# Quantifying Energy Expenditure in Osteoarthritis using ActiGraph and ActivPal accelerometers: A validation Study.

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# Abstract

*Background:* Osteoarthritis (OA) is a chronic degenerative disease targeting the body's load-bearing joints. If left untreated, the disease could progress, resulting in an individual being deemed physically disabled due to pain experienced and movement limitations associated with the condition. Physical activity is the gold-standard treatment for OA-associated symptom management and prevention of disease progression. However, sedentary behaviour and physical inactivity are common occurrences within OA. Physiological changes accompanied by the condition (such as additional muscle incorporation to compensate for instability and muscle weakness) result in a higher energy cost during movement in people with OA. Accurate physical activity prescription is known to aid in OA symptom management and improve quality of life. However, current methods of physical activity monitoring may prove inaccurate in an OA population. Current accelerometer algorithms have been validated in a healthy population. However, their accuracy in people with OA remains unclear. The higher energy cost of movement in OA may result in inaccurate energy expenditure estimations using current algorithms. Therefore, the present study aims to validate the use and accuracy of the current accelerometer and associated algorithms in predicting energy expenditure in OA. *Methods:* 8 OA participants (mean (sd) age 61.62 (9.13) years, BMI 29.13 (4.68) kg/m$^2$) were directly observed for 2 hours and instructed to complete activities of sedentary behaviour, at-home mimicked activities and light physical activity. Indirect calorimetry was used to determine actual energy expenditure during activities and compared to accelerometer-derived energy expenditure estimations using hip and wrist-based ActiGraph and thigh-based ActivPal accelerometers. *Results:* Hip ActiGraph achieved a 37.5% agreement to gas analysis energy expenditure estimations, and wrist

ActiGraph achieved a 25% agreement. Thigh ActivPal achieved a near-perfect agreement of 87.5% to actual energy expenditure estimations. *Conclusion:* The present study found that hip and wrist-worn ActivGraph accelerometers may not be valid in accurately predicting energy expenditure in OA. Research is needed to develop algorithms to adjust for the physiological changes and higher energy costs in OA. Thigh-based ActivPal accelerometers and algorithms are valid and accurate in predicting energy expenditure in OA.

## Acknowledgements

Throughout the writing of this dissertation, I have received a great deal of support and assistance.

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# Table of Contents

## 1. Contents

# 1.

# 2. Introduction

## a. History of Osteoarthritis

Osteoarthritis (OA) was first discovered and termed in 1886 by Dr John Kent Spender (1). He introduces his paper 'The early symptoms and early treatment of osteo-arthritis' by paraphrasing and agreeing with the College of Physicians' statement that "everyone who writes about rheumatoid arthritis is expected to begin with an apology for not calling it OA" (1). OA's initial pathology (when misdiagnosed as rheumatoid arthritis) was thought to be caused by nervous system deformities or abnormalities leading to bone deformities and subsequent osteoarthritic symptoms. However, in his discussion, Dr Spender states that a conscious note should be made to prevent the current pathological bias resulting from every known chronic joint disease associated with an abnormality present in an individual's nervous system (1). As research and knowledge progressed, it has been found that many factors play a role in the development of OA, which will be discussed further in this literature review.

## b. Who does OA affect, and how big of a problem is it?

OA is the most common of all the arthritis forms known to date. OA is a chronic degenerative disease targeting the joints within the body (2–6) and presenting in mild, moderate, or severe

stages (5). OA causes cartilage deterioration, joint cavity reduction, and subsequent bone friction resulting in the associated symptoms accompanying OA's presence (2–4,7–9). OA affects elderly populations, specifically ages 45 and onwards, affecting more females than males within this population (10–16). OA is known to impact the body's load-bearing joints and affects joints most commonly used during daily activities; OA has the largest prevalence and incidence rates in the knee, followed by the hip, and thirdly, affecting the hands of individuals presenting with the condition (3,5,6,16–19). OA symptoms include chronic joint pain, mobility and movement limitations, and reduced joint range of motion (5). These symptoms subsequently limit an individual's ability to perform physical activities, including those performed during exercise or daily living. Due to the movement limitations and chronic pain experienced reduce an individual's quality of life (5,13,20–23).

Osteoarthritis is highly prevalent globally and is more common in older age groups (40-80 years of age). In 2017 Hamood et al. stated that the prevalence rate of OA is estimated to be ~138 per 1000 persons (24) (Fig 1). Due to improved healthcare and increased lifespan, by 2050, the World Health Organisation estimated 20% of the world's population would comprise individuals above 60, and assuming OA's prevalence remains and does not increase, a large portion of the world's population would be in chronic pain and have a lowered quality of life- 9,735,033,900 population by 2050 as estimated by the United Nations, therefore 1,122,499,408 individuals with OA (assuming current prevalence rates do not increase) (5,7,13,20,21,23,25). Additionally, it is estimated that one-third of people with OA have severe disease that renders them physically disabled (374,166,469 individuals according to the above-estimated numbers) (2050 estimation of 130 million people)

(5,7,23,26,27). Therefore in 28 years, a significant proportion of the world's population will be living with severe disabilities.

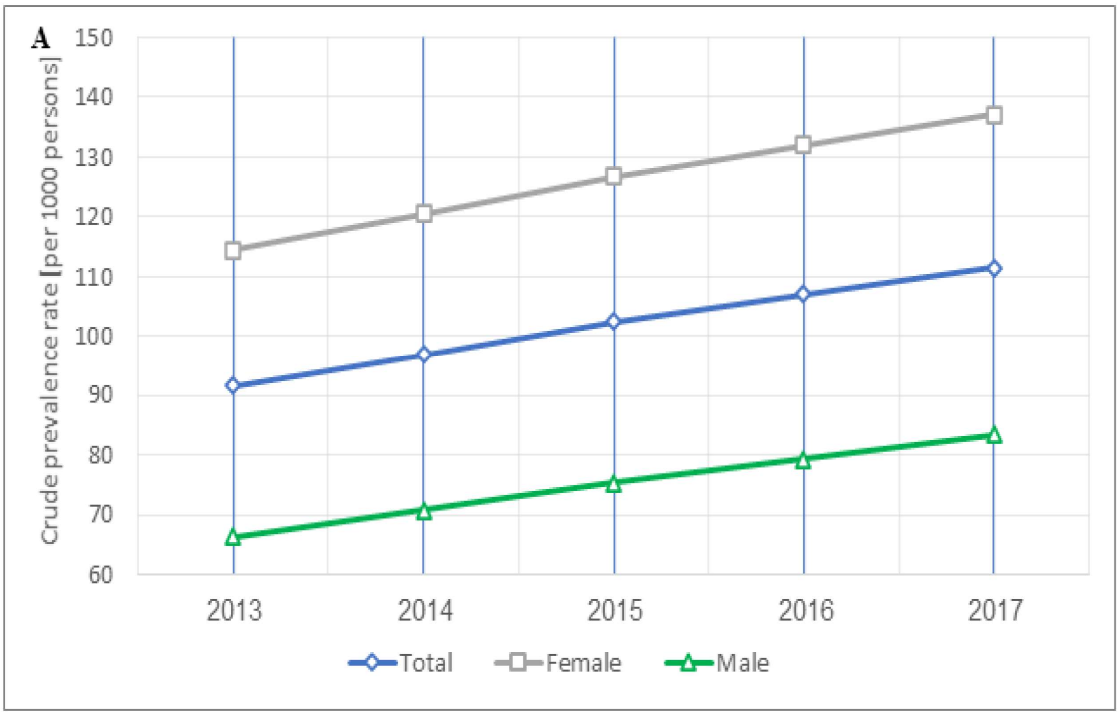



**Figure 1:** Crude incidence rates of OA from 2013-2017. Taken from Hamood et al. (2018) (24).

It is estimated that the individual cost burden of OA ranges from $42,000-$70,400 over 28 years of living with the disease - depending on whether surgery is necessary or not (28). This financial burden emphasizes the need for research to determine more cost-effective methods for managing OA, improved diagnostic approaches and technologies to diagnose and monitor

OA's progression, and determine and evaluate intervention methods to ensure the best outcomes in this population.

In New Zealand, OA has an annual incidence rate of 7000 new cases in 2013 (13). Abbott et al. found that the incidence risk of developing OA increases by 8% in people aged between 45-55 years old compared to 25-45 years of age, and a further 30% higher risk is seen in individuals aged 70 and above compared to adults of 45-55 years age group (13). In all individuals with OA, 54-56% of the population experienced no pain or discomfort, followed by individuals experiencing moderate pain or discomfort (31-40%), and finally, 6-13% of individuals experienced extreme pain and discomfort according to the Quality Adjusted Life Years (QALY) across the age groups within this study (Table 1) (13). The severe pain and discomfort experienced in people with OA can lead to this group being physically disabled, thus creating an extreme decline in their quality of life.

**Table 1**: Pain and discomfort QALY's according to different age ranges of individuals diagnosed with OA. Taken from Abbott et al. (13).

**Table 1. Quality of life utilities, by age and pain level.**

| | Pain level | | |
|---|---|---|---|
| **Age** | **No pain or discomfort** | **Moderate pain or discomfort** | **Extreme pain or discomfort** |
| **40–44** | 0.959 | 0.652 | 0.314 |
| **45–49** | 0.959 | 0.642 | 0.285 |
| **50–54** | 0.951 | 0.646 | 0.239 |
| **55–59** | 0.946 | 0.649 | 0.122 |
| **60–64** | 0.968 | 0.643 | 0.160 |
| **65–69** | 0.947 | 0.627 | 0.280 |
| **70–74** | 0.974 | 0.623 | 0.239 |
| **75–79** | 0.950 | 0.635 | 0.165 |
| 80–84 | 0.916 | 0.609 | 0.107 |

Note: QALY input was taken from the EQ-5D Tariff 2 health state preference values (Devlin, Hansen et al. 2003) derived from a survey of the NZ population (Devlin, Hansen et al. 2000). We stratified the original EQ-5D data set by level of pain (no pain or discomfort; moderate pain or discomfort; extreme pain or discomfort).

Table 1 represents the quality of life per year (QALY) of individuals suffering from OA categorized into different age groups. A healthy person with no disease suffering would achieve a QALY of 1, whereas if half the year were spent with a reduced QALY due to pain or discomfort, it would result in a QALY of 0.5. As individuals with OA age, their overall QALY decreases regardless of pain or discomfort. (13). Thus, due to OA's prevalence and associated symptoms, this table identifies that individuals with OA have a reduced quality of life regardless of OA-associated pain or discomfort. As a result, an increased need is observed to develop and integrate more cost-effective methods in treatment and management within this population. For this to occur, increased efforts are needed in the research community to better understand OA and its effect on individuals' lives to incorporate improved strategies for its treatment and management and thus improve the overall quality of life in the OA population.

The highest risk group for developing OA in New Zealand is non-Māori individuals. Non-Māori women have significantly higher QALY than Māori women (3.55 vs 3.38 respectively), and non-Māori males had a considerably higher QALY than their Māori counterparts (3.34 vs 2.6 respectively). Additionally, as seen by the above QALYs, women have been more inclined to develop OA than males.

Thus, incidence and prevalence rates in OA are higher and further increase- in older populations, resulting in a reduced quality of life observed in an elderly OA population. Further, research has shown that health inequity exists in NZ between non-Māori and Māori

individuals (29). As a result, further research is needed within OA, its affected populations, improved treatment and management strategies and approaches, and to ensure a better understanding of the disease is achieved for improved health outcomes.

### c. Joints of the Human Body

Before discussing how osteoarthritis pathology affects human movement, the normal function of joints involved in human movement will be discussed. Human movement and mobility play a crucial role in performing activities of daily living. The movement generated needs to be smooth and controlled with the desired outcome free from injury or bodily damage to achieve these action-initiated responses. Through the evolutionary development of joints, three main joints have been formed. The three main joints are; cartilaginous (or amphiarthroidal) joints, fibrous (or synarthrodial) joints, and synovial (or diarthrodial joints) (30).

The fibrous joints- also termed ‘fixed joints’- are associated with minimal or no movement and are found in joints where two bones meet and are joined with primarily fibrous connective tissue where movement restriction or prevention is required. Cartilaginous joints, known as slightly movable, are associated with minor movement between bones and connect bones through the presence of cartilage.

The most common joint in the human body is the synovial joint. Synovial joints are classified as freely moveable joints (8,31,32). They are the joints of focus in this study- specifically the knee and hip joint, as these are the most commonly affected by OA development, having the

most significant impact on daily living within this population. The basic structures present in synovial joints include articulating bones. Specialized structures include; the outer membranes, inner synovial membrane, synovial bursae, synovial fluid, and articular cartilage. These specialized structures surround the articulating ends of adjacent bones and form an enclosed structure known as the articular capsule (8,31,33). The outer fibrous capsule connects to the bone and forms additional mergings with surrounding structures, such as ligaments and tendons, to further strengthen the joints' durability (8,31,33). Synovial joints' inner membrane comprises highly specialized cells that secrete synovial fluid- known as synovial cells (8,34,35). The synovium is a highly porous membrane that attaches to the cartilage margins on the adjacent bones' articulating surfaces. Along with the synovium cells, the synovium's primary function is to secrete a thick viscous liquid into the joint cavity known as synovial fluid. This slimy fluid plays a crucial role in lubricating the articulating surfaces of adjacent bones to reduce and minimize friction within the joint capsule (8,34).

Another structure within the joint that aids in reducing friction is the articulating cartilage found at the articulating ends of adjacent bones. Both the articulating cartilage and the synovial fluid play a crucial role in minimizing friction between the adjacent bones and aiding the joint's smooth movement. The articulating cartilage, known as hyaline or type II collagen cartilage, is a thin layer of smooth specialized spongy cartilage that appears 'glass-like' and translucent on articulating surfaces in both synovial and cartilaginous joints (36). The articulating cartilage's function prevents friction between the bones and protects the bones if they would come in contact (such as when longitudinal impact forces are experienced by the joint). The absorption of the synovial fluid aids in the cartilage's properties of articulation, lubrication, shock absorption, and nourishment of the cartilage- the

synovial fluid is the cartilage's only nutrition source due to an absence of blood supply (31,34). The joint cavity in synovial joints allows a broader and more free range of motion by the joint while allowing the articulating bones to move smoothly and pain-free. Due to these additional functional characteristics of synovial joints, the joint can move through a more comprehensive range of free movement. Synovial joints are classified as diarthrosis- New Latin borrowed from Greek translating to 'articulation of free movement.'.

Additional structures aid in the joint's strength, durability, and free movement. Some synovial joints have been found to have specialized fibrocartilage structures located between the articulating surfaces within the joint. The fibrocartilagenous structure often appears in a circular or oval shape and as an articulating disc or a meniscus (usually a large 'C' shaped disc for the latter) (8,33). Indeed, the fibrocartilage structures have different structural properties depending on where they are found; it has been shown that these structures share a common function of aiding in smooth movement within the joint. Other structures in synovial joints include sacs of lubricating fluid (often found in areas where friction may be experienced between skin, muscles, tendons, or ligaments), known as a bursa. Bursae are often found in synovial joints near bony joints such as the knee, hip, or shoulder (Fig 2). Bursae aid in movement by creating a separation between external bodily structures preventing friction from forming and, thus, preventing damage (8,30). Tendon sheaths are also found in synovial joints and protect muscle tendons that cross over a joint from friction. Tendon sheaths comprise small connective tissue sacs filled with lubricating fluid -similar to bursae but much smaller. Tendon sheaths can be found throughout the body, such as in the hands and feet (Fig 3).

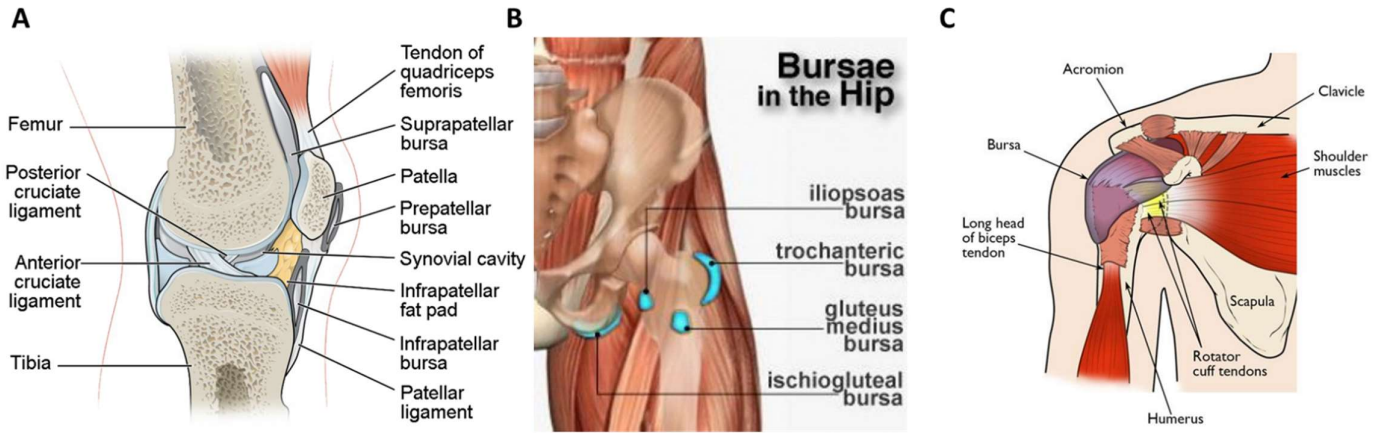



**Figure 2:** Diagrams of bursae found in the Knee (A), Hip (B), and Shoulder (C) (37–41).

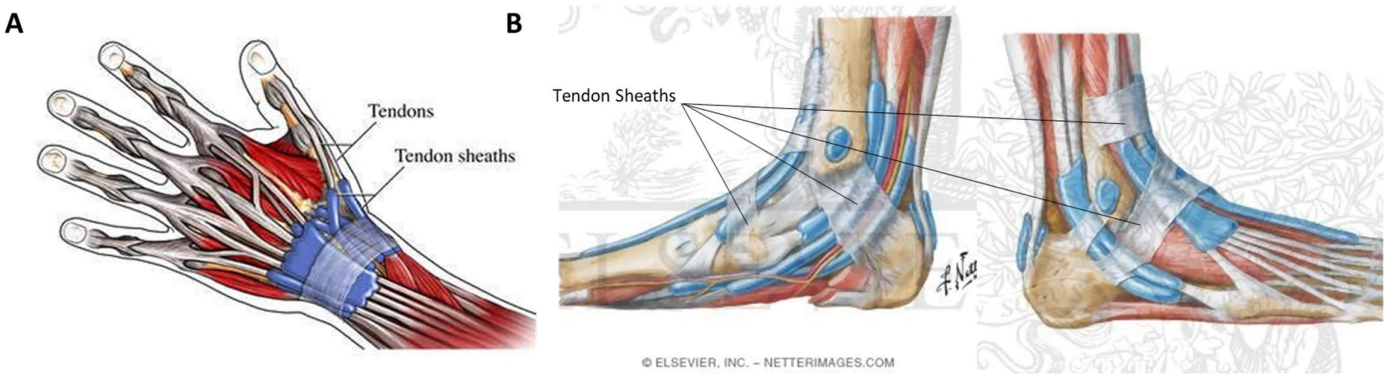



**Figure 3:** Diagrams of tendon sheaths found in the Hand (A) and Feet (B) (42,43).

Synovial joints are found in areas where a wide range of motion is needed and aid in smooth, pain-free movement. Synovial joints have six (6) different joint types occurring in the human body. These joint types include; condyloid, saddle, pivot, gliding, hinge, and ball and socket joints (the latter two being of focus in this report) (8) (Fig 4).

Hinge joints are formed when one bone articulates with an adjacent bone in a concave-convex manner- often compared similarly to a hinge on a door (44)(Fig 4(E)). However,

unlike saddle joints, hinge joints only permit movement in one direction- flexion and extension. Typical hinge joints can be found in the hand, foot (interphalangeal), and elbow (between the ulnar and humerus) joints. These hinge joints are classified as ‘common hinge joints. However, the human body has adapted to create a ‘modified’ hinge joint that permits slight movement in additional planes. This ‘modified’ hinge joint can be found in the knee (allowing for some rotational movement) and the ankle (allowing adduction and abduction, or inversion and eversion) (5,45). The modification of the knee joint comes from its skeletal arrangement and cartilaginous, ligamentous, and tendinous structures allowing the incorporation of other movement ranges such as slight adduction and abduction without causing damage or discomfort to the knee. The knee consists of three bones that articulate within the knee joint; the femur (thigh bone), tibia (shin bone), and patella (knee cap) (34,46–48). Each point of articulation within the knee joint (femur, tibia, and patella) is covered with specialized hyaline cartilage to prevent friction during movement. Each knee joint has two menisci present, the lateral and medial menisci. These menisci absorb shock and impact when the knee moves and aid in stabilizing the femoral condyles on the tibial plateau to prevent dislocation (46–48). The joint capsule surrounds the knee’s articulation area, cartilage, menisci, ACL, and PCL, fusing with the MCL and passing posteriorly to the patella (forming the patellar retinaculum) (49). Three muscle groups, accompanied by their respective tendons, aid in the ability and strength of the knee joint. These muscle groups include the anterior thigh muscles (quadriceps muscles), posterior thigh muscles (hamstrings), and the posterior lower leg muscles (gastrocnemius and soleus). The tendons of these muscles, along with the patella tendon, allow for flexion (hamstrings) and extension (quadriceps) movements seen at the knee joint (46–48).

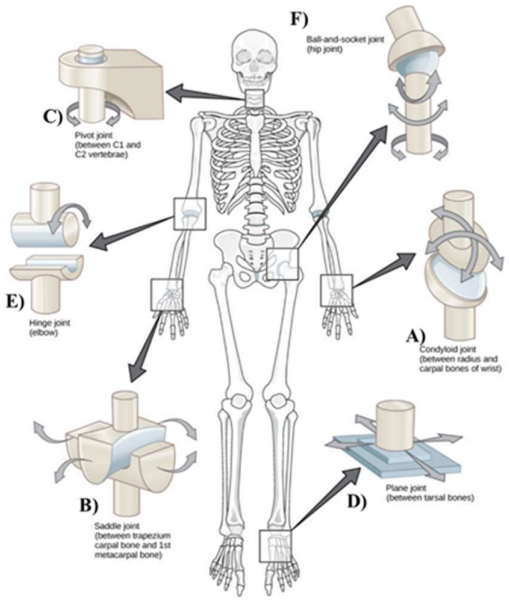



**Figure 4:** Skeletal diagram of the different synovial joints in the human body. (A) Condyloid Joint (B) Saddle Joint (C) Pivot Joint (D) Gliding/Plane Joint (E) Hinge Joint (F) Ball and Socket Joint (47)

Ball and socket joints are formed when an orb-shaped end of one bone articulates with an indentation point on an adjacent bone (44)(Fig 4(F)). This joint allows the broadest range of motion, allowing flexion and extension, abduction and adduction (thus, circumduction), and rotation along the long axis of the articulating bone. This joint can be found in the shoulder (glenohumeral joint) and the hip (acetabulofemoral joint). The hip joint comprises two articulating bones- the pelvis and the femur. The hip joint consists of the proximal end of the femur articulating with the distal inferior lateral surface of the pelvis (50–52). External to the pelvis articulation point (acetabulum) is a ring of fibrocartilaginous tissue surrounding the cup-like depression and aids in joint stabilization- similar to how the menisci stabilize the

knee. Like the knee joint, at the articulation site, both ends of the hip joint bones are covered in articulating hyaline cartilage- the head of the femur and the internal surface of the acetabulum. This articulating cartilage has been observed within the hip joint to be thickened in areas where more weight-bearing forces are experienced. Ligaments in the hip joint increase hip stability and support. In the hip, two hip ligaments are found- intracapsular and extracapsular. The intracapsular ligament found in the hip is the ligamentum teres femoris (otherwise known as the foveal ligament or ligament of the femur head), whereas the extracapsular ligaments encompass the iliofemoral ligament, pubofemoral ligament, and ischiofemoral ligament (50–52). These ligaments together create the joint capsule of the hip. As a result, the hip joint is one of the most robust and stable joints in the human body (51). The joint capsule is thickened anterosuperiorly, where the most tremendous weight-bearing forces are experienced in the hip, and thinner posteroinferiorly, where the minor weight-bearing loads are experienced (50–52). Muscles surrounding the hip joint and aid in its stability include; the gluteus maximus, semitendinosus, semimembranosus, and the long head of the biceps femoris as flexors, major and minor psoas, iliacus, pectineus, and rectus femoris as extensors, adductor magnus, longus, brevis, gracilis, and pectineus as adductors, gluteus medius and tensor fascia latae as abductors, tensor fascia latae and gluteus minimus as internal rotators, and gluteus maximus, gemellus superior and inferior, obturator externus and internus, quadratus femoris, and the piriformis muscles as external rotators of the hip (51).

Therefore, the knee and hip joints are specialized structures adapted to aid in free-living movements in individuals. These joints encompass many specialized structures which aid in smooth, pain-free movement. If these structures become comprised (in the case of OA), the function becomes a limiting factor in the movement of individuals. Thus, extreme care needs

to be placed on these joints, and if a disease does result in reduced function of the joint, it severely impacts the daily living of individuals. Therefore, if more research is conducted surrounding these joints- especially on OA's effect on them- it would result in faster and improved outcomes in individuals. Thus, it would result in a reduced decline in quality of life if OA impacts these joints.

### d. Pathophysiology of Osteoarthritis

Osteoarthritis affects the synovial joints and their associated specialized structures (synovium, joint capsule, articulating cartilage, articulating bones). OA has been extensively studied since its discovery to better understand causes, risk factors, and pathological processes associated with the disease. OA is a degenerative joint disease with two forms of pathology- primary and secondary pathology. Primary OA pathology is idiopathic, meaning no specific known cause (5,6,53,54). Secondary OA pathology usually accompanies and presents secondary to other pathological conditions (such as rheumatoid arthritis or trauma) (6,13,55). Basically, the pathological process of OA development can be summarized as 'the permanent loss of articular cartilage, exposing the underlying articulating bone and abnormal growth of bone in joints.' This process can be initiated by multiple different factors(56). OA occurs in a non-inflammatory mediated pathology absent of the human immune system influence (2,5,8). Among clinicians, OA is known as the gradual wear and tear- more commonly in a load-bearing joint- of a synovial joint resulting in abnormal mobility, stiffness, and pain experienced by patients (5,57–60,60–64).

The pathological process of OA development initializes when there is an imbalance between cartilage wear and degradation and chondrocyte repair. This imbalance results in cartilage loss and structural abnormalities in the joint (5,6,8,36,65,66). In the initial stages of OA, the chondrocytes of articular cartilage undergo rapid proliferation. This proliferation results in chondrocyte clusters in the joint (Fig 5). Following formation, these clusters result in the rapid influx of water and some pro-inflammatory cytokines (IL-1 Beta and TNF-Beta) into the synovial joint, resulting in the excessive and unnecessary production and secretion of matrix metalloproteases (MMPs) (67). The raised levels of MMPs in the joint cavity result in pro-inflammatory mediators, collagenase, protease, and the rapid degradation of proteoglycans (responsible for the hydration and sponge-like properties of the articular cartilage) by the surrounding chondrocytes (5,35,65,67–69). As a result, the articular cartilage does not receive adequate nutrients and becomes brittle and vulnerable to damage, and the synovium becomes inflamed and produces a less viscous synovial fluid. Additionally, the MMPs target the healthy existing type-II collagen in the joint and slowly 'chip' away at the already brittle surface layer (35,67). Gradually, this inadequate perfusion and degradation of the articular cartilage results in fissures and clefts in the cartilage (Fig 6)- usually exacerbated by the compressive forces experienced in the joint (58,70,71). As a result, the formation of the fissures and clefts results in a reduced range of motion that the OA-affected joint can complete, reducing the ability to perform normal movement and impacting an individual's daily function resulting in reduced movement.

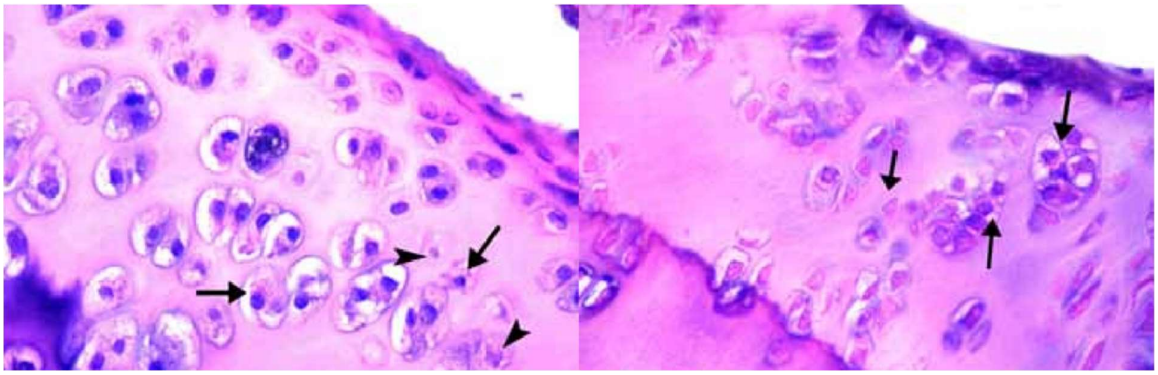


**Figure 5:** Histological image of typical hyaline chondrocytes (arrowheads) and chondrocyte clusters (arrows) present in mild OA (72).

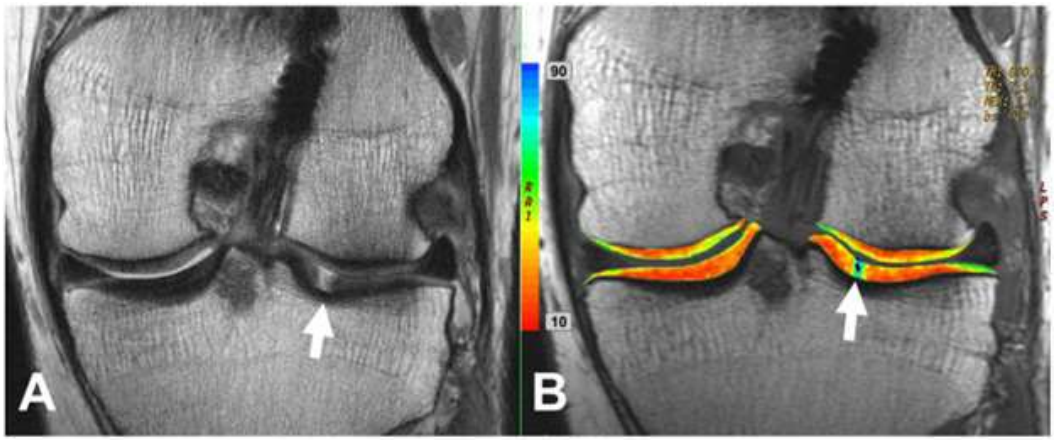



**Figure 6:** MRI images of cartilage clefts in the knee (73).

Over time, the fissures and clefts become larger and result in the death of chondrocytes near these areas of articular cartilage trauma (74–76). The death of surrounding chondrocytes causes cartilage to slough off from the articular surface of bones following the compounded effect of reduced perfusion and chondrocyte decline (16,59,77,78). This sloughed cartilage remains in the joint and floats around within the synovial fluid- termed intra-articular loose bodies or "joint mice" (Fig 7). These loose bodies compromise the structural integrity and stability of the joint and leave individuals feeling their joint 'catching' or 'giving out' beneath them through specific movements (65,68). As a result of the loss of cartilage and chondrocytes at the articular ends, the subchondral bone is forced to the surface. This causes the subchondral bone to become the new articular surface of the joint. The exposure of articulating bones within the joint result in these surfaces experiencing friction in the joint when movement occurs and load-bearing within the joint being placed directly onto the bones with an absence of shock absorption- previously absorbed by the cartilage. Bone friction and load-bearing result in increased pain experienced in OA and discomfort and the symptomatic algesia observed within an OA population (65,79–81). Indeed, this is an adaptive tactic of the body to aid in joint stabilization and repair; however, the subchondral bone does not have the beneficial properties as cartilage has for smooth movement, and the resulting friction results in the formation of ivory bone (eburnation) (Fig 8 A) (35,65,68). As an outcome, the affected joint undergoes rapid matrix remodelling to protect the subchondral bone and prevent any further damage to the joint. This matrix remodelling ramifies in increased density of the subchondral bone (sclerosis) and the formation of bony outgrowths/ osteophytes (bone spurs) into the joint (Fig 8 B and C, respectively). The formation of bone spurs results in a reduced range of motion experienced in the joint to limit joint mobility to prevent further damage by compressive and mobile forces (5,6,65,68,71).

Due to this, the formation of bone gaps appears near the spurs. These bone gaps have been observed to trap synovial fluid and eventually lead to fluid-filled spaces in the subchondral bone termed fibrous walled cysts (6,8,68). Further, this pathophysiological process in OA of synovium inflammation and subchondral bone adaptions becoming the new articular surface of the joint, sclerosis and the formation of spurs and fibrous walled cysts result in these structures releasing additional pro-inflammatory cytokines, collagenase, protease, and MMP's resulting in the further progression of OA. Due to the pathophysiological processes observed in OA development and progression, individuals experience a reduced range of motion ability of the OA-affected joint and report experiencing pain when attempting to move further than the OA-affected joints' current range of motion (82). Movements such as transitioning from sitting to standing, standing to sitting, ascending or descending stairs or hills, climbing out of bed, walking around the house, running, picking up or placing objects on the ground, and doing household activities (such as doing dishes, folding laundry or cleaning) are all affected with OA development as a result of the pathophysiological changes of OA within the hip and knee joints (62,83,84). These changes in the ability to perform movements are due to a reduced range of motion in the OA-affected joints. Movements such as knee flexion and extension and hip flexion, extension, adduction, and abduction are all significantly reduced in OA development and progression, along with a reduced ability of the respective joints to withstand load-bearing forces (66,85,86). With further research, insights and conclusions can prevent pathophysiological changes during OA development and progression. Further research could improve tactics in treatment and management to prevent further progression of already established OA individuals' already-established changes to improve their current conditions and circumstances limiting their daily activities.

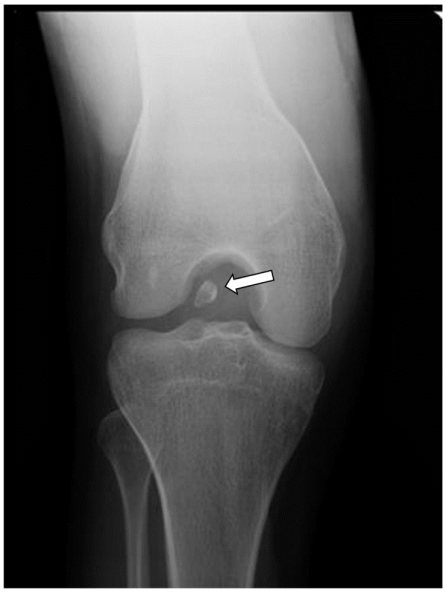


**Figure 7:** X-ray image of an individual with intra-articular loose bodies (joint mice) present in their knee (87).

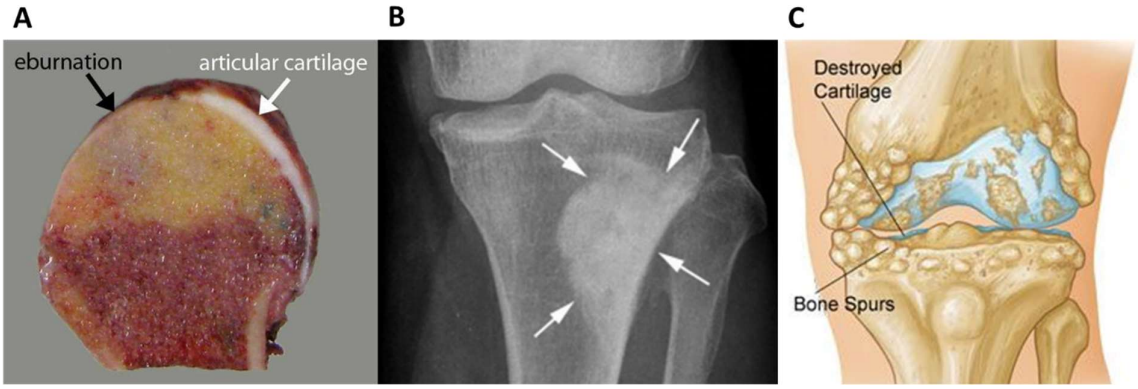



**Figure 8:** Anatomical diagram of bone eburnation (A), an X-ray image of bone sclerosis (B), and schematic diagram of bone osteophytes (bone spurs) (C), which all present in various stages and severities in OA (88–90).

### e. Diagnosis and Stages of Osteoarthritis

OA is a complex condition, with its primary pathological form being idiopathic. The main influences come from comorbid risk factors that raise an individual's susceptibility. However, OA cannot be layman diagnosed nor be diagnosed by palpation or visual inspection. OA can only be diagnosed using specialized equipment and the knowledge and expertise of a trained healthcare professional- usually an orthopaedic surgeon or specialist (91). Specialized equipment is needed for the initial diagnosis of OA. However, using this equipment for follow-up consultations would only be required to assess whether the condition has progressed (91). Equipment such as laboratory tests, radiological scans, and (in some OA conditions, such as OA of the hands) site-specific pattern associations are the most common for diagnosing OA (91). Equipment such as MRI scans, histopathology tests, and joint arthroscopes are among the more commonly used advanced practices in understanding joint damage and OA progression in the clinical setting (80,91–93). Laboratory tests cannot be used in directly diagnosing OA. Still, they can determine if the OA is primary or secondary and, if secondary, what the cause may be (such as rheumatoid arthritis) (91). The most common method for diagnosing OA is the use of radiological scans. Radiological scans aid in the visualization of the actual joint and help determine if joint space narrowing (JSN) has occurred or occurs during the progression of OA development (Fig 9). JSN narrowing occurs when the cartilage within a synovial joint is degraded and can no longer separate the adjacent bones in the joint. JSN presents in both rheumatoid arthritis and OA- the difference between these two is determined using laboratory tests (73,93,94). The third commonly used method for OA diagnosis is site-specific patterns. A site-specific pattern is an event or presence of structural or mobility abnormality presented widely within a particular joint in OA. These

have been determined through common appearances to clinics and consultants in these conditions(95). If symptoms such as genu varus (bow-legged deformity), genu valgus (knock-knees), the knee "giving out" (due to muscle weakness or meniscal damage) or locking, OA-associated pain in and around the knee, reduced range of motion, or warm joints are present in an individual visiting a clinic it could be an indication of knee OA as these symptoms are classified as site-specific patterns of knee OA. Site-specific patterns of hip OA include antalgic gait (limping in response to hip pain), pain associated around the hip area (more common in the groin but can present laterally in the hip or buttocks), limited range of motion (specifically internal rotation), and a reduced extension of the thigh (80,91). Often an individual will report to the clinic having these site-specific patterns of OA, and upon clinical inspection by the consultant, other diagnosis methods (such as X-rays, laboratory tests, MRI scans, and arthroscopes) will be used to confirm the diagnosis, determine the form of OA (primary or secondary) and to determine the stage of OA present in the individual (80,91,92).

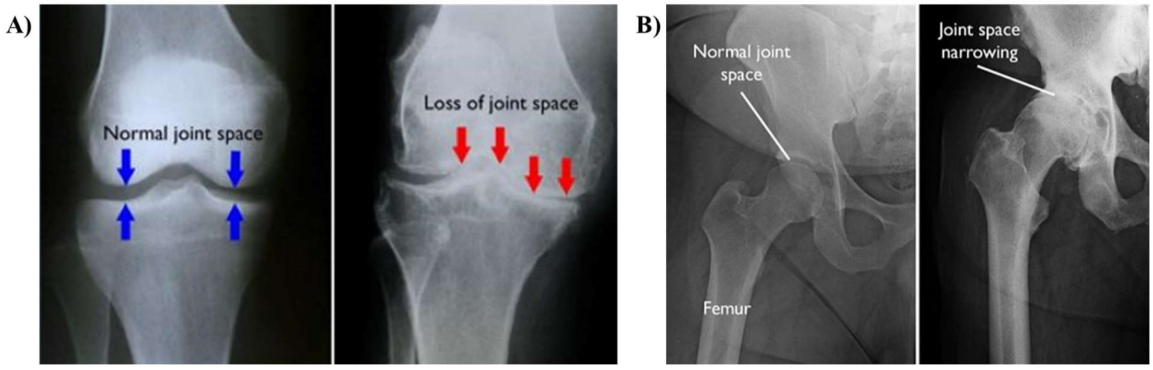



**Figure 9:** (A) Radiographical representation of a normal knee (left and blue arrows) and an OA knee with JSN (right and red arrows) and (B) of a normal hip (left) and an OA hip with JSN (Right and white arrow) (96,97).

Once it has been determined that an individual does have OA, the staging process of its development can commence. Classifying OA into a specific stage is complex and challenging as each individual presents with different morphological changes, histories, OA-associated symptoms, joint mobility, and experienced pain. However, what remains consistent is the degree of structural damage and limitations in joint mobility. Thus, the degree of structural damage (cartilage degeneration, joint space narrowing, and abnormal bone growth) has been the key to diagnosing the stage and severity of OA (80).

Three processes are involved in diagnosing OA's severity in an individual accurately. Namely, typing, staging, and grading are used to classify the severity of OA. The use of these three processes is because the classification of OA remains relatively complex due to the uniqueness of patients and the variety of associated symptoms present in an individual (80). ‘Typing” is used to classify the OA into its presenting form (i.e., primary or secondary) through the use of some of the diagnoses as mentioned earlier methods (laboratory tests, MRI scans, joint arthroscopes, X-rays) to determine if any co-morbidities or traumatic events have caused its onset. Typing usually occurs first in the diagnosis process to determine the form of OA before the stage and grade of OA. However, the last two steps of determining severity have been controversial regarding their use. Both staging and grading add relevance to and aid in determining the seriousness using different approaches but having the same final result- determining the severity of OA present.

OA appears in four different ‘grades’ once the onset of OA initiates. The first grade, grade 0, is considered to be a typical joint with no indication of JSN or articular cartilage damage and does not fall into the four previously mentioned grades (Fig 10). Grade 1 is the first of the

pathological grades of OA and is classified as such when JSN narrowing first presents unilaterally within the joint- either medially or laterally- (however, it could be absent at times) and cartilage damage is present in the form of fissures into the superficial zone when viewed under X-rays (Fig 10) (35,68,80). Grade 1 also involves slight thickening of the articular surface of the bone (periosteum) and some collagen type II expression. Grade 2 is classified when joint space narrowing appears more evidently, and the fissures within the cartilage deepen into the cartilage's middle and/or deep zones and have some cartilage loss present on X-rays (Fig 10). In this grade, periosteum thickening is more pronounced, collagen type II is still present, fibrocartilage presence is noticeable (round cells and metachromatic staining in the ECM), and some bone formation may be present (35,65,68,80). Grade 3 presents on X-rays as severe JSN along with cartilage damage in the form of fissures into the deep zones of cartilage and cartilage clefts to the subchondral bone (Fig 10). This grade is diagnosed (along with the morphological changes mentioned) when the periosteum is thickened, the presence of fibrocartilage, robust and active bone formations are present, and molecular markers such as collagen type II, type X, and type VI are present in the articular cartilage when histopathological, and other diagnostic methods are used (35,65,68,75,80). The final grade and most severe of OA (Grade 4) is classified when X-rays indicate JSN is at a maximum (articular surfaces of bones are wholly or almost in contact), and complete degradation and loss of cartilage are present on X-rays (Fig 10). This grade is accompanied by significant thickening of the subchondral periosteal bone, presence of fibrocartilage with hyalinization of the ECM (presence of chondrocyte-like cells in the lacunae of bone and strong metachromatic staining of the ECM), active abnormal bone formation into the joint (osteophytes) and the presence of collagen type II, X, VI in the basal and pericellular areas of the remaining cartilage (35,65,68,80).

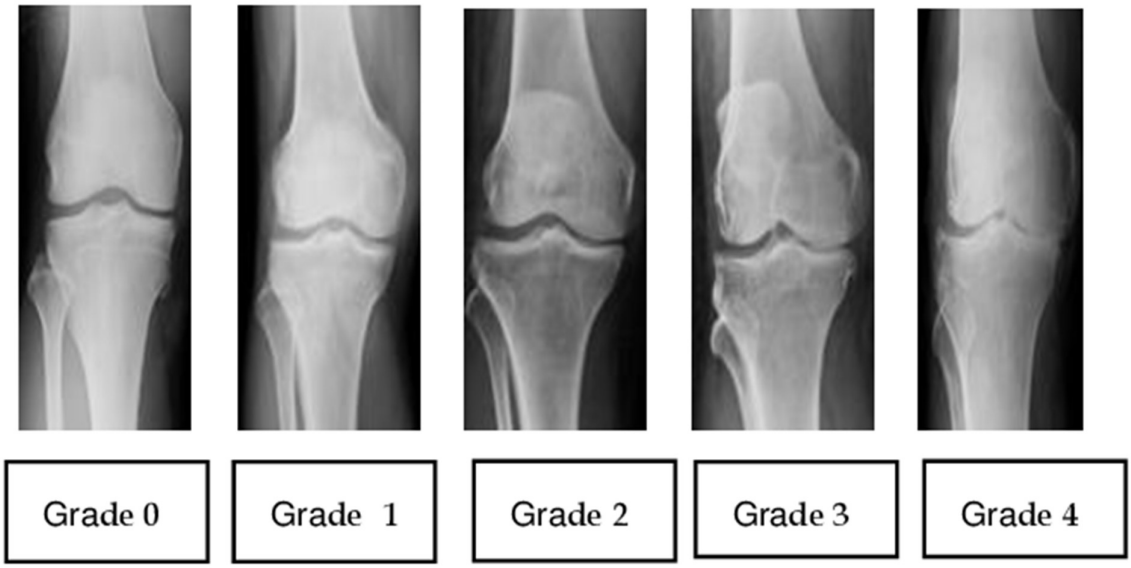



**Figure 10:** X-rays showing morphological changes in the different grades of OA development (98).

Grading of OA is done by one of two grading or staging systems. The first is the Otte method and 'grades' the OA severity, and the second uses the Mankin and Colleagues scoring system and 'stages' the OA into subgroups to grade the OA severity (80,92). Otte (1969) grades the OA severity by determining the morphological changes in bone and cartilage throughout OA development (Table 2). Whereas Mankin et al. (1971) developed a staging system where a score is determined from the histological damage present within the joint (Table 3) (80). Although these two grading systems use different approaches to diagnosing OA severity, the result remains the same as the Mankin and Colleagues scoring systems overlap and agree with the Otte grading system of OA severity (Fig 11).

**Table 2:** Table showing the grading of OA severity through morphological changes by Otte et al. (1969) (80).

| Grade | Morphology |
|---|---|
| 0 | Normal |
| I | Superficial fibrillation with no cartilage loss |
| II | Cartilage lesions present (absent of full-thickness defects)- Deep fibrillation, middle zone fissure presence and/or cartilage matric loss |
| III | Cartilage lesions (absent of full-thickness defects)- Deep zone fissures and partial loss of cartilage matric |
| IV | Complete Cartilage loss (Focally) |

**Table 3:** Table showing the staging of OA severity using histological damage scoring by Mankin and Colleagues (1971) (80).

| Feature | Score | Histological Feature |
|---|---|---|
| Cartilage structure | 0 | Normal |
| | 1 | Superficial Fibrillation |
| | 2 | Pannus and superficial fibrillation |
| | 3 | Fissure to middle zone |
| | 4 | Fissures to deep zone |
| | 5 | Fissure to calcification zone |
| Chondrocytes | 0 | Normal |
| | 1 | Diffuse hypercellularity |
| | 2 | Cell clusters |
| | 3 | Hypocellularity |
| Safranin-O staining | 0 | Normal |
| | 1 | Slight reduction |
| | 2 | Moderate reduction |
| | 3 | Severe reduction |
| | 4 | No staining |
| | 5 | Total disorganisation |
| Tidemark | 0 | Intact |
| | 1 | Tidemark penetrated by vessels |

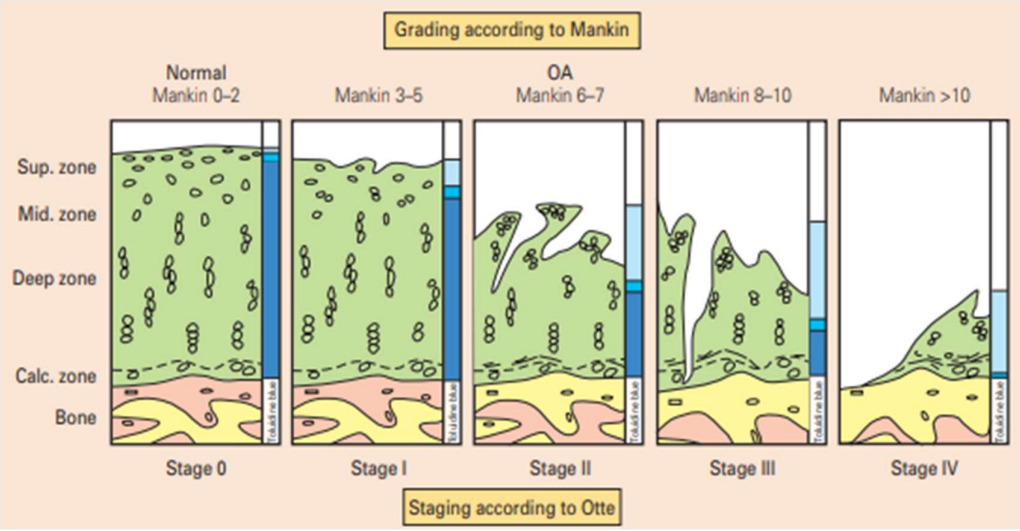
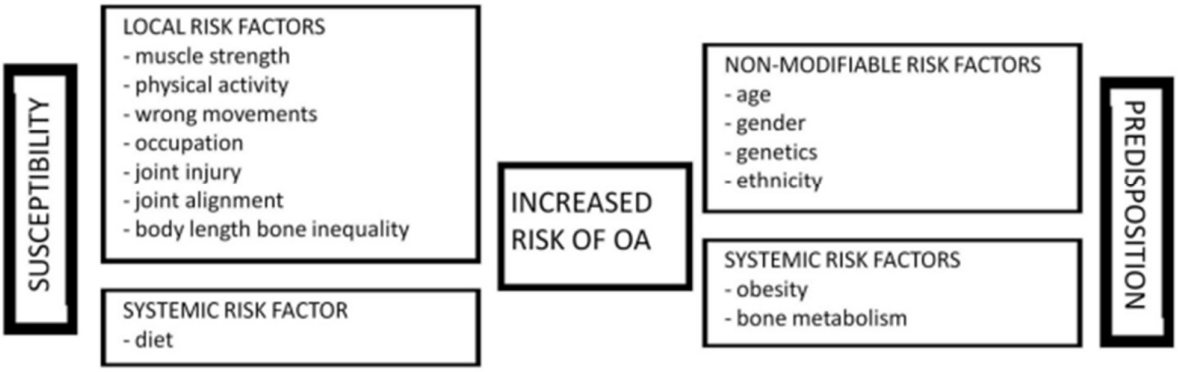



**Figure 11:** Figure representing the Mankin and Colleagues scoring system (1971) compared to the Otte grading system (1969) and how they overlap and agree with one another (80).

## f. Risk factors

Although the pathological process and development of OA are well documented, the condition has multiple factors that influence its development, and these factors differ between genders, age groups, and ethnicities (2,32,61). Research has been focused on determining the associated risk factors for the onset of both primary and secondary OA. G. Musumeci et al.(16) extensively detailed and investigated the multiple risk factors and co-morbidities associated with the onset of OA. Their review found that the developmental risk factors for OA can be separated into two main categories, namely susceptibility and predisposition risk factors (Fig 12). The susceptibility factors were determined to be local factors determined by an individual's lifestyle and are considered 'modifiable risk factors' in the general population- these include daily behaviours and habits such as diet, physical activity, and

technological use. Predisposition risk factors are considered, as they are termed- factors that are not in control of an individual- and are considered 'non-modifiable risk factors' such as age, gender, ethnicity, genetics, hereditary obesity, and bone metabolism (4,16,61,65,71,99).




(2015) (16).

**Figure 12:** The classification of OA-associated risk factors according to G. Musumeci et al. (16).

### I. Predisposition Risk Factors

The non-modifiable risk factors associated with OA onset include influences from an individual's genetics, epigenetics, gender, age, and ethnicity.

Among all the genetic sequences investigated, some key mutations have been identified as having an association with OA development (80 total)- the majority of these have determined that single nucleotide polymorphisms (SPNP) be the most relevant of these mutations (16). More specifically, it has been observed that if a SNP occurs in the genetic locus responsible for the maintenance, repair, and development of synovial joints (rs143383), OA is a definite outcome in such individuals (16,100,101). Similarly, studies have found that if SNPs occur in genes responsible for vitamin D receptors (VDR) or insulin-like growth factor 1 (IGF-1), an

individual has an increased risk for OA development (11,16). Indeed, these genetic mutations have been the most relevant in determining OA onset; however, it is crucial to comprehend that no precisely observed locus for OA onset has been identified. Its development is influenced by multiple alterations and mutations of genes responsible for protein expression. It is crucial not to conclude that a single SNP results in OA; instead, OA has an influential genetic factor that plays a role in its development.

In addition to genetic influences, some findings suggest that epigenetic effects play a role in OA development. Studies conducted by Bui et al.(2012) and Hashimoto et al. (2013) concluded that epigenetic alterations- more specifically, increased activity through demethylation - result in raised susceptibility to OA development in individuals (16,102,103).

Alongside genetic and epigenetic predispositions increasing the risk of individuals developing OA, other non-modifiable factors such as age, gender, and ethnicity play a role in OA development. One of the major influential factors in OA development has been its association with age. Indeed, research has shown that age is associated with OA development; no precise cause mechanism has been definitively found (4,12,24,65,71,104–106). Though research has attempted to find a direct factor, only hypotheses have been made about why this association exists.

One hypothesis termed the ‘Hayflick Limit’ states that chondrocytes in synovial joints only have a set number of replications throughout their lifespan. When this ‘limit’ is exceeded, the chondrocytes undergo apoptosis. This apoptotic event subsequently results in the inability of the cartilage to be repaired and replaced. It ultimately leads to the loss of articular cartilage

and, thus, the onset of OA (16,107). It has been proposed that the limited number of cellular replications allowed by the chondrocytes is a result of the loss of the telomeres protecting the genetic code within these chondrocytes responsible for their survival and function (105).

A second hypothesis claims that OA's development is a direct result of the extracellular matrix (ECM) changes that are associated with age- such as surface fibrillation, decreased reduction in tensile strength, alterations in the composition and structures of proteoglycans and ECM proteins, and the increased cross-linking of collagen (16,78). As a result of these proposed ECM changes, the synovial joint space becomes compromised, and a raised risk of tissue damage is present, explicitly following load-induced or mechanical wear and stress. This hypothesis has been tied in with the previously mentioned age-related hypothesis as it has been observed that the detrimental changes in ECM result in the extended loss of cartilage and chondrocytes. The ECM interactions are observed to play a crucial role in chondrocyte survivability. Thus, changes in the ECM could result in the loss of chondrocytes and, subsequently, articular cartilage and OA development (74).

Gender, too, has been observed to influence the development of OA across all age groups. In the age group 40-50 years of age, it has been observed that males tend to have a higher risk for developing OA compared to their female counterparts. However, the contrary is seen in the ages of 50 and above. In post-menopausal women, it has been observed that women would be more inclined to develop OA, more specifically OA of the hands, foot, and knees, compared to the males in their respective age groups (4,16,27,108,109). These observations have led researchers to believe that a hormonal influence on OA exists. Whether this hormonal influence is protective or degenerative is yet to be determined, and further research

is needed to have a definite answer; the fact remains that a gender-associated risk is associated with OA development in the population.

Although definitive reasons why age and gender influence OA development, the influence of ethnicity on its effect is somewhat controversial. One study by the National Health and Nutrition Examination Survey 1 (NHANES 1) suggested that women of African descent indicate a higher risk for knee OA development than their African male counterparts and European counterparts across all age groups (10). However, when this risk factor was investigated by the Johnston County Osteoarthritis Project (JCOAP), they found no correlations between ethnicity and the risk of developing OA (104). Interestingly, when the studies investigated the same risk factors associated with hip OA, the results were the opposite: JCOAP found ethnic differences, whereas NHANES 1 did not (18,110). Though the observations yielded no definitive outcomes on the ethnic influences on OA development, they did raise awareness of the socioeconomic, genetic, and lifestyle factors associated with OA development.

### II. Susceptibility Risk Factors

One of the most significant contributors to modern-day OA development and progression is unhealthy habits and lifestyles followed by individuals. Regarding OA, two of the most influential susceptibility risk factors are obesity and physical activity- along with a significant secondary factor affecting both; the influence of technology promoting the increased incidence of sedentary behaviour and physical inactivity (111–113).

Daily living and habitual lifestyles have reduced the consumption of healthy meals, including all needed macro- and micronutrients necessary for healthy survival. This, in turn, results in the increasing incidence of obesity observed globally (114–116). Obesity has been observed to have a direct and indirect influence on OA development. Obesity has been shown to directly influence OA development in load-bearing joints by increasing the physical and mechanical stress experienced by these joints. This results in mechanical overload experienced in joints and initiates the pathogenesis of 'obesity-induced OA' (11,14,16,71,116). Indeed, obesity-induced OA predominantly affects the body's load-bearing joints (such as the knees and hips), but the mechanism behind the pathogenesis needs to be explored. In obese individuals, the increased body mass index (BMI) results in increased weight and mechanical overload experienced by load-bearing joints. This increased overload has been observed to result in chondrocyte activation and subsequent cartilage destruction and degeneration, resulting in the initiation of OA pathogenesis (16,117). This pathophysiological process has been determined to be the primary mechanistic process involved in the direct influence of obesity on OA development. As when an individual is obese, further load-bearing stress is placed upon the already affected joints; this, in turn, would result in further cartilage degeneration and articulating bone exposure. If left untreated and unattended, this stress would result in further pathogenesis progression of OA and eventually result in an individual experiencing an extreme level of discomfort and pain that could render them physically disabled and, thus, place a more significant burden on their overall quality of life and the health system.

However, the indirect influence of obesity on OA development and progression is not as simple as its direct influence on OA development. This is due to the complexity of the

aetiological process of obesity's influence and, thus, is not entirely understood to date. Indeed, it is known that metabolic factors associated with obesity could play a role in OA development (such as raised glucose concentrations and raised adipokines); however, these influences have just been proposed by research and are not yet clearly understood (14,71,117–119). Evidence has recently been reported and hypothesized that metabolic factors in obese individuals with type 2 diabetes and raised blood glucose have been associated with OA development and progression (16,118). More specifically, it has been observed that in obese individuals with type 2 diabetes, there is a raised presence of advanced glycation end-products (AGEs) in articular cartilage collagen. AGEs have been shown to influence OA development by reducing the function of working chondrocytes and thus initiating the onset (or progressing the development) of OA (59,120,121). However, this association is not yet well understood, and further research needs to be conducted before definitive conclusions are made.

Another risk factor that substantially impacts OA development risk is physical activity and exercise. Physical activity is any bodily movement initiated by skeletal muscle contraction that results in energy expenditure (122). Exercise is any bodily movement that enhances an individual's fitness and improves overall health and wellness (122). The effects of physical activity and exercise on the risk of developing OA are two-fold. High levels of excessive physical activity or exercise have also been detrimental to the joint, especially those that excessively apply weight on the joint and execute incorrectly. The raised mechanical stress load and occurrence have been associated with an increased risk for OA development susceptibility (16,123). When excessive physical activity and load are placed on some load-bearing joints, it results in the influx of water into the joint and, as a result, causes

compositional changes in the ECM and cartilage and, thus, cartilage deformation (16,58,124). Researchers have also determined that continuous repetitive movements likewise impact the development of OA. In a trial conducted by Messier (2009), their study observed that some occupations that require regular and repetitive movements of certain joints resulted in those joints having a raised risk for OA development (16,125). Their study concluded that individuals who partake in repetitive movements due to their occupation risk for localized OA development were double their counterparts who did not participate in daily repetitive movements as part of their occupation (16,125).

Although excessive repetitive exercise can increase the risk of developing OA, a lack of exercise and physical activity predisposes an individual to develop OA. When a lack of physical activity, also known as physical inactivity, is present, the observed result weakens postural and movement muscles, resulting in an individual being more inclined to have an incorrect posture and incorrect execution when performing some actions (16). This incorrect posture and movement adaptations could result in excessive strain on some load-bearing joints, such as the spine, knees, and hips, resulting in trauma and the risk of developing secondary OA or progressing the exiting OA in an individual (16,77,126,127). Sedentary behaviour is any activity resulting in low energy expenditure during sitting, laying or resting activities (128). In addition to the postural and movement adaptations, physical inactivity and high sedentary behaviour increase the risk of becoming obese (111,129,130). As mentioned above, adipose tissue development to a level that considers an individual obese could develop primary OA by overloading the more weight-bearing joints.

It has been determined that physical activity and moderate exercise are beneficial for preventing the onset and progression of OA (84,119,126,131,132). It aids in the correct movements in our body and prevents articular cartilage alterations and the subsequent weakening of joints (16,133). Thus, a moderate level of physical activity is the most beneficial for preventing the onset of OA and slowing its progression, improving the mobility of joints, and alleviating the pain experienced in OA individuals (16,133).

### g. Effects of OA on health outcomes

Although there is evidence for the benefits of engaging in exercise for people with OA (which will be discussed later), the condition results in restricted or limited movement of the affected joint. Many reasons for the limited movement in people with OA exist, such as inflammation, joint mice presence, subconscious and conscious awareness, and muscle weakness. The degree of inflammation experienced restricts the range of motion that the joint usually follows, accompanied by the experienced pain or discomfort (9,16,35,55,65,79,125). Along with the inflammation caused by OA onset, cartilage slough off could result in the joint becoming caught during its normal movement and resulting in the 'locking' feeling of a joint typically observed in OA, the cartilage slough off debris (known as joint mice) affect the movement of the joint by catching in areas and causing the joint to be prevented from continuing through the movement. As a result, an individual either stops the movement and attempts to avoid it in the future (as the locking tends to be painful and uncomfortable) or pushes through it, forcing the joint to become unlocked, thereby causing more pain, damage, and inflammation (8,53,58,134,135). Once an individual becomes aware of the inflammation, limited movement, experienced pain, or OA presence, conscious and subconscious awareness

of the affected joint (136). This awareness results in the joints avoided use or altered movement (136,137).

The avoided or altered movements observed in OA populations result in lowered usage of normal movement muscles around the affected joint. Avoided use of a joint could further damage the joint and surrounding tissues and result in OA progression (35,53,136,138,139). This, in turn, results in muscle atrophy and strength loss in the working muscles. As a result, movements that were previously avoided or altered now become even more problematic as it puts strain on other working muscles usually not used in those specific movements, and the weakened muscles usually used in such actions tend to become weaker than before, causing them to be unable to perform those movements (80,134,136,140–144). As a result, people with OA have a higher energy expenditure for simple movements due to increased movement by incorporating additional muscles to aid in balance and stability while standing or moving (140). Although this is the case, individuals with OA also tend to participate less in physical activity when compared to a healthy population and, overall, have a lower observed daily energy expenditure (119,131,145).

In OA, most individuals experience a degree of chronic pain and discomfort in their joints and throughout their movements during their everyday sedentary activities and other forms of light, moderate and vigorous physical activities (4,13,65,80,126,134,144). In addition to the chronic presence of pain and discomfort experienced, it has been reported that muscle weakness in normal postural and movement muscles has been observed, along with incorporating additional forces from non-postural muscles for postural control and pain alleviation through movement (66,85,142,146,147). As a result, any form of physical activity

tends to be reduced in an OA population, resulting in an increased prevalence of a lower rate of physical or (in some cases, associated with severe pain and discomfort) physical inactivity in individuals suffering from OA (147). Along with lowered physical activity levels, regular movements affect individuals with OA. Daily movements become altered in response to the pain and discomfort experienced, compensating for the muscle weakness experienced through OA development and progression (53,134,148). All these alterations and pathophysiological processes associated with OA tend to become problematic. They could advance OA to more severe stages, encouraging the further weakening of postural and movement-initiated muscles, thus provoking the increased prevalence of physical inactivity observed within an OA population (63,149).

Muscle weakness and additional muscle usage for postural and movement control incorporation mutually occur in an OA population. Although these occurrences are not lifestyle changes that reduce an individual's QALY at first, it could progress to more severe stages that could result in limited movement and mobility due to both experienced pain and immobility due to immobility, muscle weakness stiff joints. Thus, this occurrence in OA development must be considered and observed when prescribed diagnosis and treatment options. The theory is hypothesized that muscle weakness in OA development and progression results in instability during standing and motion (76,140,144). Thus, the physiological incorporation of additional non-postural muscles to improve balance during these activities is observed (53,58,134,150,151). This incorporation of non-postural muscles for assistance in balance maintenance is the cause for the aforementioned observed result of increased energy expenditure and demands from a body with OA presence within it (9,134,152,153). Muscle incorporation varies depending on the joint affected by OA. For

example, if OA is found within the knee, additional postural control was observed in the anterior tibialis to assist the normal postural leg muscles such as the quadriceps, vastus medialis, and triceps surae (53,60,60,66,138,154). Muscle weakness results from the reduced usage of the muscles due to the pain and discomfort experienced associated with OA (63,64,143,155). Pain avoidance is a common occurrence in OA individuals. As a result, muscle atrophy occurs in postural muscles (80,123,144). A consequence of the observed muscle atrophy is a reduction of balance in OA individuals, and the development of a 'fear of falling' mindset ensues (81,136). This fear originates from an individual becoming aware of their imbalance and fearing that if they do fall, an injury will transpire, worsening their pain and possibly worsening their current condition (81,136). The reduced balance and muscle weakness observed in OA results in individuals attempting to avoid scenarios and situations where there may be a risk of acquiring an injury through falling.

### h. Pharmacological and Non-pharmacological Management of OA

Pharmacological and surgical interventions are applicable for the management and treatment of OA, and some non-pharmacological lifestyle interventions have been validated as viable treatment options. The preferred method of OA for OA is observed in literature as a combination of pharmacological and lifestyle interventions that can be prescribed and incorporated from the diagnosis of the condition depending on symptoms and pain severity presented (3,11,12,91,137,156). In contrast, later stages of OA may need surgical interventions for their management.

OA intervention methods can be categorized into two main groups, conservative and radical intervention methods (157). Conservative methods are interventions focused on improving joint function and mobility. They aim to reduce OA-associated symptoms through pharmaceutical and exercise prescriptions, patient education, assisted devices, and dietary modifications (54,157–159). Radical methods include more direct approaches to mitigating the effects of OA, such as surgical replacement of the affected joints and replacement with a prosthesis (22,23,54,68,137,157). Along with these clinical management methods available, non-pharmacological and non-clinical management procedures have been determined to aid in pain relief and improve the mobility of affected joints. These conservative intervention methods include physical exercise programs, diet modifications, hydrotherapy, acupuncture, patient education, assistive devices, warming approaches, and psychological techniques (11-13,48,49,94,98,143,145-151).

Conservative intervention methods include treatments to reduce pain and discomfort experienced by an individual with OA while preventing further progression of the condition (157). This approach uses pharmacological and non-pharmacological intervention methods to reduce experienced pain and induce weight loss in an individual, ranging from pain management through medication to prescription exercise (54,137,158,159). These two common treatments will first be discussed. Exercise and physical activity are also effective management tools for OA and will be discussed in a later separate section.

Radical intervention methods are usually brought in as a last resort where all attempts of conservative interventions have proved unsuccessful, and OA has progressed (23,86,157,166,167). Radical intervention methods include total or partial joint replacement

surgery (3,137,166,168). However, the later stages of OA are not of focus in this study, so radical intervention methods will not be discussed in great detail.

*Pain medication*

Three pain analgesics are used to decrease experienced pain in patients: non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and acetaminophen. NSAIDs include ibuprofen; opioid prescription drugs for pain alleviation include morphine, and acetaminophen includes medications such as paracetamol (169,170). With each drug prescription comes pain alleviation experienced by a patient accompanied by the negative side effects and risks associated with their abuse and long-term effects. NSAIDs are the most common over-the-counter (OTC) pain medication that does not need prescriptions. NSAIDs reduce pain by inhibiting and blocking enzymes responsible for prostaglandin production and release- thus, their use in OA by mitigating prostaglandin function and hindering the progression of OA (3,171,172). More potent forms of NSAIDs can only be received through a prescription and are used to alleviate pain at a moderate level (170,173). These NSAIDs tend to have a higher risk of developing negative side effects such as indigestion, drowsiness, headaches (among the lighter side effects), stomach ulcers, allergic reactions, and liver, kidney, or heart complications (being the more adverse of the associated negative side effects) (173).

Opioid pain analgesics have a strong affinity for their receptors and, as a result, bind in abundance to these receptors, resulting in an individual experiencing sensations of pain relief (169,174,175). However, the side effects of opioid use are typically worse than those associated with NSAIDs and, at times, can result in addiction to their usage (169,174,175).

Opioids are more commonly used in patients with moderate to severe pain and often are not given repeat prescriptions due to their addictive properties (169,175). Opioid usage side effects range from common pain analgesic side effects such as drowsiness, confusion, constipation, euphoria, and slowed breathing to more severe side effects such as drug addiction, dangerous drug-drug (reactions with any current prescribed or OTC medications), and drug-alcohol interactions, hypoxia, short-term and long-term psychological effects, and neurological effects (such as coma, brain damage or even death)- the latter two both being a result from opioid-induced hypoxia (169,175). Careful consideration must be taken before prescribing this class of pain analgesics to patients, along with protocols for aiding patient relief to come off of prescription opioid usage in case an addiction does occur (169,175).

Acetaminophen's method of pain alleviation is brought about by raising pain tolerance in individuals, thereby reducing the intensity of experienced pain (3,171,176). However, similarly to NSAIDs and opioids, acetaminophen usage has adverse side effects. Long-term use or taking dosages above the recommendations have been observed to have moderate acute (rash, hives, difficulty swallowing, swelling, and difficulty breathing), as well as severe adverse side effects (jaundice, severe allergic reactions, anorexia) (3,177).

*Weight loss*

Weight loss has been shown to have beneficial results for OA-symptom management in individuals who have the possibility of reducing their body weight (3,17,125). Excessive body weight has been shown to place a larger load on affected joints; thus, an increase in body mass results in further wear and tear of an OA-affected joint (86,125). Thus, through

interventions aiming at reducing current body weight in people with OA who present as overweight or obese, a reduced load would be placed on the affected joints, preventing or delaying the progression of the OA rate (3,17,115,125). Weight loss for OA management is unique to each individual. However, common approaches are used to obtain the desired weight reduction outcome. Approaches such as exercise prescription, dietary interventions and modifications, and patient education have all been shown to reduce OA-associated symptoms by reducing the body weight of individuals with OA who can lose excess weight (3,17,115,125,178,179). In addition, weight loss aids by mitigating the effects of excessive weight and obesity, preventing OA progression -especially weight loss through exercise (180). Exercise aids by improving skeletal muscle mass strength and density (allowing experienced forces to be handled better by the joints) and reducing excessive fat accumulation and intramuscular fat accumulation- the latter two contributors to hyperleptinemia and thus the inflammatory responses observed in OA (79,115,116,118,180). In clinical studies, the primary focus of dietary modifications involves proper nutrition (16,23,86,115,125), as increased load-bearing due to obesity is a significant risk factor in OA development and progression. Significant weight reduction in -these populations (3,17,17,54,86,115,125,178) is associated with 48-67% improvement in pain and symptoms (181).

*Total joint replacement surgery*

If OA progresses to later stages of the condition, clinicians and surgeons may use radical methods such as surgical interventions to alleviate persistent pain symptoms in individuals and improve mobility and joint support simultaneously (157). The indication for joint

replacement surgery is that all other conservative measures have been exhausted, and pain persists. Joint replacement therapy, otherwise known as joint arthroplasty, involves removing an entire joint (plagued by either dysfunction or an arthritic condition) and replacing it with an artificial orthopaedic prosthesis (22,23,137,157). As termed by the 'radical' approach, this treatment is often the final line of treatment once other conventional approaches have been unsuccessful in pain alleviation and disease progression.

During surgical joint replacement (both THR and TKR), the proximal end of the distal bone at the joint end is removed and replaced – this is known as cemented joint replacement. Joint replacement surgery is a successful intervention for managing and treating OA and associated symptoms (27,137,156,166,182). However, disadvantages are present with cemented joint replacement. They include cement breakdown, which could result in inflammation and infection and could end up in other areas of the body (such as the lungs), which could be life-threatening- however, this is extremely rare. There is a higher risk of complications for individuals who have undergone spinal surgeries (166). Cementless joint replacements have advantages and disadvantages, such as the elimination of both short-term bonds (cementless offering a long-term bond between the prosthetic and the bone) and the elimination of cement breakdown and debris as advantages and limiting patient factors such as low bone density restricting the ability of this surgery to be performed and long recovery periods (23,157,166,183,184). THR is usually performed once the arthritic condition of OA has reached a point when the patient can no longer cope with the experienced pain, and mobility becomes extremely limited or even impossible (137,185). The return to the normal functioning of an individual following THR is roughly six weeks, accompanied by some rehabilitative physiotherapy- allowing the patient to become accustomed to the artificial joint

replacement (137,185). Similarly, TKR replaces the arthritic joint if present in the knee (23,137,186).

Although THR and TKR are a means to eliminate immobility and alleviate OA-associated pain, some disadvantages are associated with the procedure. Often, individuals who have previously undergone either of the surgical processes must return to their orthopaedic surgeons. The return to their surgeons is more common to replace some of the worn pieces of the artificial joint (such as the plastic or ceramic inserts) or to remove artificial debris from the joint and resecure the joint in place if the cement has come undone (with specific reference to cemented joint replacements) (137,166,185,186).

A study by Kramers-de Quervain et al. (2012) investigated the long-term effects of TKR on patients and how their gait was affected two years after their arthroplasty surgery. Their study found that, although patients' gait improved two years following the surgery, the weight-bearing within the replaced joint remained lower than in the contralateral joint. Their study found that the specific reason for this occurrence was other comorbidity factors that negatively affected gait improvements in TKR patients. This study emphasized that comorbid factors (such as obesity, cardiovascular disease, type 2 diabetes, etc.) must be considered when assessing gait and function improvements in TKR patients (167). Leg muscle strength assessment in the knee and hip OA prior to surgery could indicate the need to incorporate preoperative intervention strategies to strengthen weakened muscles (61,63,141,183). Strengthening these weakened muscles would aid in recovery and ensure that the return to everyday living of TKR or THR patients occurs in the shortest time possible (83,157) in conjunction with reducing preoperative symptoms and improving some aforementioned

comorbid factors (83,119,137,167,187). A study by Nallegowda et a. (2003) evaluated the gait and balance function post-THR surgery and found similar results regarding the gait function of patients (188). In addition to gait assessments, this study investigated the balance control of patients following THR and compared it to both the contralateral limbs and a control group. The study observed that balance was significantly lower in the replaced joint leg than in the contralateral limbs and control groups. Their hypothesis for this observation is due to a sensory-motor deficit in these patients. Balance control was almost the normal standard once accounted for (providing extrasensory input such as vision). The specific reason for patients' sensory and motor deficits following THR is unknown. However, they did stipulate that careful consideration must be taken for follow-ups to inform and assess the patient's risk of falling (especially the elderly). A similar study by Majewski et al. (2005) investigated the balance control of patients following THR and found similar results. Their study stated that THR does aid patients in regaining mobility and balance functioning. However, they emphasized that regular follow-ups are necessary to monitor gait improvement and ensure that patients improve daily functioning while remaining cautious to prevent injury from falling (182). These studies show that THR and TKR surgeries do aid in improving the functionality of the replaced OA-affected joints. However, comorbid factors persist and need to be addressed to prevent other joints from following the same pathological pathway; these can be addressed using additional approaches such as drug and exercise prescription (5,17,17,68,189,190).

### i. Exercise

Exercise is a conservative treatment that OARSI, ACSM and current literature recommend as it aids in addressing symptoms associated with OA, limitations that present as a result of OA development and progression, and aids in reducing the psychological effects of OA development (such as the feelings of helplessness and inability to do tasks that previously were simple and easy) (17,158,191–193). Increased engagement in exercise improves OA-related pain, mobility, confidence, and OA progression prevention (125). Exercise intervention is one of the most important OA management and treatment methods (3,22,165,192–194). It is seen as the gold standard approach for mitigating OA-associated symptoms and impairments (17,22,55,86,125,194). Physical activity is recommended for any healthy individual as it reduces the risk of disease onset for many conditions (54,119,126,133,137,195). Thus, exercise is recommended on the diagnosis of OA onset if no prior exercise currently occurs (17,22,54,119,137). If exercise has occurred regularly before the onset of OA, it is recommended to continue. However, some adjustments and modifications could be made better to suit the needs and health of the OA-affected joints to prevent progression and better manage symptoms (126,196). Although exercise has an essential role in OA management, it is often recommended in conjunction with other intervention methods, such as drug prescriptions and dietary modifications, to obtain the best possible outcomes (86,125,137,197). Even in the case of severe OA where surgery is needed, an exercise prescription is recommended to reduce the aftereffects of the procedure and attempt to reduce the rehabilitation period post-op to return to normal function before surgery (23,137). However, though exercise is the gold standard approach to managing OA, a lack of physical activity is seen in people with OA (71,129,198,199).

A lack of physical activity is a prominent risk factor associated with OA development and progression (4,11,16,71,106,125,200). Studies implementing exercise programs and exercise prescriptions in daily living for OA management have shown evidence for improvements in OA-associated symptoms and disease progression (17,23,54,55,55,125,126,160,163,201). Both aerobic and resistance-based exercise interventions have shown beneficial results for OA. In their review, Roddy et al. (2005) found that improved joint function, mobility, experienced pain, and overall patient health were improved using aerobic or resistance-based exercise prescriptions in a hip and knee OA population (194).

Further, their review found that with regards to OA and exercise, no contraindications to exercise are present in the condition itself but may present with other co-morbid factors associated with the development of the condition. Though statements have been made suggesting that exercise prescription is beneficial in managing symptoms associated with the condition, it is vital to remember that each exercise prescription needs to be unique and specifically tailored to the patient presenting with OA (194). In addition, to exercise prescription and monitoring, it is suggested that patient education about their condition and management approaches be enforced in an OA population to achieve the most beneficial results (3,11,17,22,194). Exercise is observed in the literature to bring about beneficial outcomes in an OA population by promoting increased blood flow, reduced experienced pain, and improved strength and mobility of OA-affected joints. It has been proposed that supervised physical activity paired with other strategies such as weight loss interventions, patient education, and at-home physical activity would result in shorter improvement periods, have long-lasting sustained outcomes, and improve OA individuals' overall quality of life (55,125,189,194,202,203). Of the interventions listed thus far, the intervention yielding the

most positive and consistent results in an OA population- the gold-standard intervention method- is exercise prescription (3,17). Studies have shown that multiple methods of exercise prescription could be incorporated into daily living to achieve the desired outcomes in OA populations, including water-based aerobic training, land-based aerobic training, resistance training, or a combination of the three approaches (21,132,155,159,161,203–206). Although many different physical activity forms are available for people with OA, physical activity is categorized into two main subgroups- land-based physical activity and aquatic physical activity (21,159,165). Further, within the context of OA, both forms of physical activity have been investigated as a means of symptomatic and asymptomatic OA treatment (with knee OA and hip OA being the primary focus within this literature review). Both land-based and water-based physical activity positively affects OA symptoms and progression.

In a study led by Fransen et al. (2014), they investigated the effect of land-based physical activity on pain, physical function, and quality of life in individuals with OA of the hip. Their research used data from 10 randomized control trials (RCTs), which used participants with hip OA participating in land-based physical activity and assessed the outcomes on the abovementioned variables. Their review made objective high- and moderate-quality conclusions on the effect of land-based exercise on hip OA. This review found that high-grade evidence allows the understanding that the incorporation of physical activity resulted in the reduction of OA-associated pain experiences (21 vs 29 points on a 0-100 scale- where 0 was the absence of pain- in the controls) and improvement in joint-associated physical function (22 vs 29 points on a 0-100 scale -0 representing no loss in physical function- in the control groups) when investigated immediately after land-based physical activity. However, through their data review, only three studies investigated the effects of land-based physical

activity on the overall quality of life. In these studies, no physical activity was observed on the overall quality of life (estimated 50 points within the average population remained unchanged in the OA land-based physical activity group). Further, five of the 10 RCTs investigated performed follow-ups three to six months after the cessation of the study and exercise prescriptions. These studies found that the pain reduction effect of exercise was maintained months after their studies had ended (21 vs 29 points in the controls on the same 0-100 scale as mentioned before, three to six months following the cessation of physical activity). Physical function improvement was also maintained (17 vs 24 points in the controls on the same 0-100 scale as mentioned before three to six months following the cessation of physical activity) (207). Thus, their study concluded that any form of prescribed land-based physical activity proved to have beneficial short-term (three to six-month) outcomes in experienced pain and physical function of OA-affected hips (207). Similarly, other studies have had similar results, proving that land-based physical activity reduces OA-associated pain, improves OA-affected joints, and could improve the overall quality of life following physical activity and short-term periods afterwards (3,17,19,159,203,207,208).

Following their findings on land-based physical activities' effect on OA in the hip, Fransen et al. conducted another study investigating the same effect on OA of the knee (2015). Their systematic review used data from 55 studies and found compelling evidence that land-based physical activity benefits symptomatic-OA management and treatment. Their study observed strong evidence for pain reduction and quality of life improvement and moderate evidence in physical function improvement. They observed that land-based physical activity resulted in reduced experienced pain (12 points vs 44 points in the control group on a scale of 0-100 and 0 indicating the absence of pain) and improved quality of life (47 points vs 43 points in the

control group on a scale of 0-100 and 100 indicating the best quality of life) immediately after the physical activity session. In addition, moderate-confidence evidence showed that land-based physical activity improved physical function (28 points vs 38 points in the control group on a scale of 0-100, with 0 being the absence of loss of physical function) immediately after any land-based physical activity (209). The data indicated that at six months of follow-ups, OA-associated pain was further reduced by 6 points (range 3-9 points using the same 0-100 scale as mentioned above) and an improvement in physical function by an additional 3 points (range 1-5 points on the same 0-100 scale as above) (209). Thus, they concluded that land-based physical activity provided a short-term beneficial reduction in experienced pain and improvements in quality of life and physical function two to six months after cessation of prescribed physical activity and observed that the improvement of symptoms is considered moderate (immediate) to small (due to the two to six months period) but comparable to outcomes in drug intervention studies. (209). However, they do state that a limitation of this investigation is that the study subjects were not blinded in their investigated data and hypothesize that some form of the placebo effect may be present within these participants. Similarly, multiple additional studies have found similar results, proving the beneficial effects of land-based physical activity on OA of the knee (3,13, 49, 94,98,143,148,151,185,193–196). This shows evidence that the implementation of exercise, no matter the form, yields beneficial results in people with OA by reducing associated symptoms and improving the quality of life with the disease.

Besides land-based physical activity, water-based physical activity (otherwise known as hydrotherapy) is as effective in reducing OA-associated experienced pain, improving in physical functioning of the joint, and improvement in the overall quality of life of OA

patients (161,162,164,165,204,210–212). In a study conducted by Dias et al. (2017), hydrotherapy was investigated as a possible effective method for symptomatic OA in older women assessing its effect on pain and physical function. Their study consisted of 73 women aged over 65 that had OA of the knee separated into a control group (education protocol only) and a hydrotherapy group (hydrotherapy and education protocol). The hydrotherapy intervention consisted of water-based exercises (such as aquatic-based walking, jogging, single-leg balancing, or lunges) twice weekly for six weeks. At the end of their study, they found that the hydrotherapy group had better results for all variables (pain reduction, physical function improvement, and joint-associated muscle strength improvement). (162). Additional studies have been conducted to investigate similar outcomes within OA populations and found similar results pertaining to the beneficial outcomes such as pain reduction, physical function and quality of life improvements, and OA joint-associated muscle strength improvement and concluded that water-based physical activity achieves similar beneficial outcomes to that of land-based physical activity in the context of OA (161,162,164,165,204,210,211,213). Such studies, such as Luciana et al. (2008), investigated whether water-based therapy had different results than land-based interventions in an OA population. Their study comprised 64 participants (average age 59 years)- randomly assigned to either water-based or land-based physical activity- with knee OA and monitored for improvement in OA symptoms for 18 weeks. Stretching movements were included and kept constant during land-based and water-based intervention groups. Land-based activities consisted of prone bodyweight hamstring curls, standing body weight calf raises (additional 1kg ankle weights were provided if needed), and walking exercises (forward, backward, lateral, and forward knee raises). For water-based exercises, forward, backward, lateral, and knee raise walking was utilized while the participants were submerged in water. There was a

significant reduction in experienced pain, stiffness, and improvement in physical function). There were no significant differences between land-based and water-based intervention groups (30.9 mm reduction in VAS for land-based exercise and 35.2mm reduction in VAS for water-based exercise. The study concluded that the type of physical activity does not influence the desired outcome of improved OA symptoms; instead, any form of physical activity can bring about these desired outcomes (204).

The psychological impact of OA also influences the progression of the disease, sedentary and physical inactivity, and a person's overall quality of life (191). Not only is there significant evidence that exercise is beneficial to physical function, but exercise also has excellent benefits to psychological health. Besides aiding in OA-associated physical symptoms, physical activity aids in improving psychological conditions, resulting in improved moods, motivation, and self-sufficiency in self-management of their condition. People with OA tend to suffer from ill-health beliefs, lack of self-confidence, helplessness, and loneliness and may suffer from depression (191). This results in a downward psychological spiral as OA-sufferers tend to develop a lowered confidence in themselves (133,191,214,215). This inability to complete tasks they previously could not complete without assistance has developed psychological conditions such as anxiety and depression- common conditions observed within OA populations (17,191,214,215).

Patient education and exercise address the physical and physiological impact of OA and improve the psychological and psychosocial effects of the disease (3,17,54,86,133,191,205,216). Sharma et al. (216) observed an increase in the incidence and prevalence of anxiety and depressive symptoms in an OA population. These symptoms were

found further to reduce an individual's overall quality of life and result in OA's progression. Further, their review found that these associated symptoms worsened other OA-associated symptoms, such as experienced pain- which increased (216). Exercise has been shown to improve healthy people's moods and psychological diseases and disorders (205). Hence, implementing exercise prescriptions in people with OA would aid in improving the depressive and anxious mind states that are present.

Further, Fitzgerald et al. (217) found that a vast improvement in confidence levels increased in their study sample of 152 OA individuals. Their study found that exercise and patient education aided in building confidence in movement and the ability to perform movements free of aided assistance, reducing fear of falling and improving stability and self-sufficiency (217). Therefore, besides aiding in physiological improvements in OA-associated symptoms, exercise has shown to improve the psychological burden of OA by aiding in reducing the feelings of anxiety (fear of falling) and depression that occurs following the onset of OA and aid in improving mood, outlook on exercise, confidence, and self-sufficiency.

Overall, exercise is a first-line treatment for people with OA as it improves associated symptoms of pain, joint mobility and function, and overall quality of life. However, OA impairs the ability to move and limits physical function making it difficult to engage in exercise. These movement alterations and incorporation of non-postural muscles increase energy necessities in work needed for normal working muscles around an OA-affected joint. As a result, it is observed that physical activity levels are lower than healthy individuals, and sedentary behaviour levels are high. Low physical activity and high sedentary behaviour are problematic as physical inactivity increases the risk of OA progression and impacts physical

function, reducing the overall quality of life and possibly increasing the burden on the health system and the individual. Therefore, intervention strategies are needed to address these activity limitations and aid in incorporating exercise and physical activity into daily living as a more feasible approach for people with OA engaging in physical activity and exercise. However, understanding the activity habits of people with OA is important to understand what types of activities are feasible for people with OA to engage in. Before discussing methods of monitoring these activity habits.

## j. Measurement of Activity and Energy Expenditure

### I. Calorimetry

Energy expenditure is measured by directly monitoring or estimating an individual's heat transfer and generation. The use of calorimetry can do this. Calorimetry monitors heat generation and changes during a chemical reaction within an individual to estimate the number of calories burned during or needed to complete an activity. Thus, the heat generated and given off during the normal physiological processes (Fig 13) within the human body can predict individuals' energy expenditure and requirements. Previously, calorimetry indicated the energy expenditure of an individual through monitoring the heat gain and loss within the body, primarily- known as direct calorimetry (218,219). However, this method caused discomfort in individuals undergoing these measurements and did not have a pleasant experience (152,218–220). Though this method produces accurate and reliable results while allowing repeatability, a more comfortable method was developed using energy expenditure predictions through calculations of data from oxygen consumption, carbon dioxide production, and water content in expired air- known as indirect calorimetry (218–220).

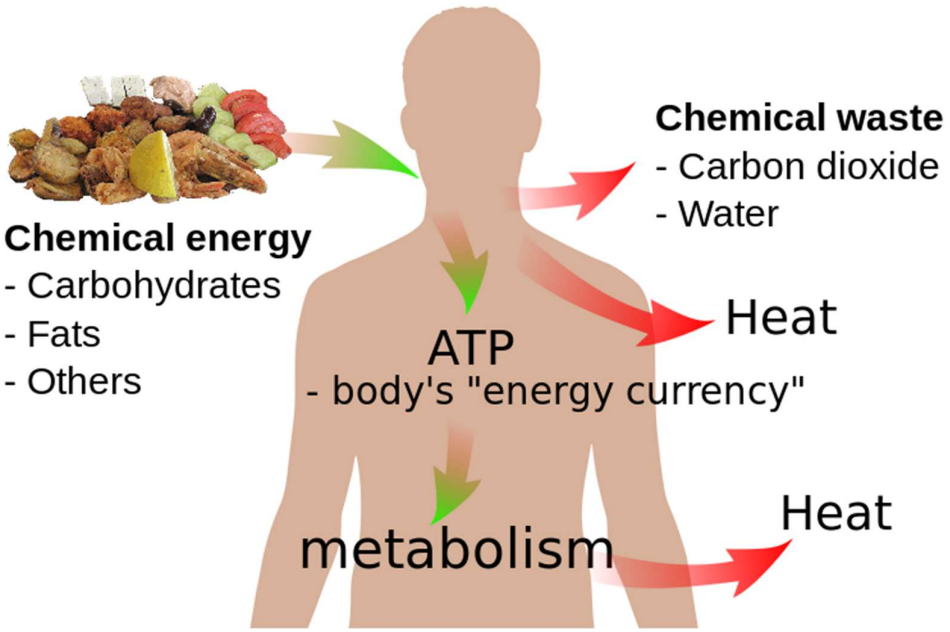



**Figure 13:** Normal physiological processes that contribute to heat generation and loss (221).

Calorimetry provides information about energy requirements by monitoring and predicting the human body's heat gain and loss. Direct, indirect, and non-calorimetric methods obtain heat gain and loss(152,218–220).

Direct calorimetry directly measures the heat generation and output of the human body through expensive setups and equipment such as calorimeters. This equipment focuses explicitly on and measures the body's heat loss by monitoring an individual's radiative, convective, and evaporative heat loss. Direct calorimetry methods include three principal forms of calorimeters- convection systems, isothermal systems, and heat sinks- however, these methods are not crucial for the scope of this study. They, therefore, will not be discussed (219).

Indirect calorimetry makes use of monitoring and obtaining data pertaining to oxygen consumption, carbon dioxide production, and water vapour expiration and inputs the collected data into specific formulas to estimate the energy expenditure of an individual (152,218–220)- which is the principal focus with regards to calorimetry in this study. There are four main forms of indirect calorimetry; total collection systems, open-circuit indirect calorimeter systems, confined systems, and closed-circuit systems (219).

Total collection systems can be divided into rigid and flexible total collection systems. The difference between the two systems is mainly involved in the capturing vessel used (219,222). Expiratory open-circuit systems- such as the one used in this study- has the added advantage of being a portable system that can monitor and analyze the contents of expired air during free-living activity (219,222,223). Estimates of $O_2$ consumption and $CO_2$ production are drawn from changes in air concentrations in inspired and expired air of the subject (219).

Direct calorimetry is a costly method for energy expenditure estimations- with the prices of equipment being extremely high to build and operate (>$1 000 000) (219). Compared to indirect calorimetry, which is a far cheaper alternative yielding the same energy expenditure estimation results without significant loss in accuracy or precision (219,222,223).

In addition to being vastly more costly than their indirect counterpart, direct calorimetry machines require one permanent technician, who requires vast expertise to operate and maintain the equipment. Whereas the indirect approach usually would need the assistance of a superior with some expertise in its use or simply following the instruction manual provided by the developers (219,222,223).

Though indirect calorimetry has provided a more comfortable method to measure energy and heat expenditure in individuals, this method of energy expenditure has one major drawback and limitation. Both forms of calorimetry cannot successfully and comfortably measure energy expenditure in free-living individuals (i.e., energy expenditure throughout the day of individuals). Accelerometers accompanied by algorithms developed through research can obtain accurate energy expenditure estimations while measuring free-living conditions without discomfort or additional bulky equipment.

## II. Accelerometers

The estimation of energy expenditure research previously found that indirect calorimetry technology tends to become uncomfortable for subjects over prolonged study and wear periods- becoming more problematic in free-living monitoring as seen in animal and some human behaviour studies (151,152,224–227). Thus, research was conducted to develop more comfortable and ease-of-use technologies to solve these problems. This research resulted in discovering and implementing energy expenditure estimations through acceleration algorithms. Studies have determined that by monitoring the acceleration of the limbs and torso of a subject, their energy expenditure can be estimated using specific algorithms and calculations (150,151,224,228,229). This was determined by concluding that the majority of energy expenditure from a subject is generated and caused by movement, and thus, by monitoring, tracking, and 'counting' these movements and moments- with the additional use and aid of heart rate monitors- energy expenditure can be estimated to the accuracy of indirect calorimetry with no significant differences in acquired data from each (151,224,226,228). There are three main types of accelerometers readily available; uniaxial

(x/ y/ z), biaxial (x&y/ x&z/ y&z), and tri-axial (x,y, and z altogether) for determining body positioning and acceleration- in one plane, two planes or three planes of movement, respectively. Each method obtains data using the same principle, using acceleration forces to determine the amount and intensity of performed activity. These acceleration values are inputted into algorithms and calculations developed alongside calorimetry to predict activity intensities accurately and, therefore, energy expenditure (225,226,230). Activity scores are the result of the algorithms using acceleration values in individuals. However, these activity scores use cut-points tailored to suit healthy populations for accurate activity intensity and energy expenditure estimations (231–233). Cut-points have been developed to determine sedentary behaviour and light, moderate, and vigorous physical activity in healthy people. Sedentary behaviour is determined if acceleration counts (counts/min) in ActiGraph or epochs in ActivPal accelerometers fall beneath the minimum value of the acceleration of the body part to classify the movement as light physical activity- below 100, 2,860 counts/min for hip and wrist-based accelerometry, respectively and 18.75 epochs/min for thigh based accelerometry) (228,230–235). This is followed by increasing cut-point ranges to determine light, moderate, and vigorous intensities of physical activities, respectively. However, it is currently unknown whether these same cut-points would accurately predict activity intensities and subsequent energy expenditure in people with OA.

All three types of accelerometers use the same technology for tracking body positions and changes (150,226,228,229). Regarding the technology within the accelerometers, two principal forms are present- piezoelectric crystals and microelectromechanical systems (MEMS). The latter system proves more beneficial than the prior as MEMS have shown exceptional sensitivity compared to piezoelectric crystal systems, and the internal mechanism

has been observed to be insensitive to temperature changes experienced by the device. In contrast, crystals have expanded or retracted due to temperature changes (229). Accelerometers monitor physical activity in individuals by tracking the acceleration of the specific limb of an individual to it is attached (147,150,227–230). The acceleration is monitored and stored (known as 'activity counts' or 'epochs') and is tracked over a specific period - ranging from every second to every minute (226,227,229). However, the monitoring and storage of these 'counts' cannot quantify nor justify the energy expenditure of an individual alone and, thus, cannot estimate the caloric output of an individual (227). Therefore, metabolic and physical activity research determined that device-specific and action-specific calibration is needed to quantify energy expenditure through accelerometry data (227,229).

The energy expenditure calibration unique to each accelerometry device used today has come from previous research. Studies that monitored acceleration through daily living (physical activity, daily activity, and sedentary household activity) alongside metabolic calorimetry have been used to determine the relationship between limb and torso acceleration and energy expenditure (using both direct and indirect calorimetry) (150,225–228,230). During these studies, accelerometer epoch data and calorimetry oxygen consumption data were collected simultaneously during specific activities. This collected data would be plotted against one another in a linear regression model to obtain a calculation/equation. This equation could be implemented within the specific accelerometry devices used in the study and used as an algorithm for predicting an individual's energy expenditure while performing specific activities based on the algorithm (227–230). It is important to note that any physical activity monitored by an accelerometer device needs a unique algorithm. Since every activity has

different energy requirements, each needs a unique algorithm to predict the energy expenditure accurately. These algorithms have been developed through research by associating the different energy requirements during a specific activity (measured by either direct or indirect calorimetry) and relaying it over to the tracked movement and acceleration of devices of the accelerometers while performing the selected activities. Hence, multiple studies (including validation studies) have been conducted to determine these algorithms, including the validity and accuracy of these specific algorithmic recognition patterns (147,150,224–230,236).

### k. Habitual activity behaviours in people with OA

People with OA have reduced levels of physical and increased occurrences of sedentary behaviour and the increased presence of physical inactivity (16,71,106,136,147). The fear and pain avoidance approach results in reduced physical activity levels and high levels of sedentary behaviour in their daily lives (58,61,68,81,106,126,136,147,152,154).

Knowing how much physical activity people with OA do in free-living environments is essential, especially for people with OA. People with OA experience movement limitations, making it difficult to engage in activities of different intensities that accumulate over the whole day. The information that can be obtained on how much activity an individual engages in helps prescribe exercise interventions to achieve realistic and acceptable goals and progression to manage osteoarthritis independently.

According to the ACSM, 150 hours of moderate exercise per week is recommended for individuals with OA to aid in managing OA symptoms and progression prevention (17,22,54,137,192). However, in people with OA, this recommendation is not fulfilled. In an OA population, it is observed that reduced physical activity is present. In an investigation conducted by Bindawas et al.. (199), it was observed that a higher incidence of physical inactivity was observed in an elderly OA population. Their study sample was assessed using the Physical Activity Scale for the Elderly (PASE) and grouped into four groups depending on their current physical activity levels. Their study found that their study population of OA individuals took part in less physical activity and had reduced function during movement than a healthy population. This was observed as a reduction in gait speed during a 20-m walk test and increased OA-associated pain in their respective OA-affected joints (199). Reduced physical activity and increased sedentary behaviour have been associated with increased adipose storage throughout the body and thus, resulting in weight gain and increased load-bearing on OA-affected joints (113,130). This increased load experienced by the affected joints and the reduced mobility within the joint could further degeneration of the existing cartilage, osteophyte formation, inflammation, and pain experienced within the joint (16,116,118,142).

Although practical, objective measurements of physical activity have been observed to be consistently overestimated in an OA population. A study conducted by Liu and colleagues (2016) found that subjective measures of physical activity were found to be ~7min/day higher compared to objective measures in their cross-sectional report of 554 OA individuals (10.8 vs 17.9. min/day, respectively) (237). Correlations were run between self-reported and objective

physical activity levels and found weak to moderate correlations between self-reported and objectively determined physical activity levels (237).

Dunlop, Liu, and other studies highlight that a lowered physical activity is present within an OA population (associated with OA progression and worsening of OA-associated symptoms) and that physical activity is overestimated in self-reported compared to actual physical activity levels in an OA population (5,237–242). Having accurate, objective measures of physical activity within an OA population will aid in treatment and management approaches to improve symptoms, prevent disease progression, and improve the overall quality of life.

Dunlop and colleagues (2011) investigated an objective measurement within an OA population to determine if physical activity guidelines are being met. Their investigation used data from 1,111 49-84-year-olds who had radiographic knee OA from the Osteoarthritis Initiative study. In their study, cross-sectional accelerometry data were obtained from daily living to determine if physical activity guidelines were met (≥150 min per week including ≥10 min moderate-to-vigorous physical activity). They found that a small minority of the study population achieved these guidelines, where only 12.9% of males and 7.7% of females with knee OA met these guidelines. Further, through accelerometry data, this study found that 40.1% and 56.5% of men and women were inactive (having no participation in moderate-vigorous physical activity lasting 10 minutes or more in a week) in their population, respectively (238). This study highlights the importance of objectively predicting the level of physical activity in an OA population.

Physical activity aids people with OA by improving their OA-affected joints' mobility. Physical activity aids mobility by promoting muscle strengthening and lubrication of the articulating cartilage. This increased muscle strength supports joints better and aids in the prevention of any further damage and injury (57). Further physical activity aids in reducing experienced pain by incorporating and activating some central pathways responsible for inhibitory actions (such as increased serotonin levels through the reduction of serotonin transporter expression and increased opioid release into the central nervous system). Thus, initiating regular physical activity would result in the increased occurrence of this inhibitory pathway within the central nervous system and, thus, result in the observed decline in experienced OA-associated pain within this population (243).

In a study by Lee et al. (239), they investigated the effects of moderate-vigorous physical activity in the OA initiative study. Their study observed that gait speed and overall movement were fast in individuals who regularly participated in physical activity to aid knee OA. Their study observed that gait and sit-to-stand were significantly improved when regular physical activity occurred (3.88 vs 4.33 feet/second and 25.9 vs 31.1 stands/minute, respectively) (239). Their study concluded by stating; “Being less sedentary was related to better physical function in adults with knee OA,” and used their data and findings to emphasize the need to encourage the increased occurrence of physical activity for improved function and quality of life and reduce the occurrence of physical inactivity and sedentary behaviour in an OA population (239). Further, a study by Fernandes et al. (2010) investigated the effects of patient education and OA-associated symptom improvement between supervised and at-home physical activity in a clinical population. Their study found that symptom improvement occurred in both groups throughout the 16-month intervention period; however, no difference

in OA-associated pain improvement was observed between the two groups. Though significant improvements in physical function were greater in the supervised physical activity group, the 95% confidence interval was vast. This outcome determined that supervised physical activity may aid in more significant physical function improvements than at-home physical activity. However, the extent to which the greater benefit is unknown. It may not be substantial enough to conclude that supervised physical activity alone is the only way to improve physical function in OA (244). This study, along with others, supports patient education and out-of-clinic physical activity as essential intervention methods for OA treatment (3,17,22,160,244,245). Although these findings are relevant to OA management and treatment, it is essential to note that beneficial outcomes through patient education and at-home physical activity prescription, accurate activity levels, and energy expenditure data need to be acquired to develop personal education and treatment regimes (194,246–250). Again, this information highlights the importance of accurate physical activity and energy expenditure acquisition for OA intervention approaches.

Further, O'Reilly et al. (251) found that exercise- even home-based prescriptions- resulted in improved outcomes when experienced pain and function were investigated. Their study included 191 people with OA aged between 40 and 80 years of age who had mild to moderate knee OA. Their study sample was split into no intervention strategy and a simple at-home exercise prescription intervention (daily resistance exercises consisting of isometric and isotonic hamstring and quadriceps exercises) and assessed self-reported pain and function outcomes- the primary outcome being pain changes in the knee using the WOMAC and secondary outcomes being pain changes on VAS and WOMAC for pain and function while climbing stairs. Their study found an improvement in WOMAC pain score was observed by

22.5% in the simple at-home exercise group compared to the control group (who surprisingly had an improvement of 6.2%) during WOMAC self-reported pain. Further, they observed a reduction in VAS pain scores compared to the control group and found that physical function had improved drastically by 17.4% in the at-home exercise prescription group. Thus, they could conclude that incorporating any exercise regime, even a simple at-home-based exercise programme, yields beneficial results for pain outcomes and improvement in the physical function of OA-affected joints (251).

Thus, exercise is a vital tool for OA management. Its incorporation into daily living yields beneficial outcomes in OA-associated self-reported experienced pain improvement, physical function, and movement mobility of OA-affected joints (21,126,158,163,201,203,206,251). Reduced pain, increased physical activity, improved mood, and self-sufficiency can be achieved by accurately prescribed exercise intervention suited to the needs and desired outcomes of patients suffering from chronic clinical conditions such as OA (20,163,201,203,205).

However, not much is known within OA populations regarding how much of the home life is spent being sedentary or participating in some form of physical activity to aid in beneficial outcomes. What is known is that it is common within this population to remain sedentary and physically inactive at home. However, the actual degree of time spent sedentary is not precisely known (16). Therefore, increased research is needed to answer how much at-home living is spent on sedentary behaviour and active time. Studies such as Lee et al. (239) and Sliepen et al. (147) have observed that a higher incidence of sedentary behaviour is present in people with OA, possibly due to increased AO-associated experienced pain during movement

and the inability to perform certain activities as a result from their limited movement condition. Increased sedentary behaviour is typically worrisome as it promotes further progression of OA and, thus, worsens OA-associated symptoms. Further research will aid in developing prescription exercise interventions to accommodate OA individuals better, achieve desired results within the time frame, and improve their overall quality of life while improving joint function and mobility and reducing OA-associated joint pain (137,203,245,252).

In individuals with OA, current literature suggests that the modifiable risk factors in OA contribute to lower physical activity levels in people with OA (4,5,24,85,91,104,147). However, to address these modifiable risk factors by improving physical activity levels, accurate monitoring and representations of experienced movement are needed (129,225,226,230). The use of accelerometers can achieve this by predicting activity levels in an OA population. Accelerometer use has been used to classify knee and hip movements resulting in energy expenditure predictions using cut points and thresholds (21,238,240,253–255).

The higher energy cost of movement in people with OA compared to a healthy OA-free population is the leading cause of concern for treatment strategies as it could produce inaccurate results regarding basal energy requirements. As a result, current methods for measuring caloric expenditure and physical activity levels may not be able to produce accurate outcomes for an OA population. This is due to the higher energy expenditure observed in OA individuals due to higher energy needs from weakened muscles to perform actions they previously could perform with ease but are not avoided

(70,76,115,134,140,153,256). Thus, atrophy has ensued, the incorporation of additional muscles to aid in movement, stability, and reflexed when joints give out, resulting in higher energy consumption during basic everyday movements, and finally, higher energy consumption from reflexes and reactions in response to pain (heightened heart rate and blood pressure among some). Thus, a need is to develop a more objective approach in accurately predicting energy expenditure in movement-limiting disabilities such as OA.

However, these studies assumed that current accelerometer algorithms accurately predict activity intensities and energy expenditure in people with OA. However, these algorithms have not been assessed in people with OA who may experience movement limitations and/or increased energy cost of movement. No literature is presently investigating the validity of their use within an OA population.

Thus, although physical activity guidelines for exercise to aid in OA management and treatment are present, it has been observed that they are not adhered to, and actual levels are overestimated in an OA population. Further, it is evident that people with OA do not meet the current guidelines for physical activity (17,54,137,144,257). This is a result of OA-associated joint experienced pain, reduced functionality of the affected joints, reduced mobility, and psychological decline associated with the onset and progression of the condition (61,104,214,258). The benefits of physical activity within an OA population highlight its incorporation into everyday living to improve associated symptoms, functional ability, and self-sufficiency. Although it is known that physical activity aids in the improvement of OA-associated symptoms, current cut points and thresholds for determining energy expenditure are calibrated to those of a healthy population, free from any movement limitations. Although

healthy population cut points and thresholds are suited to healthy people absent from movement limitations, they are used in movement-limiting conditions such as OA. Thus, it is unknown whether these cut points and thresholds are suited for people with OA and would subsequently determine accurate energy expenditure. For accurate personal intervention prescription through clinical and at-home physical activity and patient education, accurate and objective energy expenditure estimations are required to aid in achieving sustainable beneficial, and maintainable results.

## l. Summary

OA is a chronic degenerative disease that affects load-bearing joints such as the knees and hips (8,11,54,79,104,109,259). With its current pathophysiology known, this disease progresses if left untreated and unaddressed, results in an individual's quality of life regressing which could degrade to such a point where individuals suffering from OA could be deemed physically disabled (9,54).

Although physical activity is beneficial for OA symptom improvement and disease progression prevention, a lifestyle of sedentary behaviour and physical activity is observed in an OA population (147,199). In people with OA, reduced physical activity due to the avoidance principle has been observed to result in disease progression and worsening of OA symptoms (126). In addition, due to the pain experienced, inflammatory responses and incorporation of additional muscles to compensate for the lack of muscular strength and stability surrounding the joints, the amount of work needed by the body is increased. Therefore a higher activity intensity and energy cost is experienced in people with OA (22,61,125,126,139,144,162,245). Using accelerometry to inform exercise interventions to manage OA could be beneficial in incorporating exercise into daily living and achieving the desired outcomes of reducing OA-associated joint symptoms. The problem is that little is known about the accuracy of current accelerometry algorithms in an OA population. Accurate energy expenditure and activity level estimations are needed for beneficial exercise prescriptions for this approach to be successful.

Correct and accurate algorithm application would allow more precise exercise prescription and could incorporate dietary interventions to reduce body weight and reduce load-bearing on joints through prescribed exercise (9,134,256). Though many different activities have already been studied (and have established algorithms using accelerometers for energy expenditure), not all populations have algorithms specifically suited to their unique energy expenditure. Some 'gaps' in population algorithms are still current today. A current understanding and pattern for activity counts measured by accelerometers and associated energy expenditure are present in a healthy population. However, the same is not present in people with OA. This is concerning as the energy expenditure within an OA population is significantly higher than that of a healthy population (153,256). Due to the increased energy cost of movement observed in an OA population, these algorithms may not accurately predict the energy expenditure in an OA population using current acceleration calibrated algorithms and equations. Therefore, using the same algorithms for both populations may result in inaccurate results within the OA population. Inaccurate energy expenditure results in inadequate exercise prescriptions within this population, resulting in delayed improvement of symptoms, worsening of associated symptoms, and possible injury. So, through the validation of current algorithms, information pertaining to more precise approaches can be utilized and developed to manage OA symptoms and prevent disease progression. Achieving valid and accurate predictions would result in a more specific treatment approach regarding diet modifications, exercise prescription, and condition education, resulting in better patient responses and improved overall quality of life within this population.

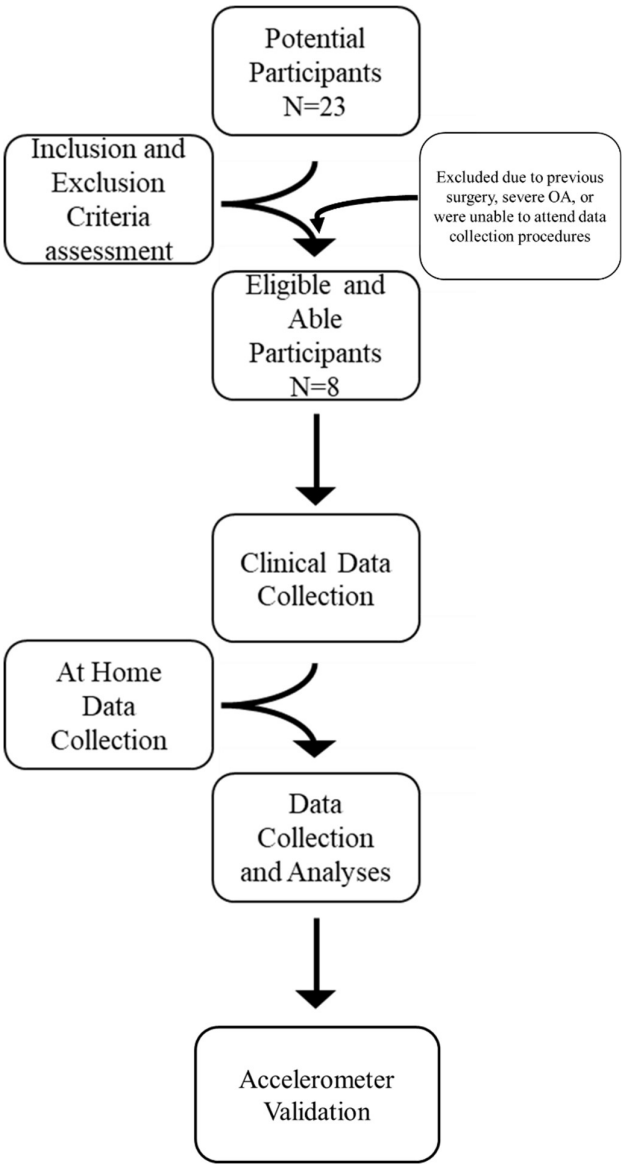
Thus, this study aims to fulfil this objective and validate current algorithms and accelerometers in an OA population to determine if their use and outcomes are correct in individuals with movement-limiting disabilities such as OA.

# 3. Aim

A lack of physical activity is present within an OA population, and detailed and correct information regarding physical activity and energy expenditure is needed for accurate diagnoses and treatment prescriptions. However, one limitation of current accelerometer use is that it is unknown whether current algorithms used in healthy individuals would obtain accurate and correct information regarding physical activity and, therefore, energy expenditure estimations in an OA population. Therefore, this study aims to determine whether commonly used accelerometers and current validated activity thresholds for a healthy population can accurately predict energy expenditure and classify movement intensities in people with OA.

# 4. Methods

## a. Study design



### b. Ethics

This study was approved by the Auckland Health and Research Ethics Committee on 20/11/2020 for three years. Reference number AH3131.

### c. Study Population

The study population was males and females between 40 and 80 years who had mild to moderate stages of OA in either their hip or knee unilaterally or bilaterally. The participants were referred to the University of Auckland Health and Rehabilitation clinic by the orthopaedic surgeon they visited at their outpatient Medical Center in Green Lane, Epsom.

### d. Inclusion Criteria

Our study required that the participants had no previous surgical history related to OA or the joint affected and were able to take part in light forms of physical activity for the data collection procedure.

Participants were considered eligible if they had mild or moderate OA present in either their knee or hip unilaterally or bilaterally primarily- confirmed by the orthopaedic surgeons at Greenlane Medical Center (214 Green Lane West, Epsom, Auckland, 1051) after viewing their x-rays. Further, they were eligible to participate in the study if they were within the age range and consented to participate in the research.

### e. Exclusion Criteria

Potential participants were excluded from taking part in this study if they experienced any absolute contra-indication to exercise (260). These contra-indications included; they had any recent significant changes in their resting ECG (indictive of ischemia), uncontrolled cardiac dysrhythmia causing symptoms, hemodynamic compromise, any current (within the past two days at the time) acute cardiac events (including myocardial infarctions), unstable anginas, symptomatic severe aortic stenosis or the presence of a known or suspected dissection aneurysm. Other exclusion criteria included signs of acute myocarditis or pericarditis, acute pulmonary embolus or infarction, symptomatic severe aortic stenosis, or acute systemic infection (along with symptoms such as fever, body aches, or swollen lymph glands) if the participant fell outside of the selected age range, unable to take part in any forms of physical activity, had previous surgery that was OA related or surgery of the OA-affected joint (OA associated or not).

### f. Participant recruitment

Potential participant contact details were obtained from the Orthopedic surgeons at Greenlane Hospital, Auckland, New Zealand- with consent from their patients. These potential participants were sent information about the study. If they agreed to participate, a participant information sheet (PIS) was sent to them detailing the procedures of the study and all inclusion and exclusion criteria needing to be met to participate in the study. After that, if the potential participants were eligible to take part in the study, the researchers and participants agreed upon a date and time for data collection.

### g. Equipment and Calibration

All equipment was set up and calibrated before the participant arrived at the health and rehabilitation clinic at the Department of Exercise Sciences to ensure the most time-efficient data collection. No equipment calibration was needed for the heart rate monitors. Accelerometers were individually calibrated following calibration instructions in user manuals and calibration programs for both ActivPal and ActiGraph accelerometers (ActiLife (ActiGraph, Florida, USA) and PAL software suite (3M Healthcare, Neuss, Germany), respectively). Gas calibration equipment was calibrated following calibration procedures listed in the calibration manual and user guide from the Cortex Medical Calibration kit (Cortex Medical, Leipzig, Germany) and following the Operators Manual Metamax® 3B (Cortex Medical, Leipzig, Germany).

### h. Clinical Data Collection Procedures

Data collection took place at the Health and Rehabilitation Clinic in the Department of Exercise Sciences University of Auckland. A single data collection session was needed per participant and lasted between one and a half hours and two hours. Upon arrival, participants were taken into an assessment room to be briefed on the types of equipment placed on them and the activities they would participate in). Participants were reassured that they could stop if they felt uncomfortable during data collection and then asked to complete a consent form to partake in the study. After that, six accelerometers were placed on them, one on each wrist, hip, and front of their thigh.

## i. Activities

The participant and researcher moved to the exercise clinic, where a heart rate monitor (Firstbeat Technologies Oy, Jyväskylä, Finland) and the expired gas analyzer Metamax® 3B (Cortex Medical, Leipzig, Germany) were fitted onto the participant. The heart rate monitor was placed securely onto a chest strap and placed on the participant- running across their torso below their sternum (Fig 14A). The Metamax ® 3B was put on the participant in the backpack harness, and the mask was placed over their nose and mouth and securely tightened to prevent any air leakages (Fig 14B).

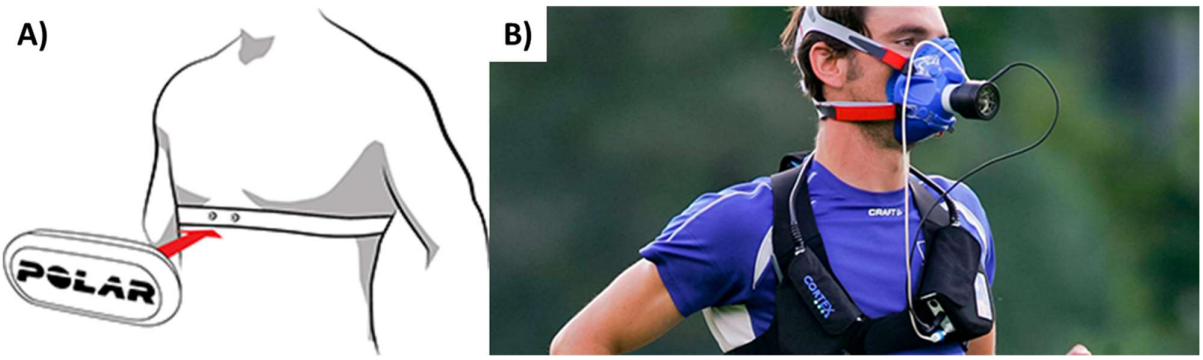



**Figure 14:** Polar Heart Rate Monitor (A) and Metamax® 3B with mask and backpack harness (B) fitted (261,262).

The participant was then asked to complete the following activities in the following order:

1) Lying down on a bed.

2) Sitting quietly at a table.

3) Sitting at a table doing some activity – e.g., computer work, reading, knitting.

4) Home activities- such as drying dishes simulated in the clinical space.

5) Home activities- such as folding laundry simulated in the clinical space.

6) Light leisure walking on the clinic's walking track (at their comfortable pace), picking up and placing weighted objects (mimicking picking up and placing objects around the home)

7) Treadmill walking at a moderate pace (~4km/h)

8) Treadmill walking uphill (3-5% incline, 4-5km/hr).

Each activity lasted 5 minutes, and the heart rate at the time was monitored. During each activity, the researcher took a short video recording of the participant.

j. Measurements

k. Physical activity and sedentary behaviour

For the measurement of movement, two types of accelerometers were used. The accelerometers placed on the left and right wrists and hips were ActiGraph wGT3X-BT activity monitors (ActiGraph, Florida, USA), and those fitted on the anterior side of the left

and right thigh were ActivPAL4 micro activity monitors (3M Healthcare, Neuss, Germany). Before placement on the subject, each accelerometer was cleared of any previously existing data and synchronized with the same computer to synchronize their built-in clocks. The ActiLife (ActiGraph, Florida, USA) and PAL software suite (3M Healthcare, Neuss, Germany) programs were used for the ActiGraph wGT3X-BT and ActivPAL activity monitors, respectively, for the purpose mentioned earlier.

The ActiGraph wGT3X-BT and the ActivPAL4 micro activity monitors are approximately the size and thickness of a standard bottle cap; therefore, they would cause minimal discomfort to the participant. The accelerometers measure and record the amount of time spent by the participant in the sitting, lying, and standing positions and record the amount of time engaged in physical activity (walking or running specifically) using built-in accelerometers and inclinometers.

Output data of acceleration counts during all three axes were recorded and downloaded - axis 1, 2, and 3, respectively- and the vector magnitude for all four wrist and hip ActiGraph wGT3X-BT accelerometers. Epoch data was recorded and downloaded for ActivPal 4micro accelerometers. Data extracted for hip accelerometers were axis 1 acceleration counts/moments, as these are the outputs that have been validated by previous studies (150). Vector magnitude acceleration counts were used during wrist accelerometry as this method has been validated as the preferred method during wrist activity monitoring (233). Finally, thigh-based accelerometry data of interest was activity counts in epochs as this is the gold standard method for activity monitoring using ActivPal accelerometers (263). Each data extraction from the relevant accelerometers was used in their raw form and compared to the

volume of oxygen consumption during the different activities obtained through Metamax 3B® gas analysis. Oxygen consumption data from the gas analysis, axis 1 from hip ActiGraph, vector magnitude from wrist ActiGraph, and activity scores from thigh ActivPal were converted to metabolic equivalent scores to determine the energy cost and subsequent experienced activity level intensities of each activity.

## l. Energy expenditure

The Metamax® 3B (Cortex Medical, Leipzig, Germany) was used for respiratory gas analysis to measure oxygen consumption and indicate activity intensity. The Metamax® 3B was connected to a computer for data acquisition. The Metamax® 3B was calibrated using the Cortex Medical Calibration kit (Cortex Medical, Leipzig, Germany) and following the Operators Manual Metamax® 3B (Cortex Medical, Leipzig, Germany). The Metamax 3B® communicated the collected data with the MetaSoft® Studio (Cortex Medical, Leipzig, Germany) software for data acquisition, storage, and representation.

The Metamax® 3B measured the concentration of gases, and the air volume expired during each activity. These data allow the MetaSoft® Studio to calculate the amount of oxygen consumed, and calories burned indirectly and the participant's metabolic rate (VO2/kg) during each activity. The output of interest was oxygen consumption ($VO_2$; ml/kg/min) which was then converted to a metabolic equivalent score (METs) to classify the activity intensity level.

### m. Heart rate

Heart rate during each activity was monitored for safety using the Firstbeat Sports heart rate monitor (Firstbeat Technologies Oy, Jyväskylä, Finland). The Firstbeat Sports heart rate monitor was connected via Bluetooth® to a tablet using the Firstbeat Sports App (Firstbeat Technologies Oy, Jyväskylä, Finland). Recording the heart rate and time at each activity point was noted to cross-reference with Metamax® 3B set time points at each activity.

### n. Questionnaires and Pain Scales

Before data collection, each participant completed a Physical Activity Readiness Questionnaire (PARQ+). This questionnaire was conducted to ensure no health or lifestyle issues were present in the participant before participating in physical activity, ensuring their safety (264).

During the third activity ( 3), Sitting at a table doing some activity), the participant was given two questionnaires. The questionnaires filled out were either the Hip Injury and Osteoarthritis Score (HOOS) Survey if OA is present in the participant's hip(s) or the Knee Injury and Osteoarthritis Score (KOOS) Survey if the OA is present in their knee(s). These questionnaires are used to determine the participant's short-term and long-term pain and discomfort due to the OA presence, hip or knee function since the OA was diagnosed, daily functioning, and quality of life affected by the OA presence (265,266).

The KOOS asks questions related to knee OA regarding function, knee-related quality of life, OA-associated pain, symptoms, and affected daily activities and is used to determine the severity of knee injury subjective to the participant. The HOOS is similar to the KOOS but asks questions related to hip OA and is used to determine the subjective OA hip influence in their daily lives.

Both the HOOS and KOOS consist of 42 questions that are dispersed across five sections, namely pain, other symptoms, function in daily living (ADL), function in sports and recreational activities (Sports/Rec), and joint-related quality of life (QoL). The mean of each question is obtained and divided by 4 (Score ranging between 0 and 4, 0 indicating extreme problems and 4 indicating none). A score for each section is then obtained and ranges between 100 (no problems) and 0 (extreme problems) (267,268). These questionnaires have been a valuable assessment tool in determining the effect of hip and knee OA on an individual's lifestyle and quality of life (269,270).

The pain was assessed prior to and post data collection procedures. Subjective pain ratings were obtained using a visual analogue scale (VAS), where participants were asked to rate their pain from 1 to 10 on a linear scale presented in front of them.

### o. Data Reduction and Representation

Data reduction occurred by averaging all collected data from participants and the variables across all participants to obtain one value to represent and compare. Data of age, height, weight, and BMI were all averaged and tabulated.

HOOS and KOOS results were tabulated as the mean of scores achieved. Only two participants had hip OA; thus, the HOOS outcomes represent 25% of participants in the study. Further, the KOOS scores represented 75% of participants in the study.

Pain VAS were reduced by obtaining all participants' median and interquartile ranges before and after data collection.

Heart rate data were obtained by accessing the Firstbeat collected data on the online site where it was stored, and minute heart rates were extracted.

Data collected from gas analysis using the Metamax 3B® was extracted through the MetaSoft software following data collection. Data collected included oxygen consumption ($VO_2$) and metabolic equivalent scores (METs).

Accelerometer data extraction involved connecting the respective accelerometers to a laptop with the Actilife and PAL software programs for ActiGraph and ActivPal accelerometers, respectively. Accelerometer data were then converted to excel spreadsheets, and timestamps were converted to actual time formats. ActiGraph data of interest was axis one acceleration moments (no./min) for hip accelerometry and vector magnitude acceleration moments (no./min) for wrist accelerometry- acceleration in the vertical axis for axis 1 and vector acceleration moments of vertical, horizontal and longitudinal axes for vector magnitude (271). ActivPal activity scores in epochs (METs/s) were the interest data for thigh accelerometry.

Each participant's gas analysis, HR, and accelerometer data were manually assessed and minute averages were extracted for $VO_2$, METs, HR, axis 1 acceleration moments, vector magnitude acceleration moments, and epochs activity scores and entered into a single data collection Microsoft excel spreadsheet. Minute axis 1, vector magnitude, and epochs activity scores for right and left side accelerometry data were used to obtain a mean minute value for hip, wrist, and thigh accelerometry for each participant during each activity, respectively.

After completing the data summary, mean values across participants were calculated to obtain mean values for $VO_2$, METs, HR, axis 1 acceleration counts, vector magnitude acceleration counts, and epochs activity scores for each activity.

Predicted activity intensity and energy expenditure were acquired in gas analysis data using calculated MET scores. MET scores (precalculated from the MetaSoft software) were compared to cut points to determine sedentary behaviour, light physical activity, moderate physical activity, and vigorous physical activity (activity levels 1, 2, 3, and 4, respectively). MET cut points below 1.25 METs are considered sedentary behaviour, between 1.25 and 3 METs light physical behaviour, between 3 and 6 is considered moderate physical activity, and above 6 METs is considered vigorous physical activity (272). Similarly, cut points for ActiGraph accelerometers were used to determine predicted activity intensities and energy expenditure for axis 1 and vector magnitudes. Axis 1 cut-points were used to determine sedentary (<100 counts/minute), light physical activity (100-1951 counts/minute), moderate physical activity (1952-5724 counts/minute), and vigorous physical activity (>5725counts/minute) (273,274). ActiGraph vector magnitude cut points for wrist-based accelerometry include <2,860 counts/min for sedentary behaviour, 2,860–3,940 counts/min

for light physical activity, and ≥3,941counts/min for moderate-to-vigorous physical activity (233). Activity scores (internally calculated by the pre-set algorithms within ActivPal accelerometers) were converted to METs by dividing the obtained activity scores by 15 (as determined using the ActivPal user guide (3M Healthcare, Neuss, Germany)) to obtain predicted MET values for each activity through thigh-based accelerometry. These MET values were then classified into activity intensities and energy expenditure in the same manner as those obtained from the gas analysis (225,275). The actual and predicted energy expenditure activity intensities were used to determine the accuracy and, therefore, the validity of the current accelerometer and algorithm used to predict energy expenditure within an OA population.

### p. Statistical analysis

Linear regression models were used to determine the relationship between $VO_2$ and heart rate, axis 1 acceleration, vector magnitude acceleration, and epoch activity scores. A Wilcoxon-Signed Rank test was used to determine if pain increase after data collection was significant.

To determine the validity and agreement between actual activity intensity and energy expenditure, energy expenditure predictions represented as experienced activity levels from hip and wrist ActiGraph and thigh ActivPal were compared to metabolic energy expenditure obtained from the gas analysis. Cohens Kappa was run to determine the level of agreement between predicted and actual energy expenditure activity intensities obtained from accelerometry data and gas analysis data, respectively (276,277). Cohens Kappa agreement

can be interpreted as follows; >0 indicating no agreement, 0-0.2 a none to a slight agreement, 0.21-0.4 a fair agreement, 0.41-0.6 a moderate agreement, 0.61-0.8 a substantial agreement, 0.81-0.99 a near-perfect agreement, and 1 indicating a perfect agreement between predictions (276). This study determined an agreement value of 0.4 and higher to be significant in validating accelerometry-based energy expenditure predictions in an OA population.

# 5. Results

## a. Participants

Twenty-three participants were recruited for the study. Fifteen did not participate due to either not meeting eligibility criteria or being unable to attend clinic data collection procedures. Heart rate data was missing from three participants during the study. This resulted from Firstbeat heart rate monitors being unavailable due to battery issues with the device. Similarly, one participant had ActiGraph accelerometry data missing. Missing ActiGraph data resulted from a faulty device, and thus, no data is present for this participant. ActivPal accelerometry data were missing from one participant. The exact cause for this is unknown. Throughout the results section laying down, sitting quietly, sitting quietly doing some work, home activity doing dishes, home activity doing washing, home activity picking up and placing objects on the ground, light treadmill walking, and incline treadmill walking will be referenced in figures and tables as activity 1-8, respectively.

The characteristics of the participants are summarised in table 4 and a participant summary of the study is seen in table 5.

Pain severity increased by 50% following the data collection procedure according to the numeric pain rating scale (NPRS) (Table 2). The increase in pain rating was not significant ($z=-1.511$, $P=0.131$).

**Table 4:** Participant characteristics.

| Variable | Domains | Mean (SD) | Median (IQR) | Minimum | Maximum |
|---|---|---|---|---|---|
| **Age (years)** | | 61.62 (9.13) | 63.00 (67.75-59.25) | 46.00 | 73.00 |
| **Height (m)** | | 1.70 (0.14) | 1.70 (1.78-1.60) | 1.51 | 1.91 |
| **Weight (kg)** | | 85.15 (22.02) | 82.50 (88.23-73.39) | 60.40 | 132.95 |
| **BMI ($kg/m^2$)** | | 29.13 (4.68) | 27.50 (33.35-26.02) | 23.59 | 36.29 |
| **HOOS Score (score/100)** | ***Pain** | 60.00 (17.68) | 60.00 (66.25-53.75) | 47.50 | 58.82 |
| | ***Symptom** | 55.00 (35.36) | 55.00 (67.50-42.50) | 30.00 | 80.00 |
| | ***ADL** | 70.59 (33.28) | 70.59 (82.35-58.82) | 47.06 | 94.12 |
| | ***Sports/Rec** | 56.25 (61.87) | 56.25 (78.13-34.38) | 12.50 | 100.00 |
| **6 Participants** | ***QOL** | 31.25 (44.19) | 31.25 (46.88-15.63) | 0.00 | 62.50 |

| | | | | | |
|---|---|---|---|---|---|
| **KOOS Score (score/100)** | ***Pain** | 65.74 (12.13) | 68.06 (75-59.03) | 47.22 | 77.78 |
| | ***Symptom** | 64.29 (16.75) | 62.50 (69.64-52.68) | 46.43 | 92.86 |
| | ***ADL** | 71.57 (18.31) | 74.26 (84.56-63.97) | 41.18 | 91.18 |
| | ***Sports/Rec** | 54.17 (26.35) | 55.00 (71.25-46.25) | 10.00 | 85.00 |
| **2 Participants** | ***QOL** | 46.88 (24.61) | 50.00 (67.19-37.50) | 6.25 | 68.75 |
| **Numeric Pain Rating Scale** | **Pre-Assessment** | 1.88 (2.03) | 1.00 (3.00-0.75) | 0.00 | 6.00 |
| **(0-10 scale)** | **Post Assessment** | 2.75 (2.49) | 1.50 (4.00-1.00) | 1.00 | 8.00 |

* For Scores Pain, Symptom, ADL, Sports/Rec, and QOL; 0 represents extreme problems, and 100 presents no problems. ADL-Joint function during daily living. Sports/Rec-Joint function during sports or recreational activities. QOL-Joint-related quality of life

**Table 5:** Study participant summary.

| | | **Participants** |
|---|---|---|
| **Male** | | 5.00 |
| **Female** | | 3.00 |
| **Joint Affected** | Knee | 6.00 |
| | Hip | 2.00 |
| **Side Affected** | Right Knee | 2.00 |
| | Left Knee | 4.00 |
| | Right Hip | 1.00 |
| | Left Hip | 1.00 |
| ***OA Stage** | Unknown | 1.00 |

| | | |
|---|---|---|
| | Mild | 7.00 |
| *OA-Osteoarthritis | | |

b. Oxygen consumption and its relationship to HR and acceleration

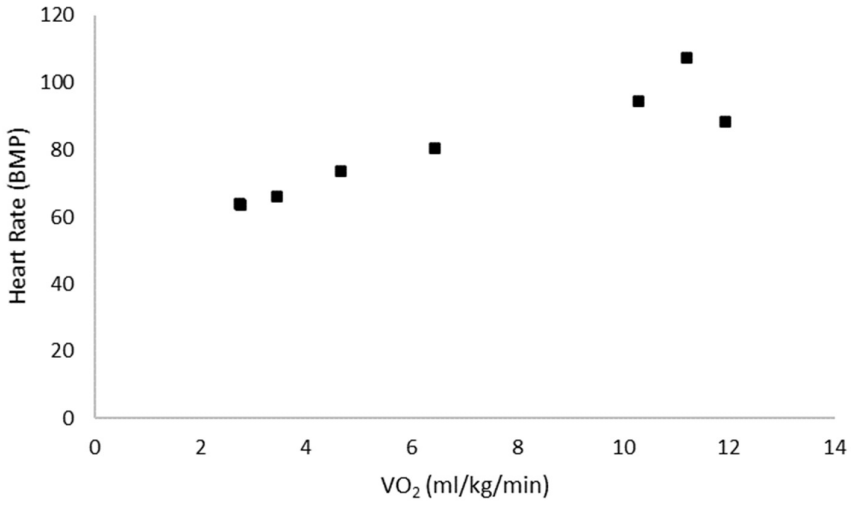



**Figure 15:** Oxygen consumption increase alongside heart rate changes using the Metamax device during home-mimicked activities

A positive linear increase was observed in $VO_2$ as heart rate increased, having a strong positive correlation ($R^2$=0.927, P<0.001) (Fig 15).

Mean (SD) values for heart rate and oxygen consumption changes during activities are represented in Figures 16 A and B, respectively.

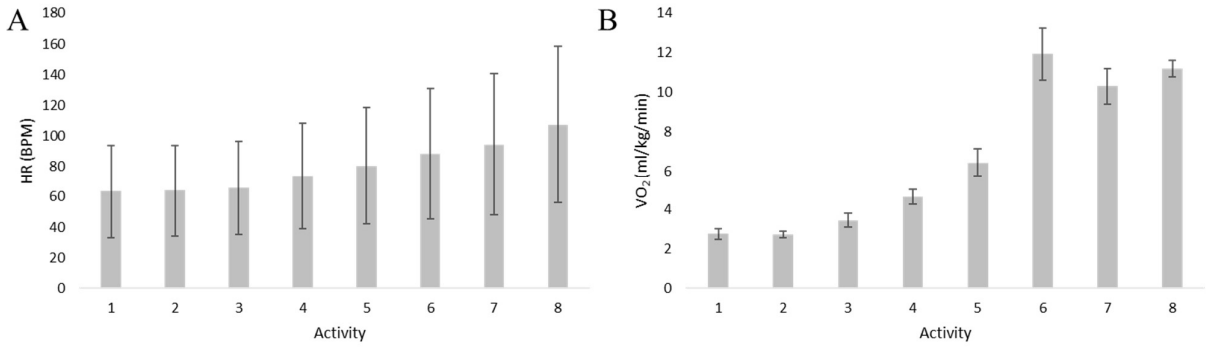



**Figure 16:** Mean (SD) values indicating the change in heart rate (A) and oxygen consumption (B) during activities 1-8.

*ActiGraph accelerometer*

Fig 17 shows the relationship between axis 1 acceleration counts recorded on the hip and its relationship to oxygen consumption determined through gas analysis.

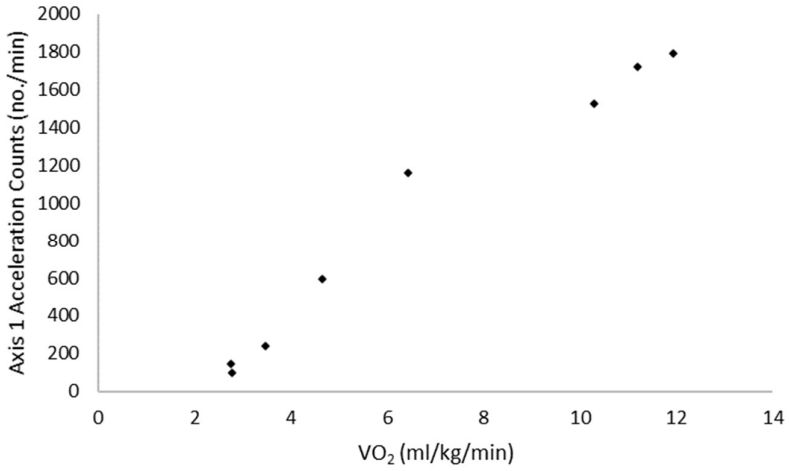



**Figure 17:** Hip ActiGraph Axis 1 acceleration counts against oxygen consumption during activities 1-8.

There was a strong positive correlation observed between axis 1 acceleration counts on the hip and oxygen consumption acquired from expired gas analysis ($R^2$=0.984, P<0.001) (Fig 17). Mean (SD) hip axis 1 acceleration counts for each activity are represented in Figure 18.

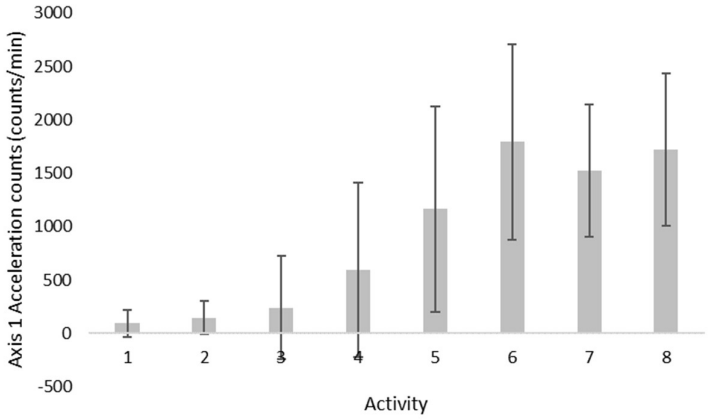



**Figure 18:** Mean (SD) values obtained from axis 1 hip accelerometry during data collection home-mimicked activities.

Figure 19 shows the relationship between wrist acceleration moments in vector magnitude and oxygen consumption during home mimicked activities conducted in the clinic. A weak positive correlation was observed but insignificant between oxygen consumption and wrist ActiGraph vector magnitude acceleration counts ($R^2$=0.357, P=0.385) (Fig 20).

Figure 20 shows all participants' mean (sd) values for each activity during data collection using wrist ActiGraph.

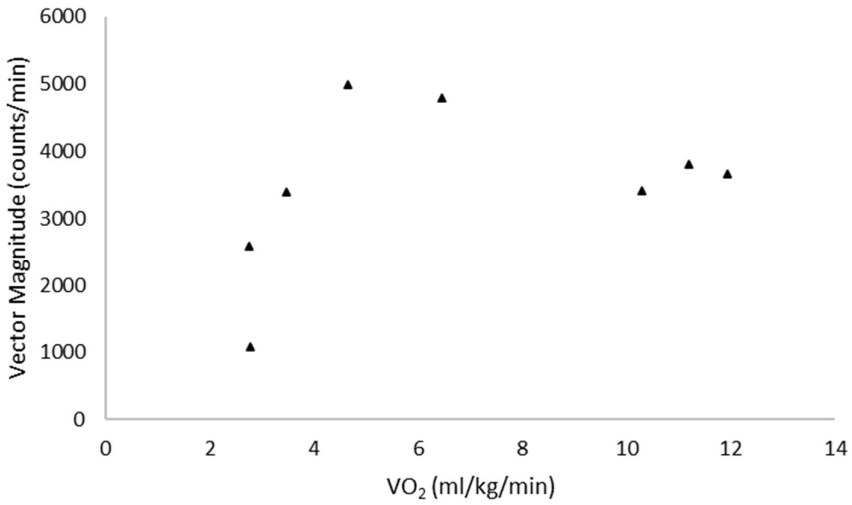



**Figure 19:** Wrist ActiGraph vector magnitude acceleration against oxygen consumption across activity 1-8.

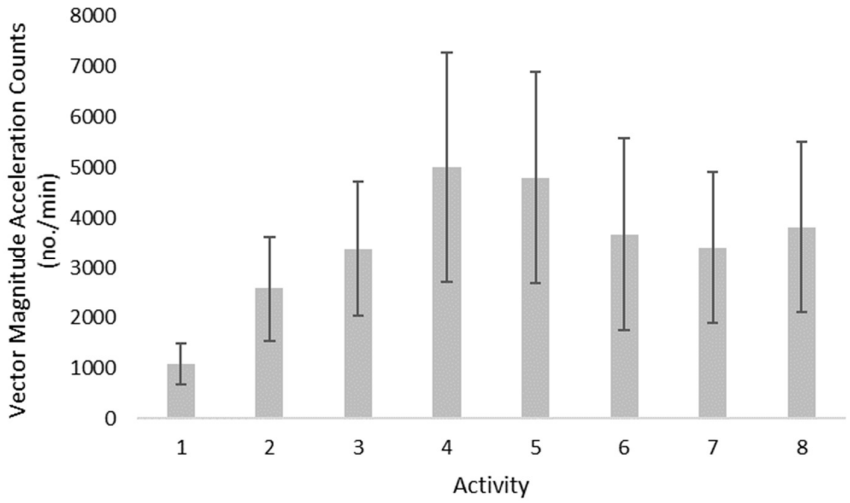



**Figure 20:** Mean (SD) values of all participants' left and right vector magnitude acceleration counts during each activity.

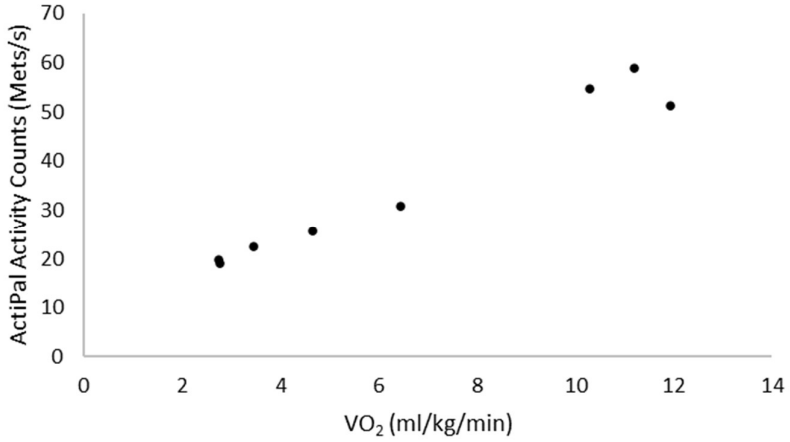



**Figure 21:** Average thigh ActivPal activity counts against oxygen consumption during clinic-based home mimicked activities.

Figure 21 shows the relationship between thigh ActivPal changes concerning oxygen consumption changes during home mimicked data collection activities. There is a significant correlation found between thigh ActivPal activity scores and oxygen consumption ($R^2$=0.976, P<0.001) (Fig 21). Figure 22 shows the mean (sd) values obtained from all participants' left and right thighs during home mimicked activities.

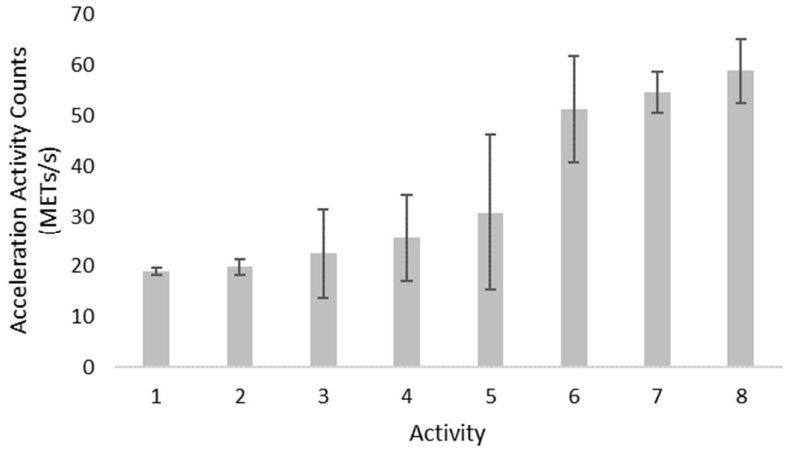



**Figure 22:** Mean (sd) values for right and left ActivPal accelerometry for all participants during home mimicked activities.

c. Agreement between Oxygen consumption and Accelerometer energy expenditure predictions

**Table 6:** Predicted activity levels according to the different methods of energy expenditure estimations.

| Activity | Metabolic-based Activity Level | Accelerometry-based Activity Level | | |
|---|---|---|---|---|
| | Oxygen Consumption | Hip ActiGraph | Wrist ActiGraph | Thigh ActivPal |
| **1** | 1 | 1 | 1 | 1 |
| **2** | 1 | 2 | 1 | 1 |
| **3** | 1 | 2 | 2 | 2 |
| **4** | 2 | 2 | 3 | 2 |
| **5** | 2 | 2 | 3 | 2 |

| | | | | |
|---|---|---|---|---|
| **6** | 3 | 2 | 2 | 3 |
| **7** | 3 | 2 | 2 | 3 |
| **8** | 3 | 2 | 2 | 3 |
| **Agreement (%)** | - | 37.5 | 25 | 87.5 |

Table 6 shows the respective activity level intensities during each activity obtained from mean oxygen consumption, axis 1, vector magnitude, and activity score recordings during data collection. Metabolic-based activity level predictions were used as a reference as this indicated actual experienced intensities during activities. Hip ActiGraph predictions had a per cent agreement of 37.5% compared to metabolic-based predictions. Wrist ActiGraph predictions obtained a per cent agreement of 25% to metabolic-based predictions. Finally, a per cent agreement of 87.5% occurred between thigh ActivPal predictions and metabolic-based predictions. Statistical Cohens Kappa coefficients found a non-significant slight positive agreement of hip ActiGraph predictions to metabolic-based predictions and a non-significant agreement of chance between wrist Actigraph predictions and metabolic-based predictions ($\kappa$=0.149, P=0.231 and $\kappa$=-0.091, P=0.692, respectively). A significant near-

perfect agreement was found between thigh ActivPal predictions and metabolic predictions ($\kappa$=0.814, P<0.001).

# 6. Discussion

The present study investigated the validity of using current algorithms of ActiGraph and ActivPal accelerometers in predicting energy expenditure in an osteoarthritis population. The study's initial hypothesis was that current algorithms were not accurate in predicting energy expenditure and physical activity intensities within a population suffering from a movement-limiting condition. The findings from this study better support this claim.

In the current population sample, participants with knee OA had higher pain, symptom, ADL, sports/rec, and quality of life (QoL) scores compared to participants with hip OA when assessed using KOOS and HOOS questionnaires, respectively (Table 4). These scores represent an individual's functional and physical capabilities and what they are and are not able to do concerning their current condition. A higher score indicates a good outcome or significantly better result than a lower score (267,268). In the current sample size, pain and QoL had median scores of 61.11 and 37.5, respectively. Pain experienced in this population was relatively lower, achieving an overall median of 50, indicating a moderate level of pain is experienced in this population. Pain occurrence is commonly observed in an OA population (4,65,100). Pain can progress to a severe state and cause an individual to be considered physically disabled (258). Pain mitigation can come about through implementing intervention methods to reduce this symptom. Intervention methods such as drug and exercise prescriptions are the common prescriptions attempting to reduce OA-associated pain- with exercise prescription being the gold standard for mild-moderate OA treatment (17,158,192). However, current energy expenditure is needed to prescribe intensities suited to an individual for adequate exercise prescription for optimal results (226,230). Therefore, people with OA

would benefit from reduced experienced pain if adequate exercise prescription occurs with accurate energy expenditure estimations.

Similarly, QoL was reduced within this population, achieving a score of 50. Although commonly seen in an OA population, this reduced experienced pain and QoL score indicates that the experienced quality of life is reduced- possibly due to increased experienced pain. Interventions are needed to improve the current QoL (5,13,106,148). Intervention methods of physical activity prescription have been shown to aid in QoL improvement, and long-term experienced pain reduction in healthy and OA populations (20,163,179,278). However, one limitation to exercise prescription is current physical and mental limitations to exercising due to experienced pain and symptoms arising during physical activity- seen in a reduced Sports/Rec score in Table 4 (125,126,136,137,160). It is common for individuals with symptomatic OA to have increased pain experiences following bouts of physical activity (119,137,158,159,255). The present study supports this statement as an increase in pain was observed immediately after the cessation of the data collection procedure, having a 50% increase according to the NPRS. Though this finding was not significant, its insignificance could be attributed to the small sample size of our study, as previous studies have found that a short-term increase in pain is observed following exercise in an OA population (159,245). The long-term effects of physical activity are more beneficial than the short-term symptoms. In an OA population, regular physical activity has been shown to reduce OA-associated joint pain and prevent the progression of the disease to later stages, hence improving an individual's overall QoL (199,243,245). Regular physical activity reduces inflammation, pain, and discomfort experienced and improves mobility, strength, and overall functionality in an OA-affected joint (22,54,61,66,82,125,137,158,162,279). This evidence suggests that

physical activity should be a priority in OA management. However, an accurate physical activity prescription must be tailored to the individual presenting with the condition. Therefore, an accurate means of monitoring physical activity prior to prescription would aid in personal physical activity treatment plans.

As seen in table 4, this sample size had a lowered sports/rec score out of the maximum achievable. This lowered score shows that reduced physical activity is present within this population, and secondly, their respective joint conditions impact their physical capabilities for participating in physical activity. Although this is a common occurrence in an OA population (57,68,71,106,131), incorporating physical activity as a treatment prescription and in daily living has significant benefits regarding their condition (57,126,131,132,145). In an OA population, significant improvements in physical function, experienced pain, mental health, physical health, and overall quality of life are observed in exercise implementation through prescription (17,19,55,133,159,179,244,280). Although it is known that physical activity incorporation aids in symptom management and quality of life improvements in OA, to achieve the optimal benefits of physical activity, accurate monitoring and measurements are needed concerning physical activity and energy expenditure estimations. Thus, accurate and valid algorithms for activity monitoring during free-living activity can achieve improved health outcomes concerning symptom management in an OA population.

As expected, the present study found that heart rate has a strong positive correlation to increases in oxygen consumption during home-based mimicked activities (Fig 15) ($R^2=0.927$, $P<0.001$). This observation was expected as it is known that physical activity increases heart rate (205). Increases in heart rate during physical activity are accompanied by

an increase in respiratory rate to accommodate the body's oxygen consumption needs (189). This observation is significant as it firstly proves the reliability of using the Metamax® as a device to accurately predict the energy estimations in OA participants using indirect calorimetry. Secondly, it provides an accurate reference for comparing energy expenditure estimations using accelerometry-based algorithms and devices (281).

Accelerometry data from hip ActiGraph accelerometers indicated a strong relationship between oxygen consumption predicted energy expenditure and hip-based accelerometry energy expenditure estimations. Interestingly, strong positive correlations were found between $VO_2$ using the Metamax® device and hip ActiGraph counts ($R^2$=0.984, P<0.001) (Fig 17). These findings signify that the relationship between hip motion and energy expenditure can be quantified and used to establish accurate energy expenditure estimations using accelerometer-based algorithms and devices in a clinical setting in an OA population. Though accelerometers have been used to determine the function of OA-affected joints (254), their use in determining energy expenditure in this population remained unclear. Previous studies have observed these findings and have been used as a valid predictor for energy expenditure and physical activity monitoring in a healthy population (230,282). Although hip accelerometry has been proven to be a helpful utility in activity monitoring, prescription, and energy expenditure estimations in healthy people, it is essential to note that hip accelerometry alone is insufficient for accurate physical activity and energy expenditure monitoring in any population. This is due to hip-based accelerometry providing accurate locomotion and energy expenditure results but inaccurate results for predicting physical activities where significant arm movement occurs (283). Thus, these findings indicate that using the hip ActiGraph

accelerometers, in conjunction with other accelerometry methods, is viable for activity monitoring and possible energy expenditure estimations in an OA population.

The energy expenditure ratings obtained from the metabolic-based activity level ratings represent the actual intensities experienced by participants during sedentary, daily living and light physical activities. When activity level ratings obtained from hip ActiGraph were compared to actual intensities, only 37.5% of predictions agreed to oxygen consumption outcomes. Further, the agreement of hip ActiGraph accelerometers only slightly agrees with the actual values of experienced intensity and subsequent energy expenditure according to Cohens Kappa ($\kappa$=0.149, P=0.231) (Table 6). These results indicate that although hip ActiGraphs show potential for predicting energy expenditure (Fig 17), the current algorithms used do not accurately predict energy expenditure in people with OA. This is due to currently used algorithms being tailored for healthy people with normal functioning joints and mobility (150,227,231,282) and not incorporating additional muscles to maintain posture and balance while standing and moving (53,140). Therefore, although hip ActiGraph has the possibility of accurately predicting energy expenditure in people with OA, current algorithms do not allow this accuracy. For accurate energy expenditure using hip ActiGraph accelerometers, new, better-suited algorithms would need to be developed to cater to the needs and physiological adaptations during OA development and progression.

Wrist ActiGraph had a very weak positive correlation to oxygen consumption increases in an OA population during at-home and light physical activities ($R^2$=0.357, P=0.385) (Fig 19). Though this finding proved to have no significance in this population, the significance could be attributed to the small sample size in our study. It is clear that wrist accelerometry using

vector magnitude values is a valid method for predicting a healthy population's energy expenditure and physical activity level (190,228,230,233,283,284). These findings may support current literature if a larger sample size of an OA population is investigated. Though it is established that wrist-worn accelerometry is a valid method for monitoring physical activity, specifically arm-based physical activity, it alone cannot accurately predict energy expenditure and whole-body motion and position changes (283). These findings indicate that wrist ActiGraph is not valid for an OA population's activity monitoring and energy expenditure estimations.

Wrist ActiGraph energy expenditure ratings only achieved a 25% agreement with metabolic-based energy expenditure predictions. This agreement was determined to result from chance ($\kappa$=0.091, P=0.692) (Table 6). Wrist accelerometry has shortfalls in predicting whole-body locomotion and overall energy expenditure (233,283). When used in healthy populations, wrist accelerometry can obtain accurate energy expenditure and physical activity level ratings during movements involving hand and arm movements. Though this has been proven in healthy people, the current study suggests that the current algorithms used within the device and the device itself for wrist ActiGraph activity monitoring are not valid in people with OA.

Although the results achieved from comparing hip ActiGraph and wrist ActiGraph accelerometry to metabolic-based energy expenditure ratings acquired non-significant p-values (P=0.231 and P=0.692, respectively), the insignificance could be attributed to the small sample size of participants present in this study. However, the current algorithms and investigated devices were observed to have missing data during hip and wrist-based physical activity monitoring, resulting in inaccurate data replicability within an OA population (285).

Further, this data loss during monitoring results in inaccurate calculations and, therefore, inaccurate activity level ratings and energy expenditure estimations. These inaccuracies may result in incorrect interpretations from medical professionals. The subsequent physical activity interventions are prescribed at a disadvantageous intensity level and thus result in delayed improvement of symptoms and an increase in the probability of disease progression within this population (286). These results indicate that current algorithms for monitoring physical activity using ActiGraph accelerometers at the hip and wrist sites are inaccurate for use in an OA population. These findings suggest that specific algorithms are needed to represent better daily free-living activity intensities and energy expenditure experienced in an OA population using hip-based ActiGraph accelerometers. By developing algorithms suited to the physiological adaptations that occur in OA, improved outcomes may be achieved through currect energy expenditure estimations and consequential exercise prescription.

ActivPAL activity score was found to have a strong positive correlation to increases in oxygen consumption during at-home mimicked activities and light physical activity ($R^2$=0.976, P<0.001) (Fig 21). These findings are supported by current literature that found that thigh ActivPAL accelerometers achieve accurate results regarding physical activity monitoring and classification and energy expenditure estimations in healthy populations (225,234). Though these studies were conducted in a healthy population, it allows further research to aid in developing algorithms to better predict energy expenditure and physical activity monitoring in a movement-limited population such as OA.

Thigh ActivPal achieved an agreement of 87.5% compared to metabolic-based energy expenditure predictions. This agreement was found to be significant and achieved a near-

perfect agreement outcome from Cohens Kappa calculations ($\kappa$=0.814, P<0.001) (Table 6). These results are supported by several arthritis studies, one of which validated the use of thigh ActivPal accelerometers in a rheumatoid arthritis population. Their study also found that thigh ActivPal resulted in accurate and valid physical activity level rating and energy expenditure results compared to indirect calorimetry methods in rheumatoid arthritis (232). Similarly, ActivPal accelerometers provided accurate information for an arthritis population for sedentary behaviour and light and moderate physical activities in rheumatoid populations (234,235,287). Though investigations have yet to be conducted to validate their use during vigorous-intensity physical activity, the same is needed within an OA population following the results from this validation study. The findings from this study suggest that current algorithms and calculations pertaining to thigh ActivPal devices are valid for accurate physical activity level predictions and energy expenditure estimations through accelerometry in an OA population.

### a. Limitations

A significant limitation of this study was that the current Covid-19 pandemic affected the ability to interview and collect patient data. The Covid 19 pandemic resulted in a smaller than estimated sample size due to the inability to attend the clinic for data collection and the fear of patients catching the virus.

A second limitation is the occurrence of faulty equipment. During data collection, heart rate monitors and accelerometers occurred faulty errors of either battery problems or data recording issues. As a result, some data was missing from some participants in the study and

may have altered our findings. If a larger sample size is achieved, it may eliminate the effect of missing data on results and yield clearer findings for results of hip and wrist ActiGraph predictions in estimating energy expenditure in an OA population.

### b. Conclusion

The present study found that ActiGraph wGT3X-BT accelerometers possibly are not valid for accurate estimations and predictions of energy expenditure in an OA population. To support this statement better, more research is needed to understand their use within an OA population. However, the increase in acceleration counts in axis 1 and vector magnitude moments are correlated to increases in oxygen consumption during physical activity. Therefore, further research may prove possible to develop new and better-suited algorithms to accurately predict energy expenditure in an OA population using hip and wrist ActiGraph wGT3X-BT accelerometers. Further, the present study found that ActivPal 4 micro accelerometers are valid in accurately predicting energy expenditure in an OA population. Their use proves accurate energy expenditure predictions compared to gas analysis energy expenditure- deemed accurate representations of actual energy expenditure in any given population.

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