: *Predictors, covariates, and outcome in linear regression analysis*

7.1.3. Interaction:

Vittinghoff et al. (2004) explains that an interaction is the product of two predictors. Equation (Eq) A is an example of a model with two predictors. Eq B has two predictors and one interaction. As shown in Eq A, the two predictors change the outcome independently. In contrast, in Eq B, a new regression coefficient (β_3) is calculated for the product of the two predictors. If β_3 is statistically significant, an interaction occurs. An interaction considers how the level of one predictor on the second predictor changes the outcome (Vittinghoff et al., 2004).

$$\text{Eq A} \rightarrow \text{outcome} = \beta_0 + \beta_1 x_1 + \beta_2 x_2$$

$$\text{Eq B} \rightarrow \text{outcome} = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_1 x_2$$

7.1.4. Mediator:

Vittinghoff et al. (2004) describes that a mediator is a predictor variable (IV). The mediator lies between the predictor(s) and the outcome and explains how the predictor(s) cause(s) the outcome. Accounting for mediators can give information on whether the relationship between the predictor(s) and the outcome must bypass a third (mediating) variable (Vittinghoff et al., 2004). It is only possible to have mediator variable if there is a significant relationship between the predictor(s) and the outcome (Bennett, 2000).

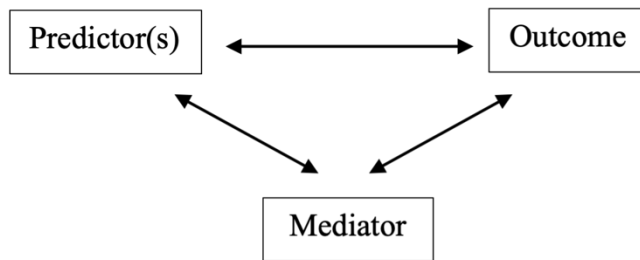


Figure 2: Predictors, mediator, and outcome in linear regression analysis

7.1.5. Moderator:

Bennett (2000) explains that a moderator is a predictor variable (IV). A moderator is a variable that can modify the magnitude and/or the direction of the relationship between the predictor(s) and the outcome (Bennett, 2000). The equation used to account for the effect of a moderator variable in regression analysis is shown in section 6.1.3 using Eq B, which is the same equation for interaction (Bennett, 2000; Vittinghoff et al., 2004).

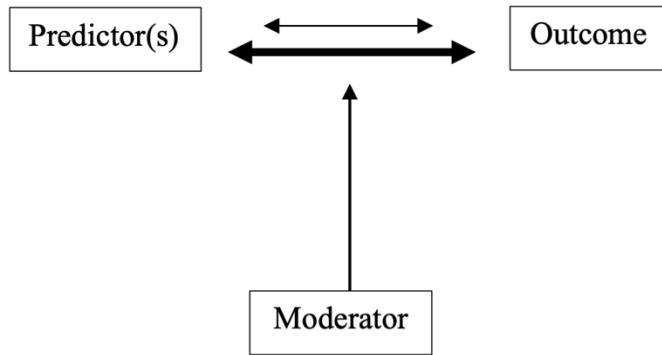


Figure 3: *Predictors, moderator, and outcome in linear regression analysis*

7.2. Objectives:

Primary objective:

1. To determine if the association between pain intensity with PA is moderated by the level of FOM in a sample with KOA.

Secondary objectives:

2. To determine if the association between local PPT values (pain sensitization) with PA is moderated by the level of FOM in a sample with KOA.

Tertiary objectives:

3. To determine if the association between pain intensity with gait speed is moderated by the level of FOM in a sample with KOA.
4. To determine if the association between pain intensity with quadriceps muscle power is moderated by the level of FOM in a sample with KOA.

7.3. Hypotheses:

Primary objective:

1. The level of FOM will moderate (i.e., increase) the strength of the relationship between pain intensity and PA in a sample with KOA.

Secondary objectives:

2. The level of FOM will moderate (i.e., increase) the strength of the relationship between PPT and PA in a sample with KOA.

Tertiary objectives:

3. The level of FOM will moderate (i.e., increase) the strength of the relationship between pain intensity and gait speed in a sample with KOA.
4. The level of FOM will moderate (i.e., increase) the strength of the relationship between pain intensity and quadriceps muscle power in a sample with KOA.

7.4. Clinical Implications of Potential Findings:

According to the College of Physiotherapists (PT) of Ontario (2023), PTs are health care professionals who aim to enhance people's mobility. PTs are often involved in exercise prescription in KOA (El-Khoury et al., 2020) and the benefit of exercise for KOA is clear (Verhagen et al., 2019). Unfortunately, people with KOA do not only face physical health barriers to exercise; they also face psychological and social barriers. A recent scoping review (n = 20 studies) showed that both experienced PTs and PT students were not confident in

recognizing psychosocial factors in people with musculoskeletal conditions (Henning & Smith, 2023). It is possible that many professions involved in prescribing and supervising exercise in KOA would, similar to PTs, under-recognize or under-estimate the importance of psychosocial factors in people with musculoskeletal conditions.

It is well known that continued adherence to PA in people with KOA is challenging. One study concluded that in KOA, those who believed that OA is a “wear and tear” condition and those who did not think that exercise therapy is effective in managing KOA are more likely to stop their exercises (Campbell et al., 2001). Due to the high prevalence of FOM in musculoskeletal conditions, FOM could play a critical moderating role in the relationship between pain intensity and PA levels. Hence, I anticipate the findings from this study will emphasize that screening for FOM using validated self-reported questionnaires should be done in all KOA patients, prior to exercise therapy. If a person has a high score on FOM questionnaires, education on the safety and benefits of PA in KOA and/or other measures to address FOM should be done in conjunction with exercise therapy during sessions with PTs.

8. METHODS:

8.1. Study Design:

A cross-sectional study design was used. A single visit (approximately two hours) to the Mobilize Clinical Biomechanics laboratory was completed. This laboratory is located at the University of Waterloo. Potential participants who showed interest in this study were screened either by email or phone call as per the request of the individual. If they were eligible and provided written consent to participate in this study, they were invited to come to the laboratory.

Participants were asked to complete the questionnaires and physical tests in the following order:

1. The Get Active Questionnaire (Appendix A) to screen for contraindications.
2. Informed consent (written and signed).
3. Questionnaires (Appendix B) on demographics.
4. Weight and height measurements (Appendix I).
5. Questionnaires on knee symptoms related to osteoarthritis (Appendix C).
6. Psychosocial questionnaires, including the FOM (Appendix D), State and Trait Anxiety (Appendix E), and Movement Reinvestment (Appendix F).
7. Questionnaire on current intake of pain and mental health medications (Appendix M).
8. The current level of pain (Appendix G) on the Numeric Pain Rating Scale (NPRS).
9. The PPT protocol (Appendix K).
10. The 6MWT (Appendix H). NPRS pre and post 6MWT.
11. Quadriceps strength and power measurements on a commercial dynamometer.
12. The final level of pain on the NPRS.

13. Three-axis commercial accelerometer, with instructions and a logbook (Appendix J), were provided for the next 7 consecutive days.

8.2. Inclusion and Exclusion Criteria:

8.2.1. Inclusion criteria:

Participants of all sexes, genders, and races were eligible for this study. Participants had to be 45 years old or older, meet the ACR clinical diagnostic criteria for KOA, which includes knee pain and at least three of the criteria below (Altman et al., 1986):

1. Age > 50 years old,
2. < 30 minutes of morning stiffness,
3. Crepitus on active range of motion,
4. Bony tenderness,
5. Bony enlargement,
6. No palpable warmth synovium.

If a potential participant reported to have pain in both knees of different intensity, only the most symptomatic knee was selected for this study.

8.2.2. Exclusion criteria:

Participants were excluded from this study if they self-reported to have any of the conditions listed below:

1. Rheumatoid arthritis or other form of arthritis,
2. Previous knee surgery in the last year,

3. Lower limb trauma in the last 6 months,
4. Any other lower extremity conditions such as gout or ankle fracture,
5. Possible or actual pregnancy,
6. Any unstable or un-monitored medical condition that prevents full participation in the study.

8.3. Recruitment:

To recruit participants, I used multiple methods, including (i) social media (i.e., Facebook, Twitter), (ii) the Mobilize Lab website, (iii) posters visible on the University of Waterloo campus and at the Center for Community, Clinical and Applied Research Excellence (CCCARE) at the Toby Jenkins Applied Health Research Building, and (iv) an existing list of potential study participants who had provided written consent to be contacted by the Mobilize Lab for future studies. Participants who were interested in this study were able to contact me either by email or through the Mobilize Lab phone line.

The Mobilize Lab is currently in the process of completing a three-year longitudinal study on KOA. Participants enrolled in that cohort were informed about the current study. In such cases, after obtaining the participants' consent to participate in this project, data on age, sex, gender, demographics and socioeconomics, race, PA data and logbook data, walking speed, knee symptoms questionnaires (all sections of the KOOS), and knee strength were shared between this project and the other research project at the Mobilize Laboratory.

8.4. Sample Size Calculation:

The sample size calculation was based on the primary research question, which has one outcome, two predictors, and one interaction effect. The relationship between pain intensity and total PA is unclear based on a recent SR-MA due to significant heterogeneity in methodology for measuring pain intensity and PA (Burrows et al., 2020). There are strong associations between FOM and pain intensity and FOM and PA levels. A SR-MA examined the difference between the level of PA in people over 60 years old with chronic musculoskeletal pain compared to those without and found a standardized mean difference of -1.74 (Stubbs et al., 2013). Hence, the strength of the relationship between the predictors and the outcome is likely medium. Sample size estimation for a relationship of small to medium strength can be obtained using a health statistic textbook by Field (2009). An ideal sample size of approximately 80 participants was required for this study. Due to monetary and time constraints for a master's level thesis, it was not possible to recruit 80 participants. Hence, we aimed to recruit 30-40 participants for this project.

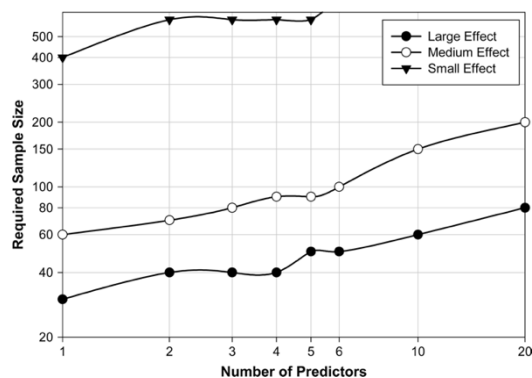


Figure 4: Field (2009), based on the work of Miles and Shevlin (2001)

8.5. Outcome Measures:

Data collection sheets and the outcome measures are provided in Appendices A-K. Descriptions of the methodologies of this study as well as the reliability and validity of the chosen outcome measures are described below.

8.5.1. Dependent (Outcome) Variable (DV):

For research question #1 and #2, the DV was PA measured by accelerometry. For research question #3 and #4, the DVs were performance on a validated walking test (walking speed) and quadriceps muscle power respectively. Details on the device used to measure knee muscle power and the walking test and their validity and reliability are listed below.

8.5.1.1. *Physical Activity Measurement:*

Accelerometry is an objective approach to measuring PA in KOA. Although an accelerometer can provide various pieces of information regarding PA, such as step count, exercise intensity, heart rate, and distance walked, the only variable of interest for this study was step count.

The equipment used for this study was a commercial three-axis accelerometer (ActiGraph - wGT3X-BT, Pensacola, Florida, United States). This accelerometer could sample data at frequencies of 30-100 Hz. Ngueleu et al. (2022) reported in their systematic review on the ActiGraph that sampling at 30Hz was most commonly used in the literature, but researchers have also used 60Hz or 100Hz. A low-frequency extension filter could be applied during data collection. Adding this filter could increase the validity of data produced by this device at low

walking speeds but could reduce the validity at higher walking speeds. This device could be worn at the hip, the wrist, or the ankle. The hip was the most common location chosen by researchers (Ngueleu et al., 2022). Hence, for this project, the device was worn at the hip, no filter was applied, and PA data was collected at 90Hz.

To minimize variability in the wear pattern among the participants, the following verbal instructions were provided: *“This is an accelerometer. It measures the number of steps you take in a day, just like your Fitbit or Apple Watch. Don’t worry about battery life or about any light blinking or turning off. You should wear this on your waist, like a belt. Please wear it from the moment to wake up to the moment you go to sleep at night. Please do not take it off during any other moment of the day. However, please take it off if you are completing any water-based tasks and activities, such as swimming or showering. Do not forget to put it back on right after. You do not have to wear it under your clothes. You can wear it on top of your pants or shirts. Please wear this device for 7 consecutive days. Do you have any questions?”*

A logbook (paper) was provided to the participants to record the date and time they put on/took off the device to evaluate sufficient wear-time per day (Appendix J). The participants were instructed to wear this device from the moment they woke up to the moment they went to bed, except for activities that involved water. The recommended minimum wear time per day for people with KOA was 10 hours of wear per day over a total of seven consecutive days (Song et al., 2010). The minimum number of wear-days from a participant for data collection for the accelerometer data to be reliable is three days (Sasaki et al., 2018). Hence, a minimum of three days with over 10 hours of wear time per day was needed for the physical activity data to be included in the analysis (Sasaki et al., 2018; Song et al., 2010).

Data processing from the accelerometer was completed using a custom Python – Visual Studio (VS) Code. Data from the ActiGraph accelerometer were imported to Acti-Life, saved as a .csv document for each participant, and imported to VS code for analysis. Data were generated from time 00:00:00 to 23:59:59 in blocks of 10 seconds (10-s epoch) (Brønd & Arvidsson, 2016). A minimum required wear time of 10 hours was denoted from the raw data and verified using the logbook. From data collections days meeting the minimum wear time, the total daily step count was calculated from all available days and the average PA measure (steps/day) was obtained from all available days.

ActiGraph produces step count data that is reliable in OA (Song et al., 2010). Step count data produced by the ActiGraph accelerometer is valid (Yang et al., 2018), showed good criterion validity (Ngueleu et al., 2022), and good reliability (ICC = 0.80) (Welk, Schaben & Morrow, 2004; Yang et al., 2018).

8.5.1.2. Six Minute Walk Test (6MWT):

Walking speed was assessed using the 6MWT. Specific instructions were found in Appendix H. This test was performed in the indoor Manulife Gym at the University of Waterloo. The gym had good lighting, a tiled level floor surface, and sufficient space to allow the researcher to walk close to the participants to ensure safety. Participants walked in a rectangle with a total perimeter of 62 meters. Chairs were placed at the four corners to allow participants to rest as needed. They were permitted to use their usual assistive devices, if any. The instruments needed for this test were a stopwatch, a measuring tool, and four chairs. A pen and paper were also used to record the total distance walked to calculate gait speed (in m/s) at the end of this test (ATS, 2002).

The test-retest reliability of the 6MWT scores in KOA is shown to be excellent, with ICC values ranging from ICC = 0.94 (post-knee surgery) (Kennedy et al., 2005) to ICC = 0.99 (primary KOA) (Ateef, Kulandaivelan & Tahseen, 2016). OARSI recommends the 6MWT to assess functional and aerobic capacity and calls it “the best available test” to assess walking abilities in the hip or knee OA population (Dobson et al., 2013).

8.5.1.3. Quadriceps Muscle Strength and Power Testing:

Commercial dynamometers are commonly used to assess knee strength and knee power in research settings (Myers, 2020; Van Driessche et al., 2018). For this study, knee extensor muscle efforts were measured on a commercial dynamometer (Biodex System 4 Pro, Biodex, Shirley, New York, United States).

The protocol was based on previous work by Brisson and colleagues (2018). Participants were securely seated on the Biodex chair, as per the manufacturer’s recommendations. Muscle efforts included isometric and isotonic contractions. First, isometric testing of the quadriceps muscles was done at 60° knee flexion (where 0° is full knee extension). The participants completed five trials of five-second contraction. A 10-second break was provided to the participants between trials. The average of three (out of five) trials with the highest peak torque (Newton-meter: Nm) was deemed maximum strength. Then, for the isotonic testing, 25% of the maximum strength value of the isometric measurement was used as the resistance level. The participants completed five knee extension contractions from 0-90° knee flexion range of motion at 25% of the maximum strength (Nm) (Brisson, Stratford & Maly, 2018). Two practice trials for the isotonic contraction were offered to participants.

Power of the quadriceps muscles was the main interest of this study. The average of the three (out of five) trials with the highest peak torque (and their associated velocity) from the isotonic setting was used for data analysis. This average was transformed to a power value using equation (1), where torque (Nm) and velocity ($^{\circ}/s$) were obtained from the Biodex. Power was normalized to body mass (W/kg) to allow comparison between participants for statistical analysis using equation (2), where a = normalized value, T = actual value, and m = body mass (kg) (Accettura et al., 2015). Velocity in $^{\circ}/s$ was converted to radian/s using equation 3.

$$\text{Eq (1)} \rightarrow \text{Power (W)} = \text{Torque (Nm)} \times \text{Velocity (rad/s)}$$

$$\text{Power unit} = 1 \frac{\text{Nm}}{\text{sec}} = 1 \text{ Watt}$$

$$\text{Eq (2)} \rightarrow a = \frac{T}{m}$$

$$\text{Eq (3)} \rightarrow 180^{\circ} = \pi \text{ rad}$$

To minimize variability among participants, the following standardized instructions were provided for the isometric and isotonic testing:

- Isometric: “*When you hear the click sound, please contract as hard as you can for 5 seconds*”. The researcher provided motivation for the participants by verbally encouraging them to “push” for the duration of the 5 second trial.
- Isotonic: “*When you hear the click sound, please push against the lever to move your leg as much and as quickly as you can.*” The researcher provided motivation for the participants by verbally encouraging them to “push” for the duration of the trial.

Commercial dynamometers provide reliable data on knee strength (Šarabon, Kozinc & Perman, 2021). The Biodex System 3 Pro produces data that is valid and reliable (Drouin et al.,

2004). The reliability for day-to-day testing and trial-to-trial testing are both good (ICC = 0.99-1.00) for position (in degrees), torque (in Nm), and velocity (in degree per second) (Drouin et al., 2004). For the knee, the reliability of isometric peak torque measurement is near perfect (ICC = 0.97) (Van Driessche et al., 2018). This device has good reliability for peak velocity (ICC = 0.90) and for peak power (ICC = 0.98) for isotonic testing at 25% of the strength obtained with isometric testing (Van Driessche et al., 2018).

8.5.2. Independent (Predictor) Variables (IV):

The IV for research question #1, #3, and #4 is pain intensity. The IV for research question #2 is PPT values obtained from an algometer. Details on the outcome measures and their validity and reliability are listed below.

8.5.2.1. *Knee Injury and Osteoarthritis Outcome Score (KOOS)*

The KOOS is a self-report outcome measure commonly used to characterize pain intensity and frequency over the past week in KOA (Appendix C). The questionnaire has 5 subscales: symptoms (7 questions), pain (9 questions), function – daily living (17 questions), function – sports and recreational activities (5 questions), and quality of life (4 questions) for a total of 42 questions. Each subscale is scored independently. KOOS-pain is the subscale of interest for this project. Each question is scored on a scale of five response options. The first option (never, none, or not at all) is assigned a score of 0. The last option is assigned a score of 4. The final score for each subscale is transformed to a score from 0 to 100 with the formula below,

where 0 is indicative of severe knee concerns and 100 is indicative of no knee concern (Roos et al., 1998).

$$\text{KOOS subsection score (from 0 – 100)} = 100 - \frac{\text{Actual raw score} \times 100}{\text{Highest raw score possible}}$$

Collins et al. (2016) performed a SR-MA on 37 studies and found that the KOOS produces data with good reliability (ICC = 0.85-0.90), internal consistency (alpha = 0.84), and adequate content and construct validity in KOA population. Instruments required are pens and paper (Roos et al., 1998).

8.5.2.2. Pressure-Pain Threshold (PPT):

PPT testing allows the researcher to quantify a threshold for mechanical pain detection in individuals with KOA. A person with pain sensitization will likely report the onset of pain at a lower PPT value (lower PPT value to trigger mechanical pain) compared to a person without pain sensitization (Rankin et al., 2022).

A scoping review with 50 studies on QST and PPT testing in KOA concluded that there is significant variation in the methodology used for PPT testing in KOA. There is variability in the location of the pressure applied (medial and/or lateral joint lines, medial and/or lateral patella, tibial tuberosity, and quadriceps muscle tendon), the rate of pressure application (from 30-50kPa/s), and the number of times pressure is applied (1-3 repetitions) (Rankin et al., 2022). There is also reported variability in the rest time between pressure application, ranging from 20-60s (Hinarejos et al., 2019; Rankin et al., 2022).

The protocol of this project was based on the most common methodology used for PPT testing as summarized by Rankin et al. (2022). A Wagner FPX 25 hand-held algometer with a head of 1 cm² (rubber tip) was used to collect PPT values (Rolke et al., 2006). Pressure was

applied at a rate of one pound per second (1 lbs/s), oriented perpendicular to the skin surface (not over clothes). The participants were instructed to say “stop” when pain was first felt (not when pain became intolerable). Pressure was applied three times at the most medial surface of the medial joint line of the knee (marked with washable marker) and three times at the most lateral surface of the lateral joint line of the knee (marked with washable marker) (Rankin et al., 2022). The order of PPT testing at these two locations was randomized. A rest period of 30s was provided to participants between trials (Hinarejos et al., 2019; Rankin et al., 2022).

Pressure was applied in lbs/s instead of kPa/s as it was easier to read one-pound increments per second on the algometer. $1 \text{ kPa} = 0.022 \text{ pound-force/cm}^2$ and $44.5 \text{ kPa} = 1 \text{ pound-force/cm}^2$. Rankin et al. (2022) mentioned that for PPT testing, researchers most commonly applied pressure at a rate of 30-50kPa/s, hence applying a force of 44.5kPa/s (1 lbs) was within the recommended range. The mean value of the three measurements for each location was recorded in pounds but later converted to kPa for data analysis and reporting.

The testing position for PPT was standardized among all participants. For the medial joint line PPT value testing, participants were asked to lie down on the ipsilateral side of the painful knee and bend their painful knee and hip to 90 degrees. A pillow was inserted between their legs for comfort. For the lateral joint line PPT value testing, the participant was asked to lie down on the contralateral side of the painful knee and bend both their left and right hips and knees to 90 degrees. Again, a pillow was inserted between their legs for comfort. The position of the participant and of the researcher for PPT testing is shown in Appendix K.

To minimize variability in the responses from participants, the following instructions were given to all participants:

“This device is an algometer, or more commonly referred as a force gauge. It has a small rubber tip. I will be applying pressure through the tip here [pointing to the medial joint line] and here [pointing to the lateral joint line]. Initially, you will likely feel pressure from the tip. As I keep applying pressure, you will start to feel pain. As soon as you start to feel pain, say “STOP” and I will stop applying pressure immediately. Remember to say “STOP” as soon as you start to feel pain, not when you cannot tolerate the pain anymore. We will repeat this process three times for each location. We will take a 30-second break between trials. Do you have any questions?”.

PPT testing produces data that are reliable in KOA population, as shown in a recent systematic review (Alqarni et al., 2018). The intra-rater reliability ($ICC = 0.887-0.924$) (Alahmari et al., 2020; Stausholm et al., 2023) and the inter-rater reliability ($ICC = 0.71-0.911$) (Alahmari et al., 2020; Stausholm et al., 2023) of data produced from PPT testing in KOA samples are both good.

In a KOA sample ($n = 27$ participants, 50 knees), the intra-rater reliability ($ICC = 0.91-0.96$) and inter-rater reliability ($ICC = 0.71$) for PPT testing were good among PTs (ranging from 1-15 years of experience) if they received training (30 minutes) and practiced the technique prior to data collection (Stausholm et al., 2023). I am a registered PT in Ontario with eight years of experience and I received two-training sessions (total of 90 minutes) with Dr. Patrick Ippersiel, who is a PT and lecturer at McGill University and has completed his Ph.D. in rehabilitation science from McGill University. After training, I obtained PPT values from 12 knees, and the reliability of PPT values that I acquired ($ICC = 0.90-0.92$) is similar to published value ($ICC = 0.91-0.96$). Details about this reliability study can be found in Appendix L.

8.5.3. Moderators: Fear of Movement Scales

The Brief Fear of Movement scale (BFMS), a 6-question self-report scale adapted from a longer questionnaire, was used for this study. Descriptions of the Tampa Scale for Kinesiophobia (TSK) (the original, longer FOM questionnaire) and the BFMS (questionnaire used in this study) are presented below.

The TSK assesses of FOM (Appendix D). The TSK is a 17-question self-report scale, where each question is scored from 1-4, where 1 signifies “strongly disagree” and 4 signifies “strongly agree”. A total score is calculated from the sum of all the scores. Items 4, 8, 12, and 16 are inverted. A total score of greater than 37 suggests the presence of kinesiophobia (Liu et al., 2021). Dupuis et al. (2023) concluded in their systematic review on the psychometric properties of the TSK that there is no study on the validity and reliability of the English version of the TSK in KOA, but the Chinese and Thai versions produce data with good internal consistency in KOA ($\alpha = 0.77-0.88$). The data produced from the TSK-17 is shown be valid and to have good test-retest reliability ($ICC = 0.80-0.99$) in people with a variety of musculoskeletal conditions (Dupuis et al., 2023). Multiple versions of the TSK have been published, including the TSK-17 (original 17 questions), TSK-13 (items 4, 8, 12, and 16 removed from TSK-17), TSK-11 (items 4, 8, 9, 12, 14, and 16 removed from TSK-17), TSK-4, and TSK-TMD (for jaw conditions).

One shortened version of the TSK, the BFMS, appears to produce useful data in OA. The BFMS is a 6-question self-report scale adapted from the TSK for the OA population. The BFMS contains items 1, 2, 9, 10, 14, and 15 from the TSK-17. In a large study ($n = 1136$), the BFMS was shown to produce data that are valid and reflect FOM in OA (Shelby et al., 2012). However, a cut-off score to indicate the presence of kinesiophobia for the BFMS has yet to be published. For this study, participants completed the TSK-17 (since there is no official published version of

the BFMS) and BFMS was calculated from the appropriate subset of questions from the TSK. Only scores from the BFMS were used for statistical analysis. Instruments required were pens and paper.

8.5.4. Covariates:

Since obesity and age are reported barriers to PA in KOA (Kanavaki et al., 2017), body mass index (BMI) and age were included as covariates. There is an inverse relationship between PA and BMI (Cárdenas Fuentes et al., 2018; Kuhle et al., 2014). According to Statistic Canada's Canadian Health Measures Survey, older people perform less PA compared to younger people on average (Statistics Canada, 2021). Other studies examining the relationship between PA and pain intensity also included age and BMI as a covariate (Brisson, Gatti & Maly, 2020).

8.5.5. Other Scales and Descriptors:

8.5.5.1. Numeric Pain Rating Scale (NPRS):

The NPRS was used to monitor pain intensity during the experiment. The NPRS is an 11-point scale from 0-10 without decimals or half points. Scores are defined as 0 = “no pain” and 10 = “worst imaginable pain”. This scale produces data that are reliable (ICC = 0.95) and valid in KOA population (Alghadir et al., 2018). Appendix G shows this scale.

8.5.5.2. *Descriptors:*

8.5.5.2.1. The State Trait Anxiety Inventory (STAI):

The STAI is a two-part self-report questionnaire composed of 40 questions: 20 questions for state anxiety (STAI-S) and 20 questions for trait anxiety (STAI-T). Anxiety can be understood as an emotion triggered by a set of actual or perceived threatening or dangerous stimuli that is expected or predicted to occur in the future (Penninx et al., 2021). State anxiety is a temporary feeling of anxiety, whereas trait anxiety is a person's likelihood to be anxious in their personality (Endler & Kocovski, 2001). Each question on the STAI-S and STAI-T is scored on a 4-point scale, where 1 indicates "not at all" or "almost never" and 4 indicates "very much so" or "almost always". The total score for the STAI-S and STAI-T ranges from 20 to 80, where higher scores indicates higher state or trait anxiety. Questions 1, 2, 5, 8, 10, 11, 15, 16, 19, 20 (STAI-S) and 21, 23, 26, 27, 30, 33, 34, 36, 39 (STAI-T) are inverted for scoring. The total score is the sum of the score of each question. A cut-off score of 40 has been suggested for the STAI-S section (Emons, Habibović, & Pedersen, 2019). However, there is no published cut-off score for the STAI-T section.

The STAI is shown in Appendix E. The STAI is widely used in research and in clinical practice (Knowles & Olatunji, 2020). The STAI is shown to produce data that is valid and reliable (Emons, Habibović, & Pedersen, 2019). Instruments required for this scale are pens and paper.

8.5.5.2.2. The Movement Specific Reinvestment Scale (MSRS):

The MSRS is a 10-question, 2-part self-report questionnaire used in older adults to assess a person's conscious attention to their movements (Uiga et al., 2020). Each question is scored on

a scale of 1 to 6, where 1 indicates “strongly disagree” and 6 indicates “strongly agree”. The total score of the MSRS, which can range from 10 to 60, is the sum of the score of each question. Higher scores on the MSRS indicate a higher tendency to intentionally control one’s own movement patterns (Uiga et al., 2020). A sample of the MSRS is shown in Appendix F. The MSRS is shown to produce data that has good re-test reliability and internal reliability (Masters & Maxwell, 2008).

8.5.5.3. Other Descriptors:

Self-reported sex, gender, race, age, demographics, KOOS subscales (not including the pain subscale), current intake of pain and mental health medications, and the baseline NPRS were included as descriptors.

8.6. Statistical Analysis:

A series of linear hierarchical multiple regression analysis was completed for each research question with the IV, DV, covariates, and moderator variable below:

- Question 1:
 - Dependent: accelerometer results (steps/day), continuous
 - Independent: pain intensity measured by KOOS-pain, continuous
 - Moderator: BFMS (for FOM), continuous
 - Covariates: age and BMI, both continuous
- Question 2:
 - Dependent: accelerometer results (steps/day), continuous

- Independent: PPT values from the algometer, in kPa, continuous
- Moderator: BFMS (for FOM), continuous
- Covariates: age and BMI, both continuous
- Question 3:
 - Dependent: walking speed from the 6MWT in m/s, continuous
 - Independent: pain intensity measured by KOOS-pain, continuous
 - Moderator: BFMS (for FOM), continuous
 - Covariates: age and BMI, both continuous
- Question 4:
 - Dependent: normalized quadriceps muscle power to body mass (W/kg) from Biodex, continuous
 - Independent: pain intensity measured by KOOS-pain, continuous
 - Moderator: BFMS (for FOM), continuous
 - Covariates: age and BMI, both continuous

Prior to model building using parametric statistics, normality testing was completed for all the variables included in the regression analysis. Normality testing was completed using the Shapiro-Wilk test (with $p < 0.05$ indicating that data differs from normal distribution). If data was found to be not normally distributed, data transformation techniques were applied. These tests were performed and analyzed using Python – VS Code.

8.6.1. Building the Multiple Regression Models:

All four regressions model were built in the same manner. First, the two covariates were entered (forced entry method). Then, the IV was entered. Finally, the interaction between the IV

and the moderator (IV x Moderator) was entered as a separate, final step. To determine if FOM (measured by the BFMS) was a significant moderator, a likelihood ratio test was completed on the second and the third model. The mathematical equations for each model for objective #1 (example) are listed below.

1. Run a linear model with all the covariates (age and BMI).

$$\text{MR. 1.1} \rightarrow E[y|x]_1 = \beta_0 + \beta_1 x_1 + \beta_2 x_2$$

$$\beta_0 = \text{constant}; \beta_1 x_1 = \text{Age}, \beta_2 x_2 = \text{BMI}$$

2. Run a second linear model with covariates and KOOS-pain values (predictor).

$$\text{MR. 1.2} \rightarrow E[y|x]_2 = \text{MR. 1.1} + \beta_3 x_3$$

$$\beta_3 x_3 = \text{KOOS-pain}$$

3. Run a third linear model with covariates, KOOS-pain, and BFMS scores

$$\text{MR. 1.3} \rightarrow E[y|x]_3 = \text{MR. 1.2} + \beta_4 x_4 + \beta_5 x_1 x_4 + \beta_6 x_2 x_4 + \beta_7 x_3 x_4$$

$$\beta_4 x_4 = \text{BFMS scores},$$

$$\beta_{5-7} = \text{interaction effect of BFMS on age (5), BMI (6), and KOOS-Pain (7)}$$

4. Determine if the two models (MR.1.2 and MR.1.3) are significantly different from each other using a likelihood ratio.

8.6.2. Understanding Beta (β) in Multiple Linear Regressions:

Beta (β) coefficient can be used to describe the unstandardized or the standardized coefficient in multiple linear regressions. All beta coefficients presented in the results section are unstandardized. The equation below is an example of a simple linear regression model, where:

y = outcome, dependent variable,

a = beta coefficient,

x = predictor variable,

b = intercept.

$$y = ax + b$$

Unstandardized beta coefficient represents the change y (outcome) per single unit of x (predictor). In contrast, standardized beta coefficient represents the change in standard deviation value of y (outcome) in one standard deviation change in x (predictor). Hence, unstandardized beta coefficient keeps the original unit of the y and x values, whereas the standardized beta coefficient is unitless and only shows change of standard deviation (Field, 2009).

9. RESULTS:

9.1. Participants' Results:

Thirty-one participants completed this study. Participants' socio-economics status (SES), including race, sex, and gender are listed in Table 1.

Table 1: Socio-economics descriptors of participants (n = 31).

Socio-economics descriptors*	
Marital Status	n = 30*
Divorced	1
Married	25
Never Married	3
Widowed	1
Number of people in household	n = 30*
1 person	3
2 persons	18
3 persons	5
4 persons	2
5 persons	2
Housing type	n = 30*
Apartment or condominium	3
House (single detached, semi-detached, duplex or townhouse)	27
Education level	n = 30*
Grade 12	5
Trade certification	1
Non-University	9
Bachelor's Degree	6
University degree or certificate above bachelor's degree	9
Employment Situation	n = 30*
Full time (>35 hours/week)	7
Part time (<35 hours/week)	1
Semi-Retired	1
Retired	14
Household work	1
Retired and Household work	2
Retired and Volunteer	1
Self Employed	1
Retired and self employed	1
Prefer not to answer	1
Total household income	n = 30*

< 20,000 \$	1
20,000 \$-50,000 \$	1
50,000\$-100,000\$	9
100,000\$-150,000\$	4
> 150,000\$	9
Prefer not to answer	6
Race	n = 31
White	29
Black	1
South Asian	1
Sex	n = 31
Female	17
Male	14
Gender	n = 31
Woman	17
Man	14

* One participant did not complete the SES questionnaire for undisclosed reasons.

Participants' descriptive variables are listed in Table 2. Participants nearly all had low baseline pain and they self-reported low anxious symptoms on the STAI-S (28.4/80) and the STAI-T (31.9/80). Three participants reported that they currently take over-the-counter pain medications regularly. Ten participants took over-the-counter pain medications as needed. One participant reported taking a prescribed pain medication as needed. Three participants reported taking a prescribed mental health medication. Two participants reported taking natural products. Fifteen participants reported that they do not take any medications.

Table 3 presents the results from the IV, DV, covariates, and moderator variables. Our participants experienced mild to moderate pain level as per KOOS-Pain (74.4/100). Figure 5 shows the scatterplots between the dependent and independent variables for each research question. Higher scores on the KOOS-Pain subsection indicates lower self-report pain intensity.

There was one missing data point which was relevant to the second research question. One participant declined completing the PPT testing due to potential risk of allergic reactions from the rubber tip from the algometer. Hence, we only have 30 data points for this variable. To

manage the missing data point for PPT, we conducted a sensitivity analysis by inputting the mean value of PPT (450.73 kPa) for the participant who declined PPT testing. Furthermore, we experienced a ceiling effect with two participants in our study with the algometer instrument. Two participants did not report any pain nor discomfort at the maximum pressure value from the algometer for 3/6 of the PPT testing trials, hence the maximum value of 25 lbs (maximum of the measuring device) was inputted for these participants for data analysis.

One participant did not have three days of minimum of 10 hours of wear time for the accelerometer; there was only one valid day from the accelerometer data (objective) and two valid days (subjective) from the logbook data. Hence, the average of the highest three days of wear time obtained from the accelerometer data (12, 9, and 8.5 hours) was used to calculate the PA value for this participant. We did not discard this data point.

With the exception of age and PPT values, all other variables for the covariates, moderator, independent, and dependent variables were normally distributed as per the Shapiro-Wilk's test. Data transformation techniques were successfully applied to age (raw age value cubed) and PPT values (raw PPT values exponent 1/3) for these two variables to be normally distributed for multiple linear regression statistical analysis.

Table 2: *Participants' descriptive variables (n = 31)*

Variables	Mean	SD	Min Value	Max Value
State Trait Anxiety Inventory-State (STAI-S) (/80)	28.4	9.4	20.0	61.0
State Trait Anxiety Inventory-Trait (STAI-T) (/80)	31.9	10.3	20.0	61.0
Movement Specific Reinvestment Scale (MSRS) (/60)	28.1	9.4	10.0	46.0
Baseline-NPRS (/10)	0.6	1.2	0.0	4.5
Isometric quadriceps muscle strength normalized to body mass (Nm/kg)	1.5	0.6	0.7	3.0
KOOS-Symptoms (/100)	70.7	14.4	32.1	96.4

KOOS-Activities of daily living (/100)	80.4	14.5	48.5	100.0
KOOS-Sports (/100)	59.2	22.6	20.0	100.0
KOOS-Quality of life (/100)	60.3	16.9	6.3	87.5

*KOOS: Knee Injury and Osteoarthritis Outcome Score, higher scores indicate lower knee concerns; NPRS: Numeric Pain Rating Scale, higher scores indicate higher pain levels

Table 3: Dependent, independent, covariates, and moderator variable results (n = 31)

Variables	Mean	SD	Min Value	Max Value
Covariates				
Age (years)	65.3	7.0	51.0	76.0
BMI (kg/m ²)	30.0	5.0	19.8	40.8
Moderator				
FOM measured on the BFMS (/24)*	11.1	3.5	6.0	19.0
Independent Variable				
Physical activity (steps/day)	6253.3	2229.1	2117.0	11811.0
Walking Speed (m/s)	1.5	0.2	1.2	1.9
Quadriceps power (W/kg)	3.10	1.71	0.40	7.55
Independent Variable				
KOOS-Pain (/100)**	74.4	15.6	38.9	97.2
PPT (kPa)***	450.73	234.42	148.6	998.18

*FOM: Fear of movement; BFMS: Brief Fear of Movement Scale

**KOOS: Knee Injury and Osteoarthritis Outcome Score

***Pressure-pain threshold. n = 30 (one participant declined this test)

9.1.1. Moderation Analysis of FOM on Pain Intensity and PA:

Tables 4 shows that FOM (obtained from scores on the BFMS) did not moderate the relationship between pain intensity (measured by KOOS-Pain) and PA (measured by the accelerometer). However, FOM scores from the BFMS moderated the relationship between BMI and PA. Our covariate model showed that there is a negative relationship between age ($\beta = -0.002$, $p > 0.05$) and BMI ($\beta = -147.494$, $p > 0.05$), but this first covariate model did not explain variance in PA ($R^2 = 0.121$, $p = 0.164$). In the next step, our covariate and IV (KOOS-Pain)

model showed similar results for age ($\beta = -0.000$, $p > 0.05$), BMI ($\beta = -86.786$, $p > 0.05$), and KOOS-Pain ($\beta = 45.590$, $p > 0.05$), but this second model did not explain variance in PA ($R^2 = 0.199$, $p = 0.107$). In the final step, our model with the covariate, IV, and FOM scores from the BFMS (moderator) model showed significant interactions for BMI x BFMS ($\beta = -90.793$, $p < 0.05$), but not for age x BFMS ($\beta = 0.003$, $p > 0.05$) nor KOOS-Pain x BFMS ($\beta = 3.628$, $p > 0.05$). This final model explained variance in PA ($R^2 = 0.525$, $p = 0.009$) with a change from the previous model in R^2 of 0.326. To confirm, a likelihood ratio test showed that adding FOM scores from the BFMS (moderator model) to the previous covariate and IV model explained more variance in PA compared to the covariate and IV model alone ($p = 0.003$, $p < 0.05$). On its own, FOM scores from the BFMS were not associated with PA in the final model ($\beta = 1326.855$, $p > 0.05$).

Table 4: Results of Hierarchical Multiple Linear Regression Models for Research Question #1. Values for the beta coefficient are unstandardized. Outcome variable is physical activity.

Outcome: Physical Activity (steps/day)		β coeff. (unstd)	p value	R ²	F value	p model
Covariates:	Age	-0.002	0.723	0.121	1.93	0.164
	BMI	- 147.494	0.078			
Covariates and IV (pain intensity from KOOS-Pain)	Age	-0.000	0.970	0.199	2.23	0.107
	BMI	-86.786	0.327			
	KOOS-Pain	45.590	0.118			
Covariates, IV, and Moderator (moderator variable is FOM measured on the BFMS)	Age	-0.041	0.049	0.525	3.63	0.009
	BMI	891.883	0.005			
	KOOS-Pain	-27.273	0.770			
	BFMS	1326.855	0.288			
	Age $\times$ BFMS	0.003	0.051			
	BMI $\times$ BFMS	-90.793	0.002			
	KOOS-Pain $\times$ BFMS	3.628	0.655			
Likelihood Ratio Test	Covariates and IV model vs Covariates, IV, and moderator					0.003

IV: independent variable; KOOS-Pain: Knee Injury and Osteoarthritis Outcome Score – Pain Subsection; FOM: fear of movement; BFMS: Brief Fear of Movement Scale.

9.1.2. Moderation Analysis of FOM on Pain Sensitization and PA:

Tables 5 shows that FOM (obtained from scores on the BFMS) did not moderate the relationship between pain sensitization (measured by the algometer) and PA (measured by the accelerometer). However, FOM scores from the BFMS moderated the relationship between BMI and PA. Our covariate model showed that there is a negative relationship between age ($\beta = -0.002$, $p > 0.05$) and BMI ($\beta = -147.494$, $p > 0.05$), but this covariate model did not explain variance in PA ($R^2 = 0.121$, $p = 0.164$). In the next step, our covariate and IV (PPT values) model showed similar results for age ($\beta = -0.004$, $p > 0.05$), BMI ($\beta = -195.779$, $p < 0.05$), and PPT values ($\beta = -673.970$, $p > 0.05$) but the overall model was not significant ($R^2 = 0.233$, $p = 0.072$). In the final step, our model with the covariate, IV, and FOM scores from the BFMS (moderator) model showed significant interactions for BMI x BFMS ($\beta = -96.288$, $p < 0.05$), but not for age x BFMS ($\beta = 0.003$, $p > 0.05$) nor PPT x BFMS ($\beta = -84.576$, $p > 0.05$). This overall model explained variance in PA ($R^2 = 0.567$, $p < 0.05$) with a change from the previous model in R^2 of 0.334. To confirm, a likelihood ratio test showed that adding FOM scores from the BFMS (moderator model) to the previous covariate and IV model explained more variance in PA compared to the covariate and IV model alone ($p = 0.002$, $p < 0.05$). In our final model with pain sensitization as IV, FOM scores from the BFMS independently explained a significant amount of variance in PA ($\beta = 2653.030$, $p < 0.05$).

To account for the missing data point for PPT value, a sensitivity analysis was completed. We imputed the mean value of PPT of our sample as the missing PPT data point in separate regression analyses for the covariates and IV model and again in the covariates, IV, and FOM scores from the BFMS (moderator) model. This sensitivity analysis yielded very similar results.

Table 5: Results of Hierarchical Multiple Linear Regression Models for Research Question #2. Values for the beta coefficient are unstandardized. Outcome variable is physical activity.

Outcome: Physical Activity (steps/day)		β coeff. (unstd)	p value	R ²	F value	p model
Covariates	Age BMI	-0.002 - 147.494	0.723 0.078	0.121	1.93	0.164
Covariates and IV (pain sensitization obtained with pressure-pain threshold values)*	Age BMI PPT	-0.004 -195.779 -673.970	0.404 0.026 0.059	0.233	2.63	0.072
Covariates, IV, and Moderator (moderator variable is FOM measured by the BFMS)	Age BMI PPT BFMS Age $\times$ BFMS BMI $\times$ BFMS PPT $\times$ BFMS	-0.033 911.502 565.373 2653.030 0.003 -96.288 -84.576	0.062 0.005 0.593 0.026 0.093 0.001 0.353	0.567	4.11	0.005
Likelihood Ratio Test	Covariates and IV model vs Covariates, IV, and moderator					0.002

* Missing one PPT value, the value of 450.73 kPa was used for statistical analysis.

IV: independent variable; FOM: fear of movement; BFMS: Brief Fear of Movement Scale.

9.1.3. Moderation Analysis of FOM on Pain Intensity and Walking Speed:

Table 6 shows that FOM (obtained from scores on the BFMS) did not moderate the relationship between pain intensity and walking speed. Our covariate model shows that age ($\beta = 0.000$, $p < 0.05$) and BMI ($\beta = -0.021$, $p < 0.05$) were associated with walking speed in people with KOA ($R^2 = 0.660$, $p < 0.05$). In the next steps of the series of regression models, we systematically added the IV (KOOS-Pain) and the moderator (FOM scores from the BFMS) and interaction variables to our models. No additional variance in walking speed was noted.

Table 6: Results of Hierarchical Multiple Linear Regression Models for Research Question #3. Values for the beta coefficient are unstandardized. Outcome variable walking speed.

Outcome: Walking Speed (m/s)		β coeff. (unstd)	p value	R ²	F value	p model
Covariates	Age BMI	0.000 -0.021	0.000 0.000	0.660	27.21	0.000
Covariates and IV (pain intensity from KOOS-Pain)	Age BMI KOOS-Pain	0.000 -0.019 0.001	0.000 0.002 0.492	0.666	17.97	0.000
Covariates, IV, and Moderator (moderator variable is FOM measured by the BFMS)	Age BMI KOOS-Pain BFMS Age $\times$ BFMS BMI $\times$ BFMS KOOS-Pain $\times$ BFMS	0.000 0.001 0.012 0.146 0.000 -0.002 -0.001	0.512 0.979 0.105 0.133 0.644 0.311 0.107	0.731	8.931	0.000
Likelihood Ratio Test	Covariates and IV model vs Covariates, IV, and moderator					0.153

IV: independent variable; KOOS-Pain: Knee Injury and Osteoarthritis Outcome Score – Pain Subsection; FOM: fear of movement; BFMS: Brief Fear of Movement Scale.

9.1.4. Moderation Analysis of FOM on Pain Intensity and Quadriceps

Muscle Power:

Table 7 shows that FOM (obtained from scores on the BFMS) did not moderate the relationship between pain intensity and quadriceps muscle power. Our covariate model shows that age ($\beta = 0.000$, $p < 0.05$) and BMI ($\beta = -0.110$, $p < 0.05$) explained variance in quadriceps muscle power ($R^2 = 0.355$, $p < 0.05$). In the next steps of the series of regression models, we systematically added the IV (KOOS-Pain) and the moderator (FOM scores from the BFMS) and interaction variables to our models. No additional variance in quadriceps muscle power was noted.

Table 7: Results of Hierarchical Multiple Linear Regression Models for Research Question #4. Values for the beta coefficient are unstandardized. Outcome variable quadriceps muscle power normalized to body mass.

Outcome: Quadriceps Muscle Power (normalized to body mass, W/kg)		β coeff. (unstd)	p value	R ²	F value	p model
Covariates	Age	0.000	0.000	0.355	7.704	0.002
	BMI	-0.110	0.047			
Covariates and IV (pain intensity from KOOS-Pain)	Age	0.000	0.01	0.355	4.953	0.001
	BMI	-0.110	0.08			
	KOOS-Pain	0.000	0.99			
Covariates, IV, and Moderator (moderator variable is FOM measured by the BFMS)	Age	0.000	0.037	0.468	2.892	0.025
	BMI	0.068	0.775			
	KOOS-Pain	0.013	0.861			
	BFMS	0.049	0.961			
	Age $\times$ BFMS	0.000	0.097			
	BMI $\times$ BFMS	-0.017	0.419			
	KOOS-Pain $\times$ BFMS	-0.001	0.831			
Likelihood Ratio Test	Covariates and IV model vs Covariates, IV, and moderator					0.200

IV: independent variable; KOOS-Pain: Knee Injury and Osteoarthritis Outcome Score – Pain Subsection; FOM: fear of movement; BFMS: Brief Fear of Movement Scale.

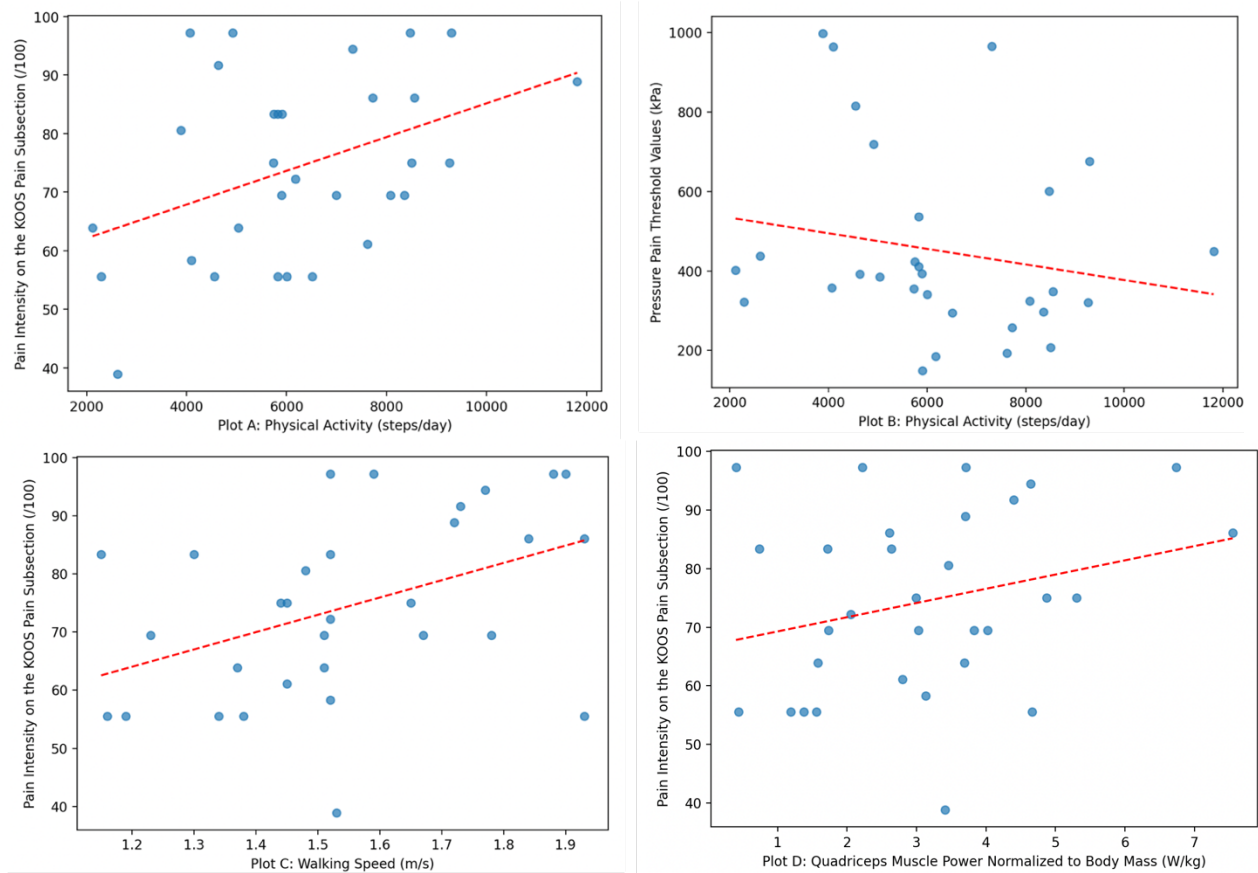


Figure 5: Scatterplot for the dependent and independent variable for research question 1-4. Higher scores on KOOS-Pain indicates lower pain intensity.

- A: Research question 1: Physical activity and pain intensity
- B: Research question 2: Physical activity and pain sensitization (n = 30 for PPT values)
- C: Research question 3: Walking speed and pain intensity
- D: Research question 4: Quadriceps muscle power (normalized to body weight) and pain intensity

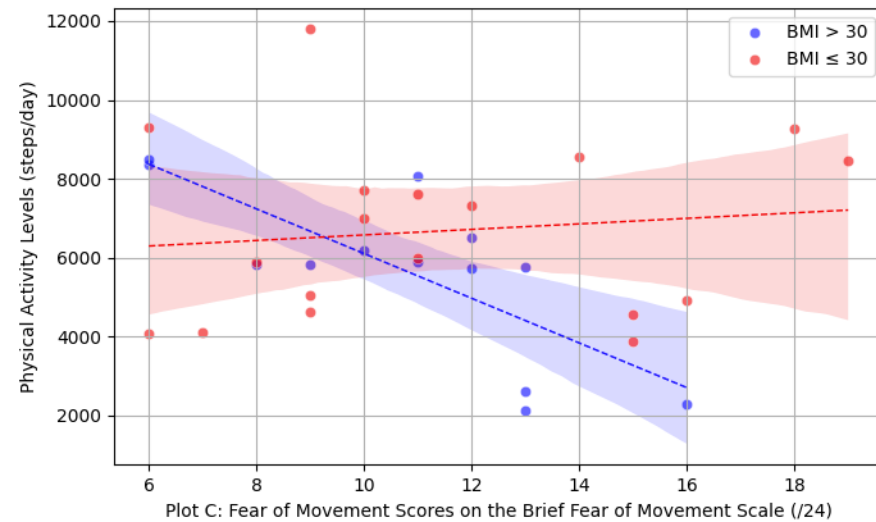
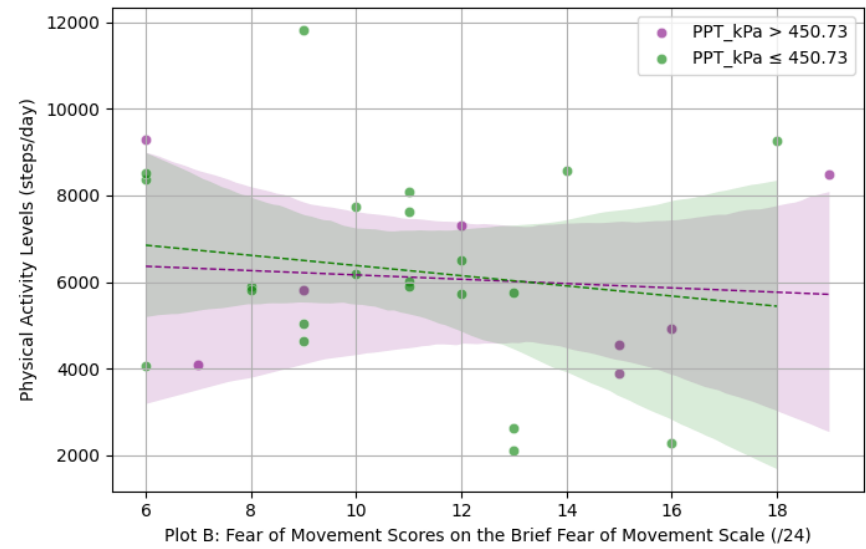
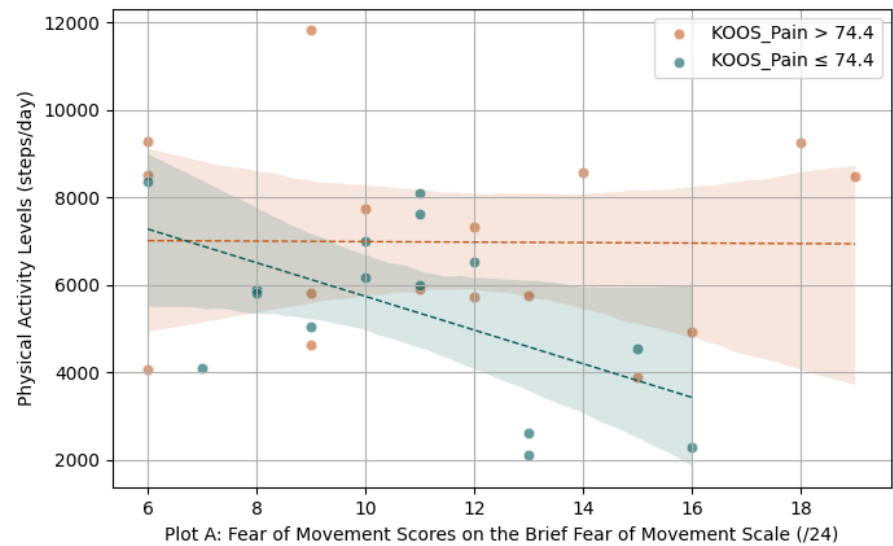


Figure 6: Interaction plots for physical activity, body mass index, and fear of movement

Plot A: Mean KOOS-Pain score is 74.4.

Plot B: Mean pressure pain threshold (PPT) value is 450.73.

Plot C: Mean body mass index (BMI) is 30.0.

10. Discussion:

The primary goal of this research project was to determine if FOM moderated the relationship between pain intensity and PA in people with KOA. Secondary, tertiary, and quaternary objectives were, respectively, to determine if FOM moderated the relationship between PPT values and PA, if FOM moderated the relationship between pain intensity and walking speed, and if FOM moderated the relationship between pain intensity and quadriceps muscle power. To our knowledge, this is the first study that examines the moderation role of FOM on pain and PA in KOA. FOM was a not significant moderator in the relationship between pain intensity (or pain sensitization) with PA in people with KOA. However, FOM interacted with BMI to explain variance in PA such that those with higher BMI and higher FOM were less likely to be physically active. A similar trend was noted between pain intensity and FOM, where those with higher pain intensity and higher FOM were less likely to be physically active. Nonetheless, on its own, FOM did not moderate the relationship between pain intensity nor pain sensitization with PA. Similarly, FOM did not moderate the relationship between pain intensity and walking speed nor the relationship between pain intensity and quadriceps muscle power.

These results are consistent with previous studies. In a study with 40 participants with KOA, FOM explained up to 19% of the variance in self-reported PA levels. Similar to the current study, their participants were overweight or obese (BMI average of 34 kg/m²), experienced moderate self-report pain intensity on the KOOS-Pain subsection (average of 54/100), and some degree of FOM (Aydemir, Huang & Foucher, 2023). A SR-MA published in 2020 shows that, in people with KOA, there is likely either no relationship or weak inverse relationship between pain intensity and total PA levels. Additionally, there seems to be a positive

relationship between lower pain intensity levels and muscle strength, muscle power, and aerobic capacity (Burrows et al., 2020). In other words, people with KOA with lower pain intensity tend to have overall better physical function in terms of muscle capacity and aerobic capacity and concurrently participate in more moderate to vigorous PA. Our findings are in line with the conclusion of this SR-MA as we found that neither pain intensity nor pain sensitization were significantly associated with PA.

10.1. Interaction between BMI, FOM and PA:

There is an inverse relationship between BMI levels and PA levels in older adults. In a study of nearly 8000 older adults, greater BMI was related to lower participation in moderate to vigorous PA (measured by accelerometry) and more time spent in sedentary behavior (Zhu et al., 2020). Similar findings on the relationship between BMI and PA were reported for people with KOA. In a study with nearly 400 participants with KOA and BMI of $>25 \text{ kg/m}^2$, higher BMI values was related with lower self-reported participation in PA (measured on the International Physical Activity Questionnaire) (Raud et al., 2020). For BMI and FOM, there are conflicting results in the literature in people with KOA. One study with participants with KOA ($n = 278$) showed that those who are obese ($>40 \text{ kg/m}^2$) presented with elevated FOM (measured on the TSK) compared to those with KOA but have a BMI $<40 \text{ kg/m}^2$ (Vincent et al., 2010). Conversely, another study with a smaller sample size ($n = 96$) concluded that there is no difference in FOM levels (measured on the TSK) in people with KOA across all BMI values (Aykut Selçuk and Karakoyun, 2020).

Taken these three variables together, clear relationships exist between elevated BMI levels and lower PA participation and higher FOM levels and lower PA participation. Our results

are in line with currently published literature and our results suggests that the interaction between the level FOM and BMI explains variance in PA levels in people with KOA.

10.2. Interaction between Pain, FOM and PA:

FOM did not moderate any association of pain intensity with PA in KOA. Further, pain intensity (from the KOOS-Pain) did not associate with PA. Various studies examined the relationship between pain with FOM and PA with FOM. In people with KOA, the level of FOM is inversely correlated with the level of PA (Aykut Selçuk & Karakorum, 2020). Higher FOM correlates with higher pain intensity (Alaca, 2019; Alshahrani et al., 2022; Aydemir, Huang & Foucher, 2022; Greenwood et al., 2023; Gunn et al., 2017; Odole et al., 2019). Our results are in line with previously published literature that suggests that the level of FOM in people with KOA is associated with lower PA levels but pain intensity is not correlated with PA levels.

Interestingly, our results suggest that FOM scores obtained from the BFMS associates with PA when pain sensitization is included as the IV, but pain sensitization (from PPT values) was not independently associated with PA. Pain sensitization occurs as a result of a heightened sensitivity of the nociceptive neurons in the PNS and/or the CNS (activation below their typical threshold) (IASP, 2021). Previous literature suggests that in people with central sensitization (such as fibromyalgia) have hypersensitivity and hyperactivation of various area of the brain (such as the insula) when stimulated with a typically non-painful stimulus (Harte et al., 2018). The posterior insula is a known to be activated in response to a painful stimulus and the anterior insula is shown to be activated in the presence of fear and anxiety (Uddin et al., 2017). In line with the literature, our results suggest that, in KOA, people with FOM and pain sensitization do not only have peripheral biological changes, but also central nervous system changes.

Understanding central and peripheral changes in people with KOA is essential for the development of treatment plans that are tailored to this subgroup of people with KOA. In terms of biological changes, any amount of exercises and PA is beneficial to people with KOA (Marriott et al., 2024). In terms of central changes, a recently published SR-MA (n = 870, 7 studies) concluded that pain education classes that focus on the comprehension of pain from a biopsychosocial viewpoint can significantly reduce reported pain intensity and pain catastrophizing in people with KOA (Lesmond et al., 2024). Additionally, another meta-analysis (n = 372, 7 studies) concluded that pain education classes in people with KOA, back pain, and other conditions can significantly reduce FOM in the short term (reduction of 13.55% on the TSK) and in the medium term (Watson et al., 2019).

10.3. FOM, Pain Intensity, and Walking Speed:

FOM did not moderate the relationship between pain intensity and walking speed in people with KOA. This finding may reflect that the study participants were unlikely to be fearful when completing the 6MWT during this study for several reasons. First, fear is an emotion triggered by a set of actual or perceived threatening or dangerous stimuli that is occurring imminently (Adolphs, 2013; Penninx et al., 2021). The environment used to determine walking speed was clutter free, leveled, and well-lit. Multiple chairs were available for sitting breaks, as needed as per standardized protocol. Additionally, because all participants for this project were recruited through an on-going longitudinal study in the Mobilize Lab, they had all previously completed this walking test at least once in the same testing location. Hence, it is likely that the familiarity of the testing location and of the task being tested resulted that the participants did not perceive this walking test as a threatening or dangerous stimulus. In psychology studies, one

single session of exposure therapy can significantly reduce the severity of various phobias (e.g., claustrophobia) (Zlomke, 2008).

Our results are in line with recently published literature which suggests that performance on a walking test is not related to reported pain intensity in KOA. One study (n = 59) found no relationship between pain at rest (measured by the visual analogue scale) and performance on walking tests (2 minutes and 6 minutes walking tests) in people with KOA (Lozano-Meca, Gacto-Sánchez & Montilla-Herrador, 2024). Though some evidence is conflicting. One study (n = 49, only females) found that FOM (measured on the TSK) does not interfere with walking abilities (measured by the 6MWT) in people with clinical KOA (Machado et al., 2022). Another study (n = 40) found that FOM (also measured on the TSK) was significantly correlated with slower self-selected walking speed (measured with motion capture) (Aydemir, Huang & Foucher, 2023) in people with KOA. Our results are in line with the study by Machado and colleagues (2022) and suggest that level of FOM on self-reported questionnaires does not interfere with walking abilities as the authors of this study also instructed their participants to walk as fast as possible for the 6MWT. In contrast, the authors in the study by Aydemir and colleagues (2023) instructed their participant to walk at their normal gait speed. The results of both of these studies should be interpreted with caution, as both groups of authors did not consider age, an important predictor of gait speed, as a covariate in their analyses.

10.4. FOM, Pain Intensity, and Quadriceps Muscle Power:

A novel contribution of this study was that we examined whether FOM moderated the impact of pain intensity on quadriceps muscle power in a sample with KOA. No other study was found that examined the relationship between FOM and knee muscle power in KOA. Only one

study showed that level of FOM plays a significant mediating role in the relationship between knee extensors strength (measured by a commercial dynamometer) and PA (measured by self-report questionnaires). In other words, higher knee extensor strength was related to lower self-reported FOM and lower FOM was related to higher PA levels (Aydemir, Huang & Foucher, 2022).

Muscle strength and muscle power are different concepts. Muscle strength is the capacity of a muscle to develop force against a resistance (Evans, 2019), whereas muscle power is the amount of torque generated at a certain velocity (speed) by a muscle contraction (Accettura et al., 2015; Reid & Fielding, 2012; Sapega & Drillings, 1983). Muscle strength and muscle power both decrease with normal age, but muscle power decreases nearly twice as fast as muscle strength (Skelton et al., 1994). Our results are in line with the current literature. It is generally well accepted that, in humans, the loss of muscle power occurs with aging and it is due to the transition of fast twitch fibres to slow twitch fibres (Miljkovic et al., 2015). This transition can be slowed with participation in exercises training (Moro et al., 2020). Age, a covariate, was the only variable that was consistently associated with quadriceps muscle power across all our models in this sample. Adding BMI, pain intensity (measured by KOOS-Pain), and the moderator variable FOM did not increase the explained variance. This suggests that a person's muscle power is vastly determined by age.

10.5. Limitations and Future Studies:

A few limitations were noted for this study. Firstly, our project consisted of 31 participants. This somewhat small sample size could contribute to a type II error (false negative) by having not enough power to detect the associations. Secondly, all participants previously

visited the Mobilize Lab and participated in at least one session of data collection for a different research project. A large study published in 2024 ($n > 4000$) showed that people who expressed interest in research studies were generally very comfortable with the English language, were working, and had higher education levels (Kim et al., 2024). This is often not the case in people with KOA in the community and our results can only be generalized to people with KOA who present with similar demographics, socio-economic status, and pain intensity as our participants. Caution should be exercised when attempting to generalize our results to individuals with KOA in the broader community, who may have different demographics and higher pain intensity. Thirdly, 29 of the 31 participants in the current study self-identified as “White”, hence one should exercise caution prior to generalizing the findings of this study to people of different racial groups. Finally, we measured quadriceps muscle power using the Biodex. Although commercial dynamometers have been validated to test quadriceps muscle strength and power, leg and knee movements on the dynamometer do not represent functional movements people with KOA must perform on a daily basis. Future projects should examine if FOM moderates the relationship between ability to perform daily functional tasks, such as ability to climb and descend stairs, and pain intensity.

PA is recommended as the first line of treatment for symptoms management in KOA, yet people with KOA clearly faces numerous physical and psychological barriers to PA, including FOM. Future studies are needed to better understand how to address FOM in people with KOA, but especially in those with FOM and pain sensitization. For FOM, it is currently not known how FOM develops, how it progresses, and who is most at risk of developing it. It is currently also not known how to either slow down or to stop its progression. For pain sensitization, there is currently no tools to clearly and easily identify those with KOA and pain sensitization. Hence,

more studies are needed to better understand FOM and pain sensitization in KOA. Furthermore, more studies are needed to understand if interventions aimed to lower FOM can translate into increased PA in people with KOA after receiving such intervention.

11. CONCLUSION:

The purpose of this study is to investigate how FOM affects the relationship between pain intensity or pain sensitization with the weekly level of PA in a sample of KOA. Additionally, this study explored how FOM affects the relationships between pain intensity, physical function, and muscle impairments (including walking speed and quadriceps muscle power) in KOA. After adjusting for age and BMI, our results show that FOM interacts with BMI, but not with pain intensity nor pain sensitization, to associate with PA. Among those who have a higher BMI, a concurrently higher FOM was correlated with less PA. Furthermore, our results show that FOM did not moderate the relationship between pain intensity with walking speed nor pain intensity with quadriceps muscle power. Since FOM worsened the impact of increased BMI on PA, future studies are needed to better understand how to reduce FOM in people with KOA.

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Appendix A: Get Active Questionnaire:



Get Active Questionnaire
CANADIAN SOCIETY FOR EXERCISE PHYSIOLOGY –
PHYSICAL ACTIVITY TRAINING FOR HEALTH (CSEP-PATH®)

Physical activity improves your physical and mental health. Even small amounts of physical activity are good, and more is better.

For almost everyone, the benefits of physical activity far outweigh any risks. For some individuals, specific advice from a Qualified Exercise Professional (QEP) – has post-secondary education in exercise sciences and an advanced certification in the area – see csep.ca/certifications or health care provider is advisable. This questionnaire is intended for all ages – to help move you along the path to becoming more physically active.

☐ I am completing this questionnaire for myself.
☐ I am completing this questionnaire for my child/dependent as parent/guardian.

PREPARE TO BECOME MORE ACTIVE

The following questions will help to ensure that you have a safe physical activity experience. Please answer YES or NO to each question before you become more physically active. If you are unsure about any question, answer YES.

YES	NO
☐	☐
1 Have you experienced ANY of the following (A to F) within the past six months?	
☐	☐
A A diagnosis of/treatment for heart disease or stroke, or pain/discomfort/pressure in your chest during activities of daily living or during physical activity?	
☐	☐
B A diagnosis of/treatment for high blood pressure (BP), or a resting BP of 160/90 mmHg or higher?	
☐	☐
C Dizziness or lightheadedness during physical activity?	
☐	☐
D Shortness of breath at rest?	
☐	☐
E Loss of consciousness/fainting for any reason?	
☐	☐
F Concussion?	
☐	☐
2 Do you currently have pain or swelling in any part of your body (such as from an injury, acute flare-up of arthritis, or back pain) that affects your ability to be physically active?	
☐	☐
3 Has a health care provider told you that you should avoid or modify certain types of physical activity?	
☐	☐
4 Do you have any other medical or physical condition (such as diabetes, cancer, osteoporosis, asthma, spinal cord injury) that may affect your ability to be physically active?	
☐	☐

.....> **NO** to all questions go to Page 2 – ASSESS YOUR CURRENT PHYSICAL ACTIVITY>

YES to any question go to Reference Document – ADVICE ON WHAT TO DO IF YOU HAVE A YES RESPONSE>



Get Active Questionnaire

ASSESS YOUR CURRENT PHYSICAL ACTIVITY

Answer the following questions to assess how active you are now.

1 During a typical week, on how many days do you do moderate- to vigorous-intensity aerobic physical activity (such as brisk walking, cycling or jogging)? DAYS/ WEEK

2 On days that you do at least moderate-intensity aerobic physical activity (e.g., brisk walking), for how many minutes do you do this activity? MINUTES/ DAY

For adults, please multiply your average number of days/week by the average number of minutes/day: MINUTES/ WEEK

Canadian 24-Hour Movement Guidelines recommend that adults accumulate at least 150 minutes of moderate- to vigorous-intensity physical activity per week. For children and youth, at least 60 minutes daily is recommended. Strengthening muscles and bones at least two times per week for adults, and three times per week for children and youth, is also recommended (see csep.ca/guidelines).

GENERAL ADVICE FOR BECOMING MORE ACTIVE

Increase your physical activity gradually so that you have a positive experience. Build physical activities that you enjoy into your day (e.g., take a walk with a friend, ride your bike to school or work) and reduce your sedentary behaviour (e.g., prolonged sitting).

If you want to do vigorous-intensity physical activity (i.e., physical activity at an intensity that makes it hard to carry on a conversation), and you do not meet minimum physical activity recommendations noted above, consult a Qualified Exercise Professional (QEP) beforehand. This can help ensure that your physical activity is safe and suitable for your circumstances. Physical activity is also an important part of a healthy pregnancy.

Delay becoming more active if you are not feeling well because of a temporary illness.

DECLARATION

To the best of my knowledge, all of the information I have supplied on this questionnaire is correct. If my health changes, I will complete this questionnaire again.

I answered **NO** to all questions on Page 1

I answered **YES** to any question on Page 1

Check the box below that applies to you:

☐ I have consulted a health care provider or Qualified Exercise Professional (QEP) who has recommended that I become more physically active.

☐ I am comfortable with becoming more physically active on my own without consulting a health care provider or QEP.

Sign and date the Declaration below

Name (or Name of Parent/Guardian if applicable) [Please print] Signature for Signature of Parent/Guardian if applicable Date of Birth

Date Email (optional) Telephone (optional)

With planning and support you can enjoy the benefits of becoming more physically active. A QEP can help.

☐ Check this box if you would like to consult a QEP about becoming more physically active. (This completed questionnaire will help the QEP get to know you and understand your needs.)

Appendix B-1: Demographics Questionnaires

PARTICIPANT ID:	DATE: (MM/DD/YYYY)
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Demographic Data Collection - Race

We aim to engage people of different races when studying health. Collecting this information will help us monitor and ensure diversity is represented in our studies.

We invite you to choose what best describes you: please **check all** that apply.

	Examples
☐ Black	African, Caribbean, Black Canadian, Afro-Latine, African American, or other African descent
☐ East Asian	Chinese, Korean, Japanese, or other East Asian descent
☐ Indigenous	First Nations, Métis, or Inuit
☐ Latine/Latinx	Latin American, Hispanic descent
☐ Middle Eastern	Afghan, Egyptian, Iranian, Lebanese, Turkish, Kurdish, or other Arab or Persian descent
☐ South Asian	East Indian, Pakistani, Bangladeshi, Sri Lankan, Indo-Caribbean, or other South Asian descent
☐ Southeast Asian	Filipino, Vietnamese, Cambodian, Thai, Malaysian, Indonesian, or other Southeast Asian descent
☐ White	British, German, Ukrainian, or other European descent
☐ Another race category	Not described above
☐ Do not know	
☐ Prefer not to answer	
☐ Prefer to self-describe	

If you chose "prefer to self-describe", please indicate your answer below:

Appendix B-2: Demographics Questionnaires (continued)

PARTICIPANT ID:	DATE: (MM/DD/YYYY)
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Demographic Data Collection – Sex and Gender

What is your sex assigned at birth?

- ☐ Prefer not to disclose
- ☐ Female
- ☐ Male
- ☐ Intersex
- ☐ Not listed

If you chose “not listed”, please indicate your answer below:

What is your current gender identity?

- ☐ Prefer not to disclose
- ☐ Woman
- ☐ Man
- ☐ Non-binary
- ☐ Prefer to self-describe

If you chose “prefer to self-describe”, please indicate your answer below:

Appendix B-3: Demographics Questionnaires (continued)

PARTICIPANT ID:		DATE:	
(MM/DD/YYYY)			

Why are we collecting this? Socioeconomic characteristics are often overlooked in research. It is our goal to include this data to understand how these factors affect disease progression.

What is your current age: _____ years old

What is your marital status?

- ☐ Never married
- ☐ Separated
- ☐ Divorced
- ☐ Widowed
- ☐ Married
- ☐ Prefer not to answer

How many people are currently living in your household, including yourself? (circle answer)

1 2 3 4 5 6 7 8 9 10+

What type of dwelling do you currently live in?

- ☐ House (single detached, semi-detached, duplex or townhouse)
- ☐ Apartment or condominium
- ☐ Seniors' housing (retirement home, assisted living)
- ☐ Hotel, rooming or lodging house
- ☐ Do not have consistent housing
- ☐ Other (please describe) _____
- ☐ Prefer not to answer

If you live in a dwelling, do you (or your spouse/partner) own or rent?

- ☐ Own
- ☐ Rent
- ☐ Not applicable
- ☐ Prefer not to answer

What is the level of education you have completed?

- ☐ Grade 8 or lower
- ☐ Grade 9-11
- ☐ Grade 12
- ☐ Trade certificate or diploma from a vocational school or apprenticeship training
- ☐ Non-university certificate or diploma from a community college, CEGEP, school of nursing, etc.
- ☐ University certificate below bachelor's level
- ☐ Bachelor's degree
- ☐ University degree or certificate above bachelor's degree

PARTICIPANT ID:		DATE:	
(MM/DD/YYYY)			

Check each option that reflects your current employment situation? (You may select more than one)

- ☐ Full-time employment (35 hours or more per week)
- ☐ Part-time employment (less than 35 hours per week)
- ☐ Self-employed
- ☐ Contract
- ☐ Seasonal, or temporary employment
- ☐ Retired
- ☐ Student
- ☐ Household work
- ☐ Caring for children or family member at home
- ☐ Unemployed
- ☐ On long-term disability leave
- ☐ Temporary leave from work (e.g. illness, parental leave)
- ☐ Volunteer
- ☐ Another option. Please specify: _____
- ☐ Prefer not to answer

What is your best estimate of the total household income received by all household members, from all sources, before taxes and deductions, in the past 12 months?

- ☐ Less than \$20,000
- ☐ \$20,000 or more, but less than \$50,000
- ☐ \$50,000 or more, but less than \$100,000
- ☐ \$100,000 or more, but less than \$150,000
- ☐ \$150,000 or more
- ☐ Don't know
- ☐ Prefer not to answer

Appendix C: KOOS

Mobilize Laboratory	
PARTICIPANT ID:	DATE:
(MMM/DD/YYYY)	

Knee injury & Osteoarthritis Outcome Score

This survey asks for your view about your knee. This information will help us keep track of how you feel about your knee and how well you are able to perform your usual activities.

Answer every question by ticking the appropriate box, only one box for each question. If you are unsure about how to answer a question, please give the best answer you can.

Symptoms

These questions should be answered thinking of your knee symptoms during the **last week**.

- S1. Do you have swelling in your knee?
Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always ☐
- S2. Do you feel grinding, hear clicking or any other type of noise when your knee moves?
Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always ☐
- S3. Does your knee catch or hang up when moving?
Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always ☐
- S4. Can you straighten your knee fully?
Always ☐ Often ☐ Sometimes ☐ Rarely ☐ Never ☐

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Mobilize Laboratory	
PARTICIPANT ID:	DATE:
(MMM/DD/YYYY)	

- P3. Straightening knee fully
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- P4. Bending knee fully
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- P5. Walking on flat surface
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- P6. Going up or down stairs
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- P7. At night while in bed
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- P8. Sitting or lying
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- P9. Standing upright
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

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Mobilize Laboratory	
PARTICIPANT ID:	DATE:
(MMM/DD/YYYY)	

- S5. Can you bend your knee fully?
Always ☐ Often ☐ Sometimes ☐ Rarely ☐ Never ☐

Stiffness

The following questions concern the amount of joint stiffness you have experienced during the **last week** in your knee. Stiffness is a sensation of restriction or slowness in the ease with which you move your knee joint.

- S6. How severe is your knee joint stiffness after first wakening in the morning?
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- S7. How severe is your knee stiffness after sitting, lying or resting **later in the day**?
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

Pain

- P1. How often do you experience knee pain?
Never ☐ Monthly ☐ Weekly ☐ Daily ☐ Always ☐

What amount of knee pain have you experienced the **last week** during the following activities?

- P2. Twisting/pivoting on your knee
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

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Mobilize Laboratory	
PARTICIPANT ID:	DATE:
(MMM/DD/YYYY)	

Function, daily living

The following questions concern your physical function. By this we mean your ability to move around and to look after yourself. For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

- A1. Descending stairs
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- A2. Ascending stairs
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- A3. Rising from sitting
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- A4. Standing
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- A5. Bending to floor/pick up an object
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- A6. Walking on flat surface
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

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Mobilize Laboratory	
PARTICIPANT ID:	DATE:
(MMM/DD/YYYY)	

- A7. Getting in/out of car
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- A8. Going shopping
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- A9. Putting on socks/stockings
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- A10. Rising from bed
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- A11. Taking off socks/stockings
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- A12. Lying in bed (turning over, maintaining knee position)
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- A13. Getting in/out of bath
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

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(MMM/DD/YYYY)	

- A14. Sitting
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- A15. Getting on/off toilet
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- A16. Heavy domestic duties (moving heavy boxes, scrubbing floors, etc)
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- A17. Light domestic duties (cooking, dusting, etc)
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

Function, sports and recreational activities

The following questions concern your physical function when being active on a higher level. The questions should be answered thinking of what degree of difficulty you have experienced during the **last week** due to your knee.

- SP1. Squatting
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- SP2. Running
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

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- SP3. Jumping
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- SP4. Twisting/pivoting on your injured knee
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐
- SP5. Kneeling
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

Quality of Life

- Q1. How often are you aware of your knee problem?
Never ☐ Monthly ☐ Weekly ☐ Daily ☐ Constantly ☐
- Q2. Have you modified your life style to avoid potentially damaging activities to your knee?
Not at all ☐ Mildly ☐ Moderately ☐ Severely ☐ Totally ☐
- Q3. How much are you troubled with lack of confidence in your knee?
Not at all ☐ Mildly ☐ Moderately ☐ Severely ☐ Extremely ☐

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- Q4. In general, how much difficulty do you have with your knee?
None ☐ Mild ☐ Moderate ☐ Severe ☐ Extreme ☐

Thank you very much for completing all the questions in this questionnaire.

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Appendix D: Tampa Scale for Kinesiophobia

Mobilize Laboratory	
PARTICIPANT ID:	DATE: (MMM/DD/YYYY)

Tampa Scale for Kinesiophobia

Scoring:

1 = Strongly disagree

4 = Strongly agree

1. I'm afraid that I might injury myself if I exercise	1	2	3	4
2. If I were to try to overcome it, my pain would increase	1	2	3	4
3. My body is telling me I have something dangerously wrong	1	2	3	4
4. My pain would probably be relieved if I were to exercise	1	2	3	4
5. People aren't taking my medical condition seriously enough	1	2	3	4
6. My accident has put my body at risk for the rest of my life	1	2	3	4
7. Pain always means I have injured my body	1	2	3	4
8. Just because something aggravates my pain does not mean it is dangerous	1	2	3	4
9. I am afraid that I might injure myself accidentally	1	2	3	4
10. Simply being careful that I do not make any unnecessary movements is the safest thing I can do to prevent my pain from worsening	1	2	3	4
11. I wouldn't have this much pain if there weren't something potentially dangerous going on in my body	1	2	3	4
12. Although my condition is painful, I would be better off if I were physically active	1	2	3	4
13. Pain lets me know when to stop exercising so that I don't injure myself	1	2	3	4
14. It's really not safe for a person with a condition like mine to be physically active	1	2	3	4
15. I can't do all the things normal people do because it's too easy for me to get injured	1	2	3	4
16. Even though something is causing me a lot of pain, I don't think it's actually dangerous	1	2	3	4
17. No one should have to exercise when he/she is in pain	1	2	3	4

Appendix E: State and Trait Anxiety Inventory

SELF-EVALUATION QUESTIONNAIRE STAI Form Y-1

Please provide the following information:

Name _____ Date _____
Age _____ Gender (Circle) M F T _____

DIRECTIONS:

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you feel *right now*, that is, *at this moment*. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

NOT AT ALL
SOMEWHAT
MODERATELY SO
VERY MUCH SO

1. I feel calm.....	1	2	3	4
2. I feel secure.....	1	2	3	4
3. I am tense.....	1	2	3	4
4. I feel strained.....	1	2	3	4
5. I feel at ease.....	1	2	3	4
6. I feel upset.....	1	2	3	4
7. I am presently worrying over possible misfortunes.....	1	2	3	4
8. I feel satisfied.....	1	2	3	4
9. I feel frightened.....	1	2	3	4
10. I feel comfortable.....	1	2	3	4
11. I feel self-confident.....	1	2	3	4
12. I feel nervous.....	1	2	3	4
13. I am jittery.....	1	2	3	4
14. I feel indecisive.....	1	2	3	4
15. I am relaxed.....	1	2	3	4
16. I feel content.....	1	2	3	4
17. I am worried.....	1	2	3	4
18. I feel confused.....	1	2	3	4
19. I feel steady.....	1	2	3	4
20. I feel pleasant.....	1	2	3	4

SELF-EVALUATION QUESTIONNAIRE STAI Form Y-2

Name _____ Date _____

DIRECTIONS

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you *generally* feel.

ALMOST NEVER
SOMETIMES
OFTEN
ALMOST ALWAYS

21. I feel pleasant.....	1	2	3	4
22. I feel nervous and restless.....	1	2	3	4
23. I feel satisfied with myself.....	1	2	3	4
24. I wish I could be as happy as others seem to be.....	1	2	3	4
25. I feel like a failure.....	1	2	3	4
26. I feel rested.....	1	2	3	4
27. I am "calm, cool, and collected".....	1	2	3	4
28. I feel that difficulties are piling up so that I cannot overcome them.....	1	2	3	4
29. I worry too much over something that really doesn't matter.....	1	2	3	4
30. I am happy.....	1	2	3	4
31. I have disturbing thoughts.....	1	2	3	4
32. I lack self-confidence.....	1	2	3	4
33. I feel secure.....	1	2	3	4
34. I make decisions easily.....	1	2	3	4
35. I feel inadequate.....	1	2	3	4
36. I am content.....	1	2	3	4
37. Some unimportant thought runs through my mind and bothers me.....	1	2	3	4
38. I take disappointments so keenly that I can't put them out of my mind.....	1	2	3	4
39. I am a steady person.....	1	2	3	4
40. I get in a state of tension or turmoil as I think over my recent concerns and interests.....	1	2	3	4

Appendix F: MSRS

The Movement Specific Reinvestment Scale (MSRS)

Instructions: Circle the answer that best describes how they feel.

	Strongly Disagree					Strongly Agree
Conscious Motor Processing						
I am always trying to think about my movements when I carry them out	1	2	3	4	5	6
I reflect about my movement a lot	1	2	3	4	5	6
I am always trying to figure out why my actions failed	1	2	3	4	5	6
I am aware of the way my body works when I am carrying out a movement	1	2	3	4	5	6
I rarely forget the times when my movements have failed me	1	2	3	4	5	6
Movement Self-Consciousness						
I am concerned about my style of moving	1	2	3	4	5	6
I am self-conscious about the way I look when I am moving	1	2	3	4	5	6
If I see my reflection in a shop window, I will examine my movements	1	2	3	4	5	6
I sometimes have the feeling that I am watching myself move	1	2	3	4	5	6
I am concerned about what people think about me when I am moving	1	2	3	4	5	6

Appendix G: NPRS

I will verbally ask the participants:

“On a scale of 0-10, where 0 = no pain and 10 = worse imaginable pain, how would you rate your pain now? Please only use integers, no half points.”

Appendix H: 6MWT

The American Thoracic Society (ATS) (2002) standardized the instructions for the 6MWT and standardized moments during the test to collect subjective data on pain. Hence, the data and tests will be collected in this order: Borg Scale (initial) → 6MWT → Borg (final).

To minimize variability among subjects, the following standardized instructions published by ATS will be read to all participants. *“The object of this test is to walk as far as possible for 6 minutes. You will walk back and forth in this hallway. Six minutes is a long time to walk, so you will be exerting yourself. You will probably get out of breath or become exhausted. You are permitted to slow down, to stop, and to rest as necessary. You may lean against the wall while resting but resume walking as soon as you are able. You will be walking back and forth around the cones. You should pivot briskly around the cones and continue back the other way without hesitation. Now I’m going to show you. Please watch the way I turn without hesitation. [Researcher shows participant walking and turning a corner of the rectangle]. Are you ready to do that? I am going to use this counter to keep track of the number of laps you complete. I will click it each time you turn around at this starting line. Remember that the object is to walk AS FAR AS POSSIBLE for 6 minutes, but don’t run or jog. Start now, or whenever you are ready.”*

Below are the minute-by-minute standardized instructions. To minimize variability, the following standardized instructions published by ATS will be read to all participants:

- At 5 minutes left: *“You are doing well. You have 5 minutes to go.”*
- At 4 minutes left: *“Keep up the good work. You have 4 minutes to go.”*
- At 3 minutes left: *“You are doing well. You are halfway done.”*
- At 2 minutes left: *“Keep up the good work. You have only 2 minutes left.”*
- At 1 minute left: *“You are doing well. You have only 1 minute to go.”*
- At 15 seconds left: *“In a moment I’m going to tell you to stop. When I do, just stop right where you are and I will come to you.”*
- At 0 seconds left: *“Stop”*

Appendix I: Data Collection Sheet

PARTICIPANT ID:	DATE: (MM/DD/YYYY)
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Data Collection Sheet:

Age (YYYY/MM):	
Height (cm):	
Weight (kg):	
Baseline pain level:	NPRS = ____ /10
PPT value trial #1	LBS
PPT value trial #2	LBS
PPT value trial #3	LBS
Pain pre 6MWT	NPRS = ____ /10
Borg pre 6MWT	
Pain Post 6MWT	NPRS = ____ /10
Borg pre 6MWT	
Pain Pre Biodex	NPRS = ____ /10
Final Pain level	NPRS = ____ /10

Appendix J: Accelerometer Logbook

Mobilize Laboratory

PARTICIPANT ID:

DATE:

(MMM/DD/YYYY)

Accelerometer Logbook

Instructions:

- Please wear the device for 7 days.
- Record the time you start to wear it (Time ON), and the time to took it off (Time OFF)
- If you had any issues with the device, please write/comment on the comments section below
- If you have any other questions, please email huaning.liu@uwaterloo.ca

Date									
Time ON									
Time OFF									
Any issues									
Other comments									

Appendix K: PPT Testing Position

This is an example for the left knee. The participant is in side-lying on a plinth. For the lateral joint line testing, the participants are instructed to have their hips and knees bend at approximately 90 degrees. A cushion or a pillow will be placed between the knees for the participant's comfort. For the medial joint line testing, the leg that is not being tested will be supported by a cushion or a pillow for comfort.



Appendix L: Personal Reliability Study for PPT

12 knees were recruited for my personal reliability study for the collection of PPT values using the algometer. Participants of all sexes and genders were eligible for my personal study. Oral consent was obtained from all participants prior to taking part of this study. Participants were notified that they are allowed to withdrawal their consent at any time during this study without needing to provide justification to this researcher.

Participants were instructed to lie down in the same testing position as shown in Appendix K. PPT testing locations were the medial and lateral joint line of the knees. Pressure was applied three (3) times at each joint line. To maximize participants' comfort and to reduce the number of times participants needed to change position on the physiotherapy plinth, the order at which the pressure was applied at the joint line was not randomized. PPT values were collected in lbs. Data was analysed in lbs and processed in Python – VS code.

Medial joint line

Knee ID	Trial 1 (lbs)	Trial 2 (lbs)	Trial 3 (lbs)
1	4.18	2.9	3.94
2	4.02	4.46	4.44
3	3.46	3.68	3.38
4	5.60	6.22	3.48
5	4.92	3.98	3.22
6	4.16	3.78	4.18
7	6.22	5.04	5.52
8	8.02	8.00	7.28
9	6.02	8.84	8.84
10	6.64	7.18	7.02
11	7.44	5.74	4.86
12	4.38	5.90	4.62

ICC (3,3) = 0.90

Lateral joint line

Knee ID	Trial 1 (lbs)	Trial 2 (lbs)	Trial 3 (lbs)
1	2.54	2.32	2.74
2	4.74	3.74	3.58
3	5.54	6.08	5.64
4	4.92	5.50	4.96
5	6.30	5.60	3.90
6	4.30	4.16	3.08
7	6.34	6.70	6.58
8	8.68	5.54	6.02
9	8.98	8.06	8.48
10	5.88	8.54	6.64
11	4.20	3.40	4.86
12	6.56	5.28	5.22

ICC (3,3) = 0.92

110

(MMM/DD/YYYY)

COMMON MEDICATIONS

Please complete this questionnaire on medications to the best of your knowledge:

Pain Medications:	Currently Taking:	List frequency, dosage & last time taken
Ibuprofen	☐	
Advil	☐	
Aspirin	☐	
Acetaminophen	☐	
Tylenol	☐	
Other Pain Medications:		
	☐	
	☐	
	☐	
	☐	
Mental Health Medications:		
Citalopram (Celexa)	☐	
Escitalopram (Lexapro)	☐	
Fluoxetine (Prozac)	☐	
Paroxetine (Paxil, Pexeva)	☐	
Sertraline (Zoloft)	☐	
Other Mental Health Medications:		
	☐	
	☐	
	☐	
	☐	
	☐	