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# Intramuscular Fat Deposition and Osteoarthritis Pathology: A Possible Overlooked Pathogenic Correlate?

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**Abstract**

Osteoarthritis, the most prevalent joint disease and one affecting many aging adults is strongly associated with various degrees of disability and high health costs. Commonly deemed largely incurable and progressive, it appears muscle fat deposition and its encroachment on muscle tissue may account for multiple adverse health outcomes, especially the osteoarthritic disease process. This mini review examines whether contemporary evidence supports a role for efforts towards preventing excess fat infiltration into vulnerable muscles as one means of reducing osteoarthritic pain and disability. To this end, research on this theme and reported as of June 2025 on this issue was sought. We found that with few exceptions and regardless of joint examined a role for muscle mass infiltration in osteoarthritis disability appears of high clinical significance.

## Introduction

Osteoarthritis, a prevalent chronic disease affecting one or more freely moving joints and characterized by progressive bone remodelling, articular cartilage degeneration and soft tissue capsular and ligamnetous alterations continues to induce appreciable levels of physical and socioeconomic disability in a high percentage of older adults no matter where they preside [1-4]. Strongly associated with a complex interaction of local and systemic factors, rather than simple ‘wear

and tear' processes [2], the disease is increasingly characterized by multiple muscle alterations including: muscle atrophy, muscle spasm, muscle contractures, muscle fibrosis and pathology. In addition, osteoarthritis appears to be mediated to some degree by the presiding degree of abnormal muscle fat infiltration or fraction.

To this end, this brief specially examines whether, a) the fat muscle ratio is a feature or predictor of severe osteoarthritis, b) possible treatments to counter this, c) the specific importance of its timely identification in older adults at risk for or diagnosed as having osteoarthritis. It was anticipated the literature would reveal a variety of studies highlighting the potential impact of excess muscle fat mass on osteoarthritic pain. It was also believed that if this thesis can be substantiated, a variety of muscle treatment approaches would be found to reduce osteoarthritis pain, including those that can minimize muscle fat gains that are age associated, diet mediated, or reactive and arise in the face of joint pathology and surgery [5, 6].

**Methodology**

To examine works that might enlighten in the aforementioned regard, the PUBMED data bases largely extending from Jan-June 2025, using the key words: osteoarthritis, pain, sarcopenia and muscle fat mass were sought. Only articles focusing on osteoarthritis and some form of muscle fat attribute and pain as related to osteoarthritis were selected for review. Described in narrative form, are some general ideas and results of diverse current studies directed towards establishing the muscle fat fraction to lean muscle mass ratios in osteoarthritis contexts. The specific topic of interest, sarcopenia was also reviewed. No systematic review was conducted, however, and points made are those that have recently emerged and comport with the author's 25 years of research showing high degrees of obesity in cases with disabling hip and knee osteoarthritis and the fact that muscle fat mass can be seen in many young adults who are healthy via body impedance measures. The article focuses largely on intramuscular fat mass, as opposed to subcutaneous fat and muscle atrophy or mass that might prove insightful in efforts to foster the well being of many older adults that can be applied at low cost or non invasively.

Accordingly, first I will highlight some general current 2025 evidence reports that allude to recently observed muscle influences or responses in the osteoarthritis disease cycle, rather than all those that have been published to date. The items chosen are those that have a bearing in the author's view on pain the hallmark of osteoarthritis, namely cartilage shock absorbing tissue degeneration changes and destruction and include the presence or encroachment of fat into the muscles of vulnerable joints. Second, some emerging evidence of a key role for health behaviors as a mediating or moderating pathogenic factor in this respect. Third, clinical implications, possible clinical directives, and future research ideas are presented.

**Assumptions**

1. Excess muscle fat mass may adversely impact articular cartilage structural features.
2. The absence of adequate nutrition may impact the risk of severe osteoarthritis via its effect on muscle composition, strength, and joint stability.
3. A failure to control body weight may prove injurious to a joint.
4. Lean muscle mass declines and increases in muscle fat ratios may provoke and perpetuate an array of unwanted joint functional outcomes and pain provoking adaptations.

Evidence that fat mass may generate pain in its own right or provoke osteoarthritis progression is potentially supported to date by a host of biomechanical and muscle composition and quality analyses, ultra sonography, imaging studies, basic studies, and biochemical approaches.

**Current Specific Findings**

While a role for muscle in the osteoarthritis pathogenic cycle is a relatively recent perspective, and increasing numbers of studies confirm its association with symptomatic osteoarthritis, the notion that muscle fat deposition or infiltration may be a potent disease muscle mediator is not widely documented, nor universally applied to a degree commensurate with its possible diverse pathogenic disease manifestations, attributes and associations. In addition, most studies either discuss methods of evaluating muscle composition as this impacts osteoarthritis in a general sense, or detail post surgical muscle fat attributes, both reactive and possibly pathological. However, among the related studies on this issue published as of June 2025 on PUBMED and PubMed Central science repositories, a fair number that focus on obesity and its implications for joint loading, highlight an independent role for muscle adipose tissue composition alterations including muscle fat deposition. Increasing numbers also indicate it may be possible to mitigate this mediating factor in some cases. For example, among these studies a specific role for physical activity [8] and an array of muscle-related structural and functional changes to address sarcopenia [a progressive muscle mass declining state] as this impacts mobility, and raises pain levels, possibly additively and extensively and sets the stage for inactivity and muscle fat fraction increases [9]. Others show a role for deforming contractures, varying degrees of muscle spasm and subnormal vector influences, plus functional changes in muscle biochemistry that have a unique or collective bearing on cartilage viability and that may implicate or lead to muscle fat excesses and infiltration as well as deficits in lean muscle mass [10-13].

Other data imply that there may be progressively harmful adverse degrees of joint loading that subsequently manifests as fully fledged osteoarthritis, as various degrees of muscle pathology and disordered biochemical expression and/or kinesiophobia or fear of moving due to pain and possible muscle inflammation [14]. Collectively, one or more of these suboptimal non physiological pathological disease states appears to have the potential to foster subnormal muscle forces and joint loading or attenuation responses, as well as marring cartilage nutrition processes, and cartilage integrity, and joint stability [15-22].

Other data reveal observations of prevailing or emergent muscle fat associated metabolic muscle alterations, alterations in muscle quality, thickness, mitochondrial muscle energetics and/or myopathy of the surrounding muscles that may impact on overall physiological reserve and adaptability as well as fostering a perpetual state of undue damage and persistent joint stresses [23], and local signs of muscle weakness. There may also be emergent indications of a gradually diminishing joint range of motion [24], and joint stiffness [25], plus abnormal degree of muscle related joint degrading biomechanics [10, 24, 26]. Moreover, it is conceivable that in the absence of effective interventions, as time proceeds muscle tension effects associated with modest intra articular pressure levels, hypoxia and short periods of synovial ischaemia an ongoing cycle of disordered joint destruction and inflammation that causes widespread central pain sensitization or neuropathic states emerges incrementally and persists to destroy the joint as follows:

This envisioned series of adverse interactions including heightened muscle strength and contractile

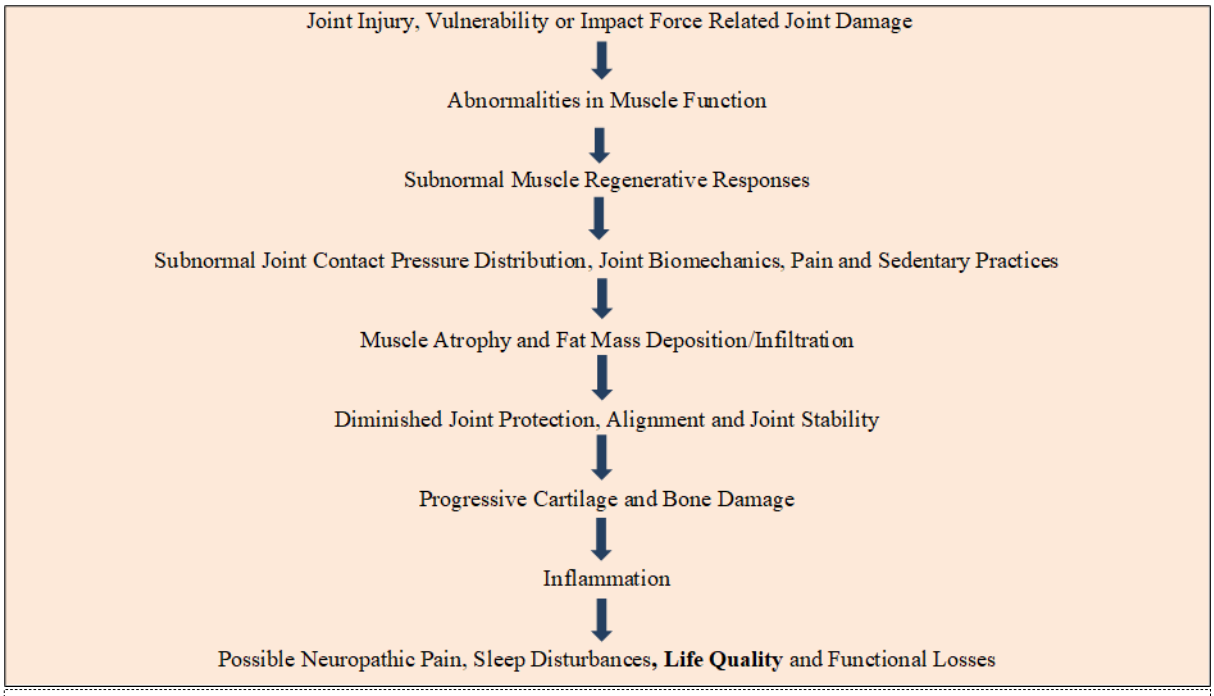


Figure 1. Hypothetical relationships between osteoarthritis pathology, pain and muscle fat deposition factors

abnormalities [26] and others that may induce or be mediated by muscle fat encroachment is indeed increasingly shown to be associated with subnormal joint biodynamical, structural and osteoarthritis joint destruction. For example, in knee osteoarthritis, the most prevalent site of osteoarthritis damage, the disease is often accompanied by a significantly reduced muscle strength capacity and a greater body mass index, wherein a large accumulated fat mass linked with greater systemic inflammation and possible inflammation mediated muscle damage may play a pathogenic role [30]. As well, this idea is consistent with known age associated degrees of the gradual onset of subnormal muscle metabolic physiological states, losses of lean muscle mass, increasingly sedentary behaviours, and possibly some neuromotor conditions.

Underlying local factors may also include possible painful muscle reactive adaptations due to persistent abnormal sensory inputs from one or more of the surrounding tissues in the presence of an increased muscle fat mass and parallel decline in muscle mass [15-20, 30] that may impact the ability to attenuate joint impact loads significantly and effectively as well as muscle quality and architecture [30]. Other research suggests persistent muscle spasm resulting from excessive stretching of diseased tissues or abnormally stimulated muscle nociceptors, myokines. or adverse metabolites may also produce a state of ischemic pain in its own right, as well as a state of poor muscle endurance and disabling muscle fatigue that is hard to mitigate [31]. Also known as myosteatosis, its presence in muscle exhibits a negative correlation with muscle mass, strength, mobility, and a decrement in muscle quality, while serving as a biomarker for sarcopenia, cachexia, and metabolic syndromes. It also induces proinflammatory changes that clearly contribute to declines in muscle function, compromise mitochondrial function, and increase muscle inflammatory responses [31].

Others show the presence of muscle fat derived inflammation may not only evoke local muscle pain signals, but may elicit more widespread pain, bone attrition, and sensory sympathetic inputs that contribute to the arthritis disease and disability cycle [32]. Unsurprisingly, the presence of a decreased quadriceps cross-sectional area and increased intramuscular adipose tissue in knee osteoarthritis has

been found predictive of downstream symptom worsening and a need for knee replacement especially in the overweight adult [33, 34].

In this regard, a longitudinal follow-up study of 4.9 years, 472 participants who developed knee osteoarthritis, and 387 cases hip osteoarthritis showed the degree of intramuscular fat in the anterior thigh was significantly associated with incident knee osteoarthritis as well as hip osteoarthritis. Dose-response relationships were also observed. The interaction and subgroup analyses supported the view that this muscle fat effect is a unique pathogenic factor and one that occurs independent of body mass index or gender [34] and may have a bearing on ongoing physical activity challenges as well as emergent alterations in both muscle architecture and degeneration and declines in functional abilities [35, 36], plus exaggerated sympathetic reflex mechanisms and more fatty tissue acquisition than not [37, 38].

It also appears muscle fat fibrosis may have a separate or combined cumulative and progressive effect on osteoarthritis structural pathology indicators [39-41], and regardless of whether this situation is causative or reactive, unless identified early on, it may be highly challenging to heighten their physical function or relieve longstanding pain or mitigate osteoarthritis, especially if there is a progressive unwillingness on the part of the affected adult to move to counter increasing pain and stiffness, widespread reflex reorganization, body mass increases, alongside muscle mass declines, joint instability, and muscle fiber atrophy. In addition, in the presence of marked instability and/or complete joint stiffening, the abnormal and awkward movements used by the individual to avoid pain and injury may throw strain on other joints, causing further pain and possible reactive diverse muscle associated adverse structural alterations as well as adverse muscle strength implications [42-44].

Recent data specifically reveal a higher degree of intramuscular fat in both knee extensors and hamstring muscles in middle-aged women with knee osteoarthritis compared with that in a healthy group. It was speculated that weakness of these muscles may to changes in their architectural properties that varies depending on the degree of muscular infiltration. It was concluded the presence of intramuscular fat in the knee muscles is an important determinant of the subjects' performance and physical function abilities and one worth examining further [44].

Other muscle based determinants that may be related to the degree of muscle fat encroachment and presence involved in osteoarthritis include declines in physical performance and quality of life as well as potential for enhancing the risk for non-communicable diseases, immobility, and disability [45]. Increasing data appear to agree upon multiple associated possible harmful degrees of reactive muscle fat deposition in the context of painful osteoarthritis such as subnormal degrees of muscle fibrosis, muscle inflammation, joint instability, and altered cartilage calcium presence [45-50]. Those muscles that may then undergo attrition and/or muscle fat encroachment may also produce slower than desirable reflex reactions that enhance the risk of incurring more extensive joint pathology and pain than those generated in the presence of sufficient fat free lean muscle mass [46-50].

Recent evidence also shows a possible role for osteoarthritis associated muscle fat infiltration [51], as well gene and protein metabolic alterations [52] that may occur alongside widespread pain, atrophic muscle weaknesses, muscle volume deficits [53] inflammation [54] and muscle architecture alterations including the presence of intramuscular fat deposition or infiltration [55]. At the shoulder joint, it appears muscle resident fibroadipogenic cells do serve as a key contributor to rotator cuff tear pathological changes [20].

While mechanical injury is the most likely cause of osteoarthritis in most instances, emerging evidence shows functional ability declines in the presence of excess muscle fat in early knee osteoarthritis symptoms that could be causative or reactive or both [56]. An increased muscle fat ratio and its presence can possibly engender multiple pathological states including various degrees of systemic inflammation, physical dysfunction, muscle and muscle metabolic impairments and pain [51, 55, 57, 58]. As applied to the vastus medialis muscle of the thigh in knee osteoarthritis, this situation also appears strongly correlated with a decline in the quality of the medial femoral cartilage [58].

As well, those cases displaying atrophic muscle weakness are likely to also display disruptions in muscle genetics, muscle inflammation, and joint instability that may progress to more detrimental muscular alterations such as declines in muscle force capacity and responsiveness [44]. Possible central processing neural mechanistic changes that occur over time may further serve to amplify the pain attributable to the local condition even after surgery in the absence of salient timely targeted intervention that embraces efforts to mitigate obesity and possible muscle fatty tissue infiltration and deposition even in the face of joint replacement surgery [76].

Although more research on diverse osteoarthritis samples of higher ages, joints other than the hip and knee joints that predominate is desirable, and more emphasis on muscle pain, inflammation, and atrophy, a role for muscle fat mass correlates that may foster extensive alterations in muscle reactivity and neural signaling at multiple levels including cartilage integrity, is a topic strongly advocated by researchers as a promising one, that cannot be ignored.

In addition, even though the source of fat infiltration and why this may enlarge and become pathogenic is not well clarified, nutrition and physical activity as well as injury appear to play a possible role beyond age and genetics and could serve as basis for intervention approaches that can reduce muscle fat encroachment safely, as well as mitigate-if not reverse- joint destruction, as indicated. As well, multiple diverse intervention modes directed at osteoarthritis pain relief or obesity prevention or both may help as well, especially if they alleviate fears of moving and anxiety.

Currently, as of June 2025, despite the limited body of research that has emerged to date and appears to basically be in its ‘infancy’, it is evident many recent osteoarthritis studies show an enormous potential for studies that explore muscle fat mass deposition and/or its expansion as a potential key pathogenic factor or co-factor requiring attention. Additionally, it appears physical therapies that address this pathogenic disease feature and especially those that can prevent or minimize its impact may greatly help to mitigate this disabling disease. Especially indicated are those strategies that encourage efforts to increase lean muscle mass, strength, power, and careful movements, while reducing pain. Also indicated are: a) weight control; b) possible muscle protein supplements; c) strategies directed towards enhancing muscle reactivity, and efforts towards avoidance of repetitive injurious joint loading activities that induce pain [20, 59-65]. Muscle stress protection in particular seems highly relevant as recent analyses reveal that in the presence of failed regeneration in injured muscle promotes a hostile microenvironment characterized by heightened inflammation, fibrosis, and denervation that may reduce the remaining muscle tissue's quality, and stimulate intramuscular adipose tissue expansion and its known lipotoxic effects on regeneration and contractile function especially in the face of a sedentary lifestyle [66].

At present, even though more solid information on this topic is necessary to acquire, it appears most clinical researchers currently assume muscle problems of some sort underlie and impact osteoarthritis pain and if minimized will prove to have a bearing on osteoarthritis outcomes. In particular, distinctive

efforts to study and address muscle fat deposition origins and impacts such as fears of movement [67], muscle strength [68, 72] pain [69], and pain behaviours [74] although rare, are realms of study that will likely prove advantageous as well as insightful. Indeed, increasing attention alone is being paid to muscle fat as a mediator or correlate of osteoarthritis and this realm of cumulative inquiry is adding a new dimension to understanding its origins and progression, and need to obviate or avert its role as a specific site for generating toxic substances with the potential to impede normal muscle function and metabolism and foster potential muscle damage [36, 71] as well as health negating body wide changes due to cross talk between fat and body tissues and pain [74]. More specific exploration on how to exploit this emergent set of understandings and their potential for effective osteoarthritis preventive as well as treatment strategies should help to greatly advance the field as cited by most current researchers, even those who conduct joint replacement surgery [76]. These observations largely support and reveal a negative role for the presence of fatty tissue in muscles around an osteoarthritis damaged joint as well as how muscle fat mass deposition and enlargement may impact joint biomechanics, muscle parameters such as coordination, flexibility, strength, contraction speed, and endurance adversely in the face of painful osteoarthritis especially in an aging population vulnerable to declines in the lean muscle mass to fat ratio [77, 78].

## Discussion

Although osteoarthritis is currently deemed a chronic progressively disabling condition with no known cure, research over the past 10 years or more has indicated that there is strong possibility that an array of muscle related factors as well as obesity can contribute to the osteoarthritis pain and disease cycle.

Conversely, a diverse array of intervention approaches that focus on maximizing muscle structure and function appear advocated to potentially reduce the degree of excess muscle fat mass often noted in this population alongside pain, so as to foster desirable outcomes, regardless of joint site and disease severity.

Excess muscle fat may also impact outcomes of surgery to replace a diseased joint, stressing its importance. Applying what we do know towards primary prevention of injuries, and the adoption of active living rather than sedentary behaviors by many will however likely foster overall joint as well as general health, while helping to reduce enormous public health resource demands from depletion, even in the face of surgical solutions and especially among those in advanced disease stages. Key supportive approaches such as enabling sound dietary practices, electrical muscle stimulation, sensory motor and strength training, and Tai Chi, are likely to prove efficacious as well as safe for many in this regard.

To achieve optimal results, however, a role for cognitions cannot be ignored, given the fact that pain is widespread and fear and depression are readily provoked among those with osteoarthritis and severe pain. Additionally, cases need to be carefully educated as to the considerable care they must take however, to avoid overexertion, muscle fatigue, and repetitive movements, which can heighten muscle pain inputs and accelerate cartilage destruction, as well, as excess sedentary practices. Additional care and careful monitoring to avoid overstretching the joint, and helping those with severe overweight to lose weight is advocated as well. As well, avoiding high frequency loading activities after periods of immobilization found to hasten cartilage destruction is clearly of additional import.

At this point, and despite limitations of this review as well as the state of the research, it appears that while osteoarthritis continues to be described as both inevitable as well as incurable, this immensely

painful disabling condition can be mediated or moderated by factors other than age or wear and tear. As such, based on cumulative and emergent evidence, it seems plausible to suggest that the osteoarthritis sufferer's wellbeing can be effectively mitigated if not reversed if efforts to minimize muscle fat invasion of vulnerable joints is forthcoming, especially if tailored to the overall health status and needs and abilities of the individual and supported by objective measures of muscle composition, force capacity, pain, cognitions, plus weight. In particular, to avert rapid or excess disease progression and disability, and its association with immense social and mobility-related losses, there appears to be an increasing body of research that supports the view that efforts to reduce muscle fat encroachment is a highly salient osteoarthritis disease mitigation strategy. Hence, even if not the key pathogenic cause of osteoarthritis, its prevention must be seen of paramount importance in minimizing osteoarthritic joint pain and dysfunction.

However, since this is by no means a universally accepted idea or practice, more studies that tease out the possible relationship between muscle factors and osteoarthritic pain along with central factors that affect pain and muscle fat encroachment are warranted. Carefully controlled intervention studies with larger samples with similar muscular and disease related characteristics conducted over extensive time periods utilizing a variety of possible interventions could prove insightful as well.

Presently, as per earlier studies, a recent study [66] that strove to characterize lower limb muscle quality in cases with knee osteoarthritis revealed an unanticipated associated of a higher degree of fat infiltration and lower normal-density in the hip muscles rather than the knee extensors (commonly targeted in isolation and thought to predominate the condition). It appears therefore that knee osteoarthritis cases may suffer in part due to associated altered levels of hip abductor and external rotator muscle metabolism alterations, including muscle fat deposition associations, rather than the knee extensors [70]. Another that assessed muscle cross-sectional areas, echo intensity, and shear modulus in the knee muscles of 24 knee osteoarthritis cases and 24 controls indicated osteoarthritis muscle and strength losses, poor flexibility and increased passive tension, and possibly reductions in its contractile components and muscle force generating capacity that may accompany knee osteoarthritis [68]. Another revealed high levels of intramuscular fat and poorer function than controls [41] with possible significant implications including pathological disease mechanisms, muscle strength, impaired muscle regeneration, and life quality outcomes [71-75].

In short, although limited, current findings strongly highlight the degree to which muscle fat infiltration and/or enlargement may play a disabling role in the osteoarthritis disease cycle, as well fostering multiple levels of focal and systemic dysfunction, severe pain, and biomechanical and metabolic challenges. Moreover, a failure to appreciate and understand the importance of identifying, tracking, and examining muscle factors such as muscle fat mass in general in the realm of both osteoarthritis research and the design of optimal osteoarthritis rehabilitation plans and their scope and sequence may be shortsighted at best and warrants more careful study and one supported by possible AI diagnostics [31].

**Key Conclusions**

While recognizing the limitations of this line of inquiry and analysis we tend to conclude:

- High degrees of osteoarthritis impairment and suffering will persist among older adults if myths about the condition and sub optimal intervention approaches remain entrenched**.**

- Efforts to unravel the profound impact of muscle fat mass on joint health as one approach will prove beneficial.
- Targeted and tailored intervention studies to prevent fat encroachment and excess weight gain in later life are likely to prove highly efficacious.
- Research that examines muscles and joints from the perspective of intramuscular fat other than the hip and knee are indicated.
- Sarcopenia and obesity prevention are strongly warranted among all aging adults.
- A study of disease free older adults and how muscle fat affects joint loading and muscle regeneration would be revealing and greatly advance the field.

Until more is known, we further conclude that although most of the initiating osteoarthritis determinants that affect many older adults highly adversely are not known and the disease is commonly deemed incurable, it seems possible too that a variety of subnormal bone-muscle interactions and biological signaling alterations that are stimulated by an enlarged muscle fat cell presence can readily impact joint biomechanics as well as joint structure, including muscle and must be considered a key disability determinant, co-factor or osteoarthritis biomarker [63] Moreover, rather than neglecting or overlooking the relevance of possible increases in disordered muscle composition, especially those attributable to injury related fatty infiltration processes, interventions to avert this encroachment or minimize it can help offset a perpetual state of progressive muscle dysfunction, neuropathic pain, cartilage failure and its disabling life quality and functional implications.

We further conclude early detection, and primary prevention here is of high import, rather than late end stage interventions and will avert much suffering, functional disability, and pain in those numerous older adult populations at risk for osteoarthritis disability. In particular, helping vulnerable aging adults to avoid adopting a sedentary lifestyle, educating them about the impact of excess body weight and joint impacts on their wellbeing and need for joint protection, and the importance of regularly participating in exercises that build strength and foster weight control are highly indicated as well.

## Final Thoughts

In addressing the growing burden of osteoarthritis, conceptually modelling to unlock and elaborate on the true nature of the condition, a holistic lens that tracks muscle composition and weight status routinely and its joint and life affirming ramifications warrants concerted study and may show how much osteoarthritis suffering can be avoided or undone.

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## Conflicts of interest

none

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