

Exercises Pursued by Older Adults with Osteoarthritis and Their Structural Impacts are Hard to Uncover; a Scoping Review of Selected 1970-2024 Studies

Ray Marks^{1,*}

¹Department of Research, Osteoarthritis Research Center, Box 5B, Thornhill, ONT L3T 5H3, Canada

Article Type: Review Article

Open Access & Peer-Reviewed Article

DOI: 10.14302/issn.2474-7785.jarh-24-5282

Received: September 2, 2024

Accepted: September 4, 2024

Published: September 10, 2024

Corresponding author:

Ray Marks, Department of Research, Osteoarthritis Research Center, Box 5B, Thornhill, ONT L3T 5H3, Canada

Keywords:

Articular Cartilage, Biomarkers, Exercise, Osteoarthritis, Older Adults, Rehabilitation

Citation:

Ray Marks (2024) Exercises Pursued by Older Adults with Osteoarthritis and Their Structural Impacts are Hard to Uncover; a Scoping Review of Selected 1970-2024 Studies. *Journal of Ageing Research and Healthcare* - 5(2):1-20. <https://doi.org/10.14302/issn.2474-7785.jarh-24-5282>

Abstract

Persons with osteoarthritis often have signs of reduced muscle strength. Some studies suggest that this strength could be improved with exercise. However, does this form of therapy improve the disease status as assessed by improvements in cartilage viability, a hallmark of the disease? This brief describes the possible usage of exercises in general, plus those known to improve strength and function, and reduce pain and whether structural impacts that favor or impede disease regression have been observed in this context among the older osteoarthritis adult population. Since exercise may also do harm, rather than good in osteoarthritis management if excessive, contra indicated, or suboptimal, what is the consensus in this regard in 2024?

Introduction

Osteoarthritis, the most common rheumatic disease is a chronic condition affecting the majority of the older population. Commonly deemed incurable, osteoarthritis is a well documented and frequent source of functional disability

and pain despite years of research and intervention attempts. In the context of the increasing aging populations worldwide, the collective costs of the disease, considered as a key determinant of an age related intrinsic capacity decline [1] are enormous. Unfortunately, its prevalence appears to be increasing [2] and increasing at an alarming rate [3].

Commonly characterized by progressive bone remodeling, bony outgrowths, and micro fractures, cartilage tissue fragmentation and degeneration, plus possible joint capsular fibrosis, ligament instability, muscle pathology, and often joint derangement and instability, osteoarthritis joints may become poorly aligned and more susceptible to cumulative or sudden joint impact forces with dire functional consequences [4]. In addition, muscles surrounding the affected joint may not only become weaker than desirable, but respond more slowly than desirable, and may thus be less able to absorb joint impact effectively. Adding to the disease burden may be ensuing bouts of accompanying joint inflammation and pain, muscle fat infiltration, decreased range of joint motion, impaired muscle reflex responses, subnormal proprioception, adverse emotional reactions, and joint deformity.

On the premise that exercise will delay muscle atrophy [5] or provide increased joint stability [6], persons with osteoarthritis are frequently encouraged to undertake exercise. While exercise can objectively improve physical performance with no documented detrimental effect [7], and may even have beneficial effects on type II collagen metabolism, especially in people without radiological osteoarthritis [8], the effects of exercise training for persons with osteoarthritis as regards its structural features and loading impacts either favorable or not have not been thoroughly examined and cannot be deduced from preclinical models or those carried out by healthy persons or persons with osteoarthritis who undergo exercise but have no radiologic measures either at baseline or after 6 weeks [9] or 12 weeks of intervention [10]. Variance due to age and disease manifestations, mode of exercise [11-13], methodological limitation in exercise protocol reporting [14] as well as exercise duration [15], frequency and dosage, the role of allied therapies [16], and exercise adherence rates are also influential factors not well articulated in randomized controlled studies and others [17-19] and cannot explain either exercise associated successes or lack of success.

Based on a sample of parallel reports it can argued that exercising can place widely varying biomechanical and physiologic demands upon the cartilage tissues and its cells and fibrous supportive surrounding matrix that may or may not stimulate cellular biosynthesis, which is the basis for the adaptation and viability of this important joint shock absorbing tissue lining [20-22]. Moreover, in some studies it could be shown that joint motion without compression could cause articular cartilage thinning, while static loading caused a decrease in chondrocyte biosynthesis. It was concluded that there may be cartilage activity thresholds below and above which the effects are minimal or destructive, as opposed to beneficial. Because the adaptive capacity of articular cartilage may be compromised in the injured, overloaded, or aged joint [23] that is heightened in the presence of lower than desirable muscle mass [24], and measures of cartilage using ultrasound produced differing results across differing exercise modes [25], it seems reasonable to examine if those recommended exercises to counter osteoarthritis are equally 'good' for all or need to be carefully designed, titrated and implemented with care in the older adult with compromised joint and muscle health until more is known even if somewhat refuted by Marriot et al. [26].

However, in addition to observations that support modest exercise as a beneficial cartilage mediating strategy, that observed in light of the above mentioned potential research limitations, plus those denoting no adverse or favorable cartilage based impact in the context of a single exercise bout in

severely damaged knees prior to surgery [27] cannot be generalized to any meaningful degree. Similarly, data extracted from healthy cartilage assays designed to discern exercise metabolic effects [28], plus those gleaned in the realm of various running related studies [29], secondary analyses [30] or the post traumatic osteoarthritis rat model must be viewed with caution [31] despite a global consensus on applying exercise as a front line strategy for improving osteoarthritis status.

Aim

This present overview aimed to examine whether exercise as applied to osteoarthritis has any impact on cartilage tissue assessed directly through radiographs, the gold standard measure in this respect. As well, resistance training in the form of isometric exercise, one of the oldest forms of exercise used for arthritis management was specifically examined and if so what radiological or its proxy measures as assessed through serum measures, biomechanical, or force measures indicate in this realm and in what regard.

Research Question

The review attempted to establish whether exercises that have been studied for many decades appear to reduce joint attrition and its progression objectively, while increasing increase muscle power and function safely and significantly in osteoarthritis contexts.

Rationale

In light of the continued osteoarthritis disease burden that is increasing rather than decreasing, along with the current emphasis on applying evidence based medical recommendations in all spheres of endeavor, versus hearsay or traditional approaches, it appears reasonable to ask if the lack of solid evidence that exercises can be applied successfully without any discrimination or on the basis of the prevailing studies to improve osteoarthritis wellbeing is based on sound science and/or takes into account its variable pathology, sub groupings, and characteristic features of osteoarthritic joint change. These features include: progressive bone and articular cartilage degenerative changes, capsular fibrosis, ligamentous damage, joint laxity, sensory (mechanoreceptor) receptor changes and extensive muscle pathology. Joint inflammation is also a consistent feature of along with pain, joint effusion, stiffness, decreased range of joint motion, muscle weakness, joint instability and deformity, and progressive reductions in the efficiency of musculoskeletal functioning. But, the question arises as to whether as applied to the older adult population, whether exercise is a panacea or can a failure to act cautiously in exercise applications in the presence of osteoarthritis induce more rather than less disability and adverse psychosocial reactions and thus more costly outcomes [32].

As well, since even modest stretching exercises may prove injurious, for example in cases that are neuropathic [33], is the blanket conclusion that osteoarthritis cases will demonstrate flexibility improvements with physical exercise participation [34] adequate for ensuring optimal benefits for all, for example in cases with joint instability? Similarly, is the idea of exercising to tolerance sufficient to achieve desired results if this protective neural sense or reflex response is subnormal [35] or the diseased limb is poorly aligned [36]. Moreover, should caution be taken to address possible adverse exercise impacts that may damage cartilage, while trying to promote more optimal functional and loading outcomes or regenerative processes [3].

Significance

The question of whether exercise has a uniformly beneficial impact on an osteoarthritis joint in the older population is a topic that warrants more scrutiny in our view because even though multiple affirmative studies imply a significant pain relieving benefit, surgery continues to be demanded by those who may have pursued exercise diligently. This may be because muscles and their physiological and structural attributes may be dysfunctional to a considerable degree in a high percentage of osteoarthritis subjects and thus benefits from exercise applications may not align with those observed in the lab. Moreover, exercise that is poorly designed or supervised [37] as well as poorly targeted and titrated may fail to improve joint status uniformly or even worse, may do more harm than good [20], for example in those with more severe rather than less severe cartilage damage [38]. Indeed, exercise that is simply employed for all cases equally, even though intuitively these may not impact differing cartilage lesion sites equally or favorably and may not be helpful for attenuating the chronic susceptibility of osteoarthritis cartilage to mechanical impacts in all cases [27] may prove highly undesirable, even if promising for cases apparently at risk for osteoarthritis [37]. As well, for similar reasons are programs of unsupervised, partially supervised, or remotely delivered internet based exercise protocols likely to prove universally efficacious or replicable in light of the challenges faced by an older adult in pain with limited function and possible depressive symptoms, low health literacy and resource access, and especially in view of the possible degree of cartilage damage that could be generated by exercising to fatigue or in the face of ligament laxity [20, 39, 40] or muscle pathology or both.

Methods

A comprehensive overview of peer reviewed publications posted on **PUBMED**, **Google Scholar**, and **PubMed Central** in any year was conducted to address the present article aims. Among these data were 9397 articles posted as of August 25, 2024 on **PUBMED** using the key words ‘*osteoarthritis and exercise*’, the total number of posted unfiltered resources numbered 9417, 160 were meta analyses, and 8718 were available in full text, but only 4763 were available on line. A total of 8922 of which 4356 were available in full text online referred to *isometric* exercise, of which 1409 were randomized trial reports dating back to 1982 with 1134/1409 randomized trials of isometric exercise related articles focusing largely on knee osteoarthritis. Very few studies examined exercise and cartilage repair associations if any, even though this may prove of high clinical relevance as well as highly insightful.

Considering the plethora of exercise associated studies cited on the three data bases currently examined, and the mostly mixed samples, study designs, and modes of treatment but few analogous or replication studies or consistent themes of exploration, we elected to focus on examining both exercise impacts in general as well as resistive modes, as observed in randomized controlled trials, and often advocated for treating arthritic joints because they involve muscle contraction without producing joint motion, and in the belief that transarticular forces can be duly minimized as result. Brown et al. [41] have also suggested that this form of exercise may prove more suitable than dynamic exercises for persons with osteoarthritis that may be more painful especially in cases with inflamed unstable osteoarthritis joints. They may also foster overall cardiovascular health, bone health, psychological health, and aid in obesity prevention [4], muscle and neural protective mechanisms that may fail in osteoarthritis [42, 43] or provide increased joint stability [44] often associated with the presence of joint degeneration. We excluded preclinical or animal based exercise or simulated osteoarthritis studies, studies focusing on osteoarthritis cases younger than 60 years of age, foreign language studies, physical activity, passive motion, internet delivered, and balance oriented exercise related studies, joint replacement surgery

associated studies, muscle stimulation and platelet rich plasma studies, study proposals, and other data bases such as EMBASE, CINAHL, and Science Direct. Only a qualitative scoping overview is provided, no subgroup studies are included unless exercise associated, and readers can refer to referenced meta-analyses for further in depth assessments [see selected references 45-50].

Current Findings

Even when earnestly sought, and regardless of data base employed, it was unusually challenging to delineate or even uncover the potential impact of formal exercise in any form on osteoarthritis associated joint structures of any sort, and what actual post exercise functional results were observed. Almost none assessed any probable joint soft or hard tissue impacts or status directly or even indirectly, and in those studies using multiple intervention formats results could not be attributed to exercise per se in many cases with any degree of certainty. Moreover, rather than testing the most widely employed and recommended forms of exercise for arthritis, most current studies failed to apply isometric exercise methods of various doses and combinations and were not those that could be readily subsumed by most older adults, such as eccentric high intensity exercises.

As well, there was little evidence regimens studied were applied with the goal of maximizing one or more outcomes based on the specificity of exercise theory, wherein exercise has both general, as well as specific effects on muscle that can be optimized. By employing vastly differing subject groups with varied degrees of osteoarthritis, where most over age 80 were not included in the study, as well as largely subjective measures, and few objective outcome assessments, loading estimations, biochemical, neuromotor, kinematic, and radiographic baseline and outcome measures, with few exceptions [eg.,51-54] it is impossible to state that exercise is universally beneficial and its effects are similar no matter how these are applied. In addition, among the many research reports reviewed, most pertaining to exercise focused on the knee joint, with few exceptions. Even in this case, where the consensus remains that pain and function improve no matter how exercise is practiced or how often [47, 55-57], with few exceptions [46], not all exercise participants are found to improve, but why this is, is largely unexplored.

Since osteoarthritis is a complex disease with many overlapping features, the assumption that all exercises are equal in impact as well as beneficial or safe in all forms and stages of this disease must be questioned given most researchers failed to confirm the presence or absence of any accompanying joint loading improvements or non improvements or worsening of joint structural stability plus inflammation, and disease biomarker status. The associated relevance of extraneous variables such as obesity, muscle metabolic and structural post exercise alterations [57-59], plus the probable mediating role of comorbidities, stress [59] and possible age related intrinsic capacity declines [1] are also hard to discern at present. Adherence as well as to what degree home exercises performed in some studies replicated the desired recommendations with high fidelity is also not duly reported or evident in many cases or negated as a factor of note [57]. Moreover, even if exercise appears 'no better' than placebo [30], the consensus that exercise participation reduces osteoarthritis pain, and improves function in the short term should be qualified more acutely. In addition, even if this is a universal finding given that there may be limitations to the extent to which pain can be attenuated in some cases a patient should have an accurate idea of what to expect. In addition to those items mentioned above, it is not clear if exercises applied in the face of any undetected probable muscle or joint sensory disturbance and movement abnormalities anticipated in the older adult will limit gains in function or not or whether more pathology than desirable might ensue. The role of medications to counter pain is also not well

controlled for and without patient education, those who do sustain pain relief may tend to function in ways that heighten joint impact inadvertently or fail to protect joints against muscle fatigue.

At the same time, even if deemed high quality as far as research design goes [56] not all published exercise regimen data may apply to all older osteoarthritis cases especially those with some form of heart disease for example who may not be studied, or where no adaptations to the studied regimen are evident or alluded to, as well as those with one or more co morbid health conditions.

Moreover, in accepting that more cases performing exercise will have less osteoarthritis pain than not, no matter how this is approached [26, 57], the data fail to clearly support this premise for large samples, or for example for hip osteoarthritis [30] or as mentioned by Hinman et al [59] where the role of extraneous variables, competing interventions, and reasons why some exercise participants do not respond favorably in all cases is often unreported, while blinding and instrument subjectivity, and reliability and fidelity of these are not always assured or discussed and where exercises may be unsupervised, applied on a limited basis, and based on complex exercise combinations [30, 60] or possible practitioner as well as patient personal preferences. Safety issues due to poorly directed and enacted exercise impacts in the face of joint damage and derangement, in particular, for example in the frail older adult with sarcopenia or bone fragility are unfortunately rarely alluded to.

Unsurprisingly, even in the realm of some key resistance or alternate exercise modes applied in a controlled manner, results remain challenging to aggregate, hard to validate, and apply with any degree of certainty. Not only do exercise approaches differ considerably, but whether these result in disease modifications that are measurable objectively, and that could help identify salient underlying explanatory and disease mediating mechanistic processes, for example the observed lack of exercise impacts on the osteoarthritis knee adduction [61] or frontal plane moments [62] and other outcomes as consistently evidenced in this body of data [See snapshot Table 1].

In addition to the snapshot above, and even when considering all currently published exercise oriented osteoarthritis meta-analyses and research studies of note it appears that despite years of endeavor no single form of exercise is found to consistently produce a pain free result for all osteoarthritis cases or appears to be of the highest merit overall. Additionally, even if sample sizes that are modest at best are discounted as non representative of the population, and very few attempts at sub group assessments are evidenced to date, why some cases respond favorably or unfavorably to exercises in general, as well as specific modes of exercise in this regard [5, 55], why some cases with osteoarthritis adhere or do not adhere to exercise recommendations [64] and why exercise does not improve depression attributes [45] even if it relieves pain - but not in all cases [74], remains hard to uncover. Even if this set of findings is affected by the application of diverse albeit limited subjective survey questions, the role of the halo effect, patient and provider perceptions, unknown reliability of measures, patient health literacy and memory challenges, lack of exercise specificity, or reflex muscle inhibition, it is impossible to deduce their individual or collective importance when considering exercise applications for older osteoarthritis cases at present. Pain too is commonly assessed using differing instruments and possible definitions and modes of expression with no parallel time based objectively derived and clinically relevant associated disease indicators, thus even here a strong basis for any form of exercise as the active variable in pain reduction is challenging to support.

At the same time, outcome indicators that might reflect the disease characteristics more closely than not are often not detailed. These might include, but should not be limited to factors such as:

Table 1. Sample of Selected Resistive Exercise Intervention Studies and Others and Impacts as Applied in Randomized Trials for Knee Osteoarthritis Showing Some Benefits, but *few* Radiographic or Cartilage Composition and Loading Biomarker Assays and Impacts

| GROUP | METHODS | CLINICAL FINDINGS | CARTILAGE ASSAY |
|-------------------------|---|--|-----------------|
| Baker et al. [63] | <i>4m High Intensity Home Based Progressive Strength Training vs Nutrition (n=46 cases > 55 yrs)</i> | + improved pain, function, strength, life quality | x |
| Bruce-Brand et al. [64] | <i>6 wk Home Based Resistance vs Neuromuscular Stimulation vs Controls (n=41, ages 55-75)</i> | + equal functional benefits, cross sectional area muscle/strength | x |
| De Zwart et al. [65] | <i>12 wk High vs Low Intensity Resistive Exercises + Vitamin D (n=177, mean age 67 yrs)</i> | + pain, function, mostly equal results | x |
| De Vita et al. [66] | <i>Quadriceps Strength Training (n=30)</i> | + strength/pain, no biomechanical effect | x |
| Holm et al. [67] | <i>12 wk Neuromuscular/Strength Training (n=64)</i> | + strength, function | x |
| Huang et al. [68] | <i>12 wk Knee Extensor Strengthening (n=58)</i> | + pain, function | x |
| Messier et al. [69] | <i>High vs Low Intensity Training (n=377, > 50yr)</i> | - pain, function, joint status equal | x |
| Kus et al. [55] | <i>Sensory Motor/Resistance Training (n=48)</i> | + pain, function, equally | x |
| Oğuz et al. [70] | <i>6 wk Exercise/Exercise and Taping (n=22)</i> | + pain, function, equally - cartilage metabolisms changes | Y |
| Øiestad et al. [71] | <i>12 wk Strength/Aerobic Training (n=168, ages 35-70 yr)</i> | + muscle strength, VO2 max - no quality of life benefit compared to standard care | x |
| Onwunzo et al. [9] | <i>Isometric Quadriceps and Straight Leg Raise Exercises (n=40; mean age 58 yrs)</i> | + pain intensity, range of motion, functional ability | x |
| Vincent et al. [72] | <i>4 m Concentric vs Eccentric Training (n =90, ages 60-85 yr)</i> | + pain, function equally | x |
| Yabroudi et al. [73] | <i>24 Sessions Resistance Exercise vs Pulsed Electromagnetic Fields (N=34)</i> | + pain and function improved equally | x |

Abbreviations: + improved; - not improved/altered; m=months; wk: weeks; yr(s)=year(s)

- a. the degree of joint effusion,
- b. joint range of motion,
- c. muscle fiber size and composition,
- d. muscle recruitment patterns,
- e. inflammatory biomarkers,
- f. body mass,
- g. functional kinetic and cognitive features,
- h. actively assessed aerobic capacity.

Additionally, attempts to overcome the presently vastly differing intervention frequency, duration, and intensity approaches to exercise that exist along with limited follow-up accounts of their impacts on key structural joint features and others are hard to generalize [7, 75]. How cases with poor health status, those who suffer from obesity as well as those who are frail physically or emotionally respond to exercise of any mode is not clear as well even if selected survey data indicate post exercise functional gains as a common observation [30, 49].

In sum, despite the goals of most clinicians – what should be done or undone or avoided when assessing a specific client’s exercise needs cannot be discerned with any degree of predictability as beneficial or optimally beneficial and safe or appropriate for achieving a set of desired outcomes [49] in light of any patient related exercise preferences [76-78]. Moreover, how exercise will impact a vulnerable joint is a complex event determined by (1) the nature of the applied load, (2) the load distribution within the joint during the specific activity and (3) the mechanical properties of the cartilage [21]. Thus despite possible favorable exercise induced reductions in pain, cartilage impacts may not be assumed appropriate, especially if pain is relived and high impacts or excessive compression inducing or fatiguing exercises are carried out by those who are not mindful of joint injury, or who undertake sub-optimal or non specific joint exercise regimens [10]. A further unknown is the probable role of suboptimal loading movements on vulnerable joints as well as the disease progression and its spread to other joints that may be perpetuated or magnified even if surgery is forthcoming [79].

To advance this line of inquiry where systematic reviews do not always concur or fail to assimilate comparable data, we propose that dedicated study is warranted here so as to protect the vulnerable older adult with osteoarthritis from a low life quality as well as from probable increasingly adverse cartilage tissue and joint impacts as based on animal models subject to subnormal joint loads. Applying similar methods to those used in the lab including more careful study selection criteria and controls plus advanced clinical and biological as well as imaging data over time relative to baseline and patient characteristics would appear to hold great promise. In particular, as attempted by Lange [4], radiographic measures applied in a standardized manner to exercise and comparable non exercise groups [58] exposed to different modes of exercise training [80] among cases with varying degrees of muscle pathology are likely to be beneficial and insightful. A concerted global effort to obtain data on various exercise applications on joint inflammation and effusion, joint stability and alignment as well as serum disease biomarker levels, muscle composition and kinetic measures over an extended time frame could prove highly revealing as well, even if not duly mentioned in the past year to any degree [2].

As well, since most older adults diagnosed as having osteoarthritis will likely differ in multiple respects [81], and not all forms of exercise may yield comparable pain and functional impacts as

observed by De Zwart et al. [65] and Pazit et al. [82], the role of careful clinical and mechanical evaluation and extending study inclusion criteria to reflect that of older adults becomes even more salient to contemplate in our view. If these exercise modes currently espoused to have similar impacts are in fact not all comparable when viewed as a whole, is tailoring exercise as indicated more likely to prove beneficial than generic approaches, especially among those that are directed to adults of high ages [80 years and above] who present with diverse degrees of disability and who may have varying needs and personal goals. Moreover, since those exercise formats tested in young healthy or older healthy adults may not apply to those with differing degrees of joint disease who are older, more focused research on what will be best for an older adult over time is indicated and should be tested against controls who do not differ on unmeasured outcomes and disease determinants or manifestations, or have dissimilar behaviors or disease attributes. Additionally, the importance of controlling for the behaviors and exposures of non treatment subjects in pilot as well as larger studies plus the impact of attention, concurrent therapies, history, and maturation effects is rarely assessed and identified. For example, those due to media messaging and where control as well as experimental subjects may adopt alternate or additional pain relieving remedies during a trial and this information should be collected at baseline and follow up. Alternately, why post exercise functional benefits may not occur, and if this is due to non adherence versus adverse alterations in cartilage based factors, which is rarely discussed or measured should be assessed to help provide insight in this regard. Why exercise impacts on cartilage – when measured - are not consistently located throughout the tissue, and why joint loading may be either unaffected by exercise [53] or not the same as another [eg., 53, 80, 83] or the same [10] is impossible in our view to discriminate [84] and cannot be inferred by any overall support that favors exercise adoption of any mode for people with osteoarthritis as far as pain and function is concerned in 2024 where few objective assessments prevail.

Even if exercise is underrated, without adequately supportive robust definitive data, the belief osteoarthritis is not curable and movement participation has no effect or can in fact worsen its presence may persist. Either way, patients may either avoid exercise or try to adopt regimens that may place undue loads on their already fragile joints and cartilage matrices, such as running or yoga or those widely touted without any validated evidence by the media, those who ‘sell’ exercise equipment or gym memberships, and science based public health preventive messages that may not be evidence based or easily performed in the home environment or nursing home, such as aerobic aquatic or resistance exercises in a pool [53] or multi pronged motor learning combined exercise regimens [30]. In addition, even if ‘exercise’ as a whole appears to have no cartilage based measureable adverse effects [75], this has not been tested in the older adult to any degree, and for any duration, and may yet present a lost opportunity. The lack of any definite exercise oriented data as far as this impacts joint biomechanics [66] may also remain a concern to the older patient who seeks such information along with the careful clinician, for example one who advocates hip strengthening for knee osteoarthritis, but is not sure why it appears efficacious [98]. This scenario may be especially compounded in the instance where very little is known about the impact of various exercises on joint health in the presence of obesity or frailty or joint instability, limited joint range of motion, bone spurs, soft tissue decrements, hyper mobility, osteoporosis, neuropathy, inflammation, cardiovascular conditions, or joint malalignment. Funders and some clinicians who are unaware of the gaps in knowledge may yet align their budgets or recommendations accordingly, and fail to pursue in depth analyses based on the view that patients can simply exercise their way to a better life, and are encouraged to keep an open mind in light of the

increasing- rather than decreasing- osteoarthritis prevalence rates among the older population and possible publication bias and areas of import that are under researched [85].

Discussion

Although osteoarthritis has been studied for more than a century, the disease appears to be more common today than ever, and remains the leading disabler of older adults. Often denoted as a disease of the articular cartilage, the tissue lining the ends of bones of freely moving joints such as the knee, this report sought to evaluate the known effects of exercise-almost universally recommended for osteoarthritis care, on measures of cartilage structure that represent the state of attrition or degradation. Exercise was analyzed because it is widely touted as being of value to the patient, and where sedentary behaviors plus muscle weakness may impair overall function and induce inflammation, dysfunction, and pain. Based largely on animal models of osteoarthritis such as the rat exposed to various exercises in those with artificial arthritis [48], it has been proposed exercise adoption will prove beneficial to joint integrity and reduce pain as opposed to a failure to exercise.

Based on the functional requirements of persons with osteoarthritis, as well as the limitations imposed by their joint pathology, it explored if exercises safely improve function and reduce pain in all osteoarthritis cases, and the degree to which this approach can impact its articular cartilage structural features favorably.

Although delimited to: studies of osteoarthritis in the older population this review reveals that despite widespread generic calls across the globe for exercise training and participation for fostering the health of older adults ideally including a combination of aerobic, muscle strengthening, and flexibility exercises for the older or aging adult, this approach may be ill considered for ameliorating cartilage attrition in the sedentary older adult with severely painful osteoarthritis, even if strongly recommended by osteoarthritis experts and others [26, 85]. Commonly recommended regardless of their degree of pathology and/or numbers and extent of any diseased joint, or concurrent comorbidities-often patients who are excluded from exercise studies [eg., 64], most exercise intervention studies used limited variations of subjective measurement approaches, did not focus on disease markers to solidify their conclusions [86] or mechanisms for explaining exercise effects on pain and function [10, 67, 87] or function in one domain but not another [35, 58, 67, 86] even if we did not include all relevant articles.

At the same time although we did review the most extensive medical data sources and those housing meta analyses and conclusions reached by leading reviewers, the body of related meta or umbrella exercise training analyses may not be robust in all respects, nor comparable. They may not for example, provide clear data on adherence issues [eg., 64], nor possible timely data as most reviewed studies were conducted in eras where obesity was not rife [eg., 24] using secondary data sets applied in a single location, and where data collected was largely subjectively assessed [9], and with no baseline osteoarthritis radiographic measure [24, 36]. The lack of inclusivity of the older adult, and the fact the bulk of studies were conducted in funded labs on populations that may not represent those older adults who have no provider, no transport, or insurance coverage or were too impaired to participate or who drop out of programs involving exercise and were not duly followed up.

Why one type of exercise is chosen and not another and how one form of exercise impacts osteoarthritis joints other than the knee or explains non uniform as well as uniform outcomes in varied osteoarthritis studies is consequently very hard to unravel [32]. Moreover, untested older adults with osteoarthritis who are often excluded from studies, may not respond in the same way as younger adults to exercises

and those that are remotely offered may not yield the same outcomes as carefully supervised exercises. Assuming older adults in pain will readily follow exercise if deemed helpful as a health strategy [10, 67, 88, 89], carrying this activity out over time may prove challenging for those in poor health as well as those with multiple physical challenges, plus possible bone, soft tissue, sensory declines, poor endurance, and inflammatory provoking micro impact injuries [64].

In addition, exercise carried out in the absence of patient education [95] may not prove efficacious if it induces excess or non physiological impacts on the diseased tissue [8, 24] even if pain appears to be reduced in various controlled studies [3]. What is meant by moderate exercise and evidence for having a ‘null’ effect in osteoarthritis cases even if advocated [90] must remain in question especially where data are deemed to be generated from lower than desirable quality research [91] and acute exercise effects in young adults [32], or on non radiographic assays and not any other [92].

Indeed, perhaps older adults with osteoarthritis are suffering in excess because even with over 100 exercise based therapy studies espouse benefits on pain and function, they still fail to provide indisputable evidence that pain relief in osteoarthritis and exercise are robustly linked [76] and its multi layered and complex presentation in the older adult in this regard is rarely measured or discussed.

Rather, there is an assumption of a ‘one size fits all’ osteoarthritis diagnoses, and that its association with exercise is a linear and a universally conclusively favorable one [93] and can be applied based on patient or doctor appraised preferences [96] despite recognition of its somewhat unpredictable site specific joint loading responses that needs to be acknowledged [99]. As well, since cartilage is exquisitely sensitive to excess mechanical or suboptimal loading impacts [94], rather than being a passive tissue, it may require sufficient post exercise or intermittent programmatic rest periods to avoid negative deformation associated cartilage load effects as found in healthy young adult men immediately post exercise that could impact metabolic and remodeling processes [97]. Alternately, the impact of both appropriate as well as possible poorly selected and implemented exercise modes on damaged cartilage as well as end stage joint degeneration cannot be readily predicted or extrapolated from such studies and needs more thorough investigation in its own right as intimated by Thudium et al. [40]. This group found cartilage tissue turnover and cartilage degradation appear to increase in response to a 3-month exercise-related joint loading training program and at 6-month follow-up, with no evident difference in type II collagen formation. Aggrecan remodeling increased more with high-intensity resistance training than with low-intensity exercise. These exploratory biomarker results, indicating more cartilage degeneration in the high-intensity group, in combination with no clinical outcome differences of the VIDEX study, may well argue against high-intensity training even if well tolerated.

In the interim, function, functional performance and life quality as well as research quality in exercise based assays remain questionable at best despite numerous study attempts [78, 100, 101]. In addition, while deemed safe no matter what mode of exercise is adopted, this cannot be validated readily for older adults and on the basis of structural joint features as well as functions of daily living and for joints other than the knee. This situation and the relevance presently highlighted, plus knowledge gaps and finding inconsistencies surely needs to be addressed promptly in multiple spheres in our view so as to not only eliminate discordant findings, but to help clinicians to better tailor their recommendations and avert modes of high impact exercise that could prove injurious. Research needs to better elaborate on how older adults living in the community safely can confidently pursue exercise recommendations without undue human and other health or societal resource demands and that can be performed regularly at low cost and without stress and fatigue effects.

Alternately, the costs of failing to do this can be expected to rise in multiple ways and especially if exercise impacts on function and life quality cannot be validated and exercise dosages applied that do have a bearing on osteoarthritis pathology remain unknown. In addition costs will rise if for example, only a small number of cases over time appear to do better than those who receive no treatment, or where treatment or its impact is suboptimal, ineffective, or possibly harmful or determined by type or groupings of osteoarthritis [101-110]. As well, if the potential for or limits of averting excess cartilage load, or more importantly enhancing cartilage reparative processes remain unknown, even the best efforts to maximize life quality and mobility options may prove unsuccessful, as well as possibly inducing or encouraging excess drug or costly invasive treatments or both. The fully fledged understanding of recorded post exercise adverse events as well as benefits remains unknown at present and may be inducing rather than alleviating suffering.

While no simplistic approach will be enlightening on its own, to make some headway in this complex realm, in tangible ways, perhaps the use of small workshop collectives, single case studies, and careful 'n of 1' single subject design efforts or follow ups of current study participants over time, can generate some helpful insights and enlightening data. In addition to careful sample selection, efforts directed towards reducing potential measurement errors, combining animal and human related studies, employing artificial intelligence diagnostic assessments [AI] and others using agreed upon sensitive assays and parameters that allow for advanced statistical analysis of the included demographic, clinical, radiographic, and musculoskeletal profiles are especially recommended.

Implications

To avoid provoking excess or preventable disability and pain and the undue expenditure of energy required by some forms of exercise, and that could reduce overall functional performance capacity, it appears careful evaluation and applications of supervised exercises of modest intensity that are not impactful on the joint[s] of the older adult with osteoarthritis and that builds on what we know can be helpful, and should be based on clinical indicators as well as radiographic, imaging, neuromotor, biomechanical and biochemical measures.

As opposed to a failure to do this, a comprehensive effort at baseline and follow up may make the difference between the immense benefits of 'precision' versus 'generic' medicine approaches that may not work for all older osteoarthritis cases.

As observed by Kong et al: [48] it appears: 1) exercise recommendations can best be served in the future by clarifying their mechanism of action, their similar and dissimilar effects, and providing or acquiring more certainty about their osteoarthritis associated disease modifying or restorative effects in the context of older adults with varying degrees of disability. 2) It will also help clinicians and researchers if publications are more widely available for patients as well as health workers who are not linked to a well funded university or college publication source. 3) Agencies guiding older adults can help by making all research accessible to them. 4) Primary care physicians and allied health personnel can conduct more regular assessments of the disease status of clients and help assure patients are well educated and have the resources they require to adhere to their recommendations.

Concluding Remarks

- Based on our concerted effort to access and synthesize or uncover any specific trends or clinically relevant observation between exercises and radiological or disease markers in older adult

populations with osteoarthritis, what is clear is the absence of such data as well as many less than robust clinical trials on varied rather than a single intervention strategy, thus claims that exercise of any mode is beneficial or harmless cannot be totally justified in our view.

- We further conclude that to foster as well as forge more firm and robust conclusions about the scope of exercise and its bearing on osteoarthritis degradation, experts in the field, clinicians and others should brook no further delay and engage interactively to support multi centric long-term larger studies to examine and validate all the nuances of the phenomenon of supposed disease modifying influences of exercise on articular tissues in both treatment successes as well as failures so as to help identify best evidence based patient directives and the utility of adopting one or more regimens of exercise by older adults with diverse forms of osteoarthritis pathology.
- To this end, we propose more efforts to carefully consider the fact that a one size fits all approach is actually foreign to other medical realms such as heart disease, osteoporosis, stroke, rheumatoid arthritis, and respiratory ailments. Additionally efforts to integrate biomechanical and laboratory measures into the evaluation of osteoarthritis cases before advising them to exercise are strongly indicated.

Final Thoughts

In the face of the mounting older population and their susceptibility to this currently incurable degenerative joint condition termed osteoarthritis, we urge the dedicated researcher and clinician to forge a pathway that can add to and shed light on the existing evidence base upon which family practitioners and others can better rely and act safely and efficaciously using strategies consistently found to be restorative, regenerative, life affirming, or preventive.

References

1. Cao X, Yi X, Chen H, et al. Prevalence of intrinsic capacity decline among community-dwelling older adults: a systematic review and meta-analysis. *Ageing Clin Exp Res.* 2024;36(1):157.
2. Courties A, Kouki I, Soliman N, et al. Osteoarthritis year in review 2024: epidemiology and therapy. *Osteoarthritis Cartilage.* 2024:S1063-4584(24)01320-7.
3. Liu K, Zhang B, Zhang X. Promoting articular cartilage regeneration through microenvironmental regulation. *J Immunol Res.* 2024;2024:4751168.
4. Lange AK, Vanwanseele B, Foroughi N, et al. Resistive exercise for arthritic cartilage health (REACH): a randomized double-blind, sham-exercise controlled trial. *BMC Geriatr.* 2009;13;9:1.
5. Rostron ZPJ, Zacharias A, Semciw AI, et al. Effects of a targeted resistance intervention compared to a sham intervention on gluteal muscle hypertrophy, fatty infiltration and strength in people with hip osteoarthritis: analysis of secondary outcomes from a randomised clinical trial. *BMC Musculoskelet Disord.* 2022;23(1):944.
6. Alkhamis BA, Reddy RS, Alahmari KA, et al. Balancing act: unraveling the link between muscle strength, proprioception, and stability in unilateral hip osteoarthritis. *PLoS One.* 2024;19(2):e0298625.
7. Lin PL, Yu LF, Kuo SF, et al. Effects of computer-aided rowing exercise systems on improving muscle strength and function in older adults with mild knee osteoarthritis: a randomized controlled clinical trial. *BMC Geriatr.* 2022;22(1):809.

8. Azukizawa M, Ito H, Hamamoto Y, et al. The effects of well-rounded exercise program on systemic biomarkers related to cartilage metabolism. *Cartilage*. 2019;10(4):451-458.
9. Onwunzo CN, Igwe SE, Umunnah JO, et al. Effects of isometric strengthening exercises on pain and disability among patients with knee osteoarthritis. *Cureus*. 2021;13(10):e18972.
10. Kjeldsen T, Skou ST, Dalgas U, et al. Progressive resistance training or neuromuscular exercise for hip osteoarthritis: a multicenter cluster randomized controlled trial. *Ann Intern Med*. 2024;177(5):573-582.
11. Coudeyre E, Pereira B, Lechauve JB, et al. Eccentric muscle strengthening using maximal contractions is deleterious in knee osteoarthritis: a randomized clinical trial. *J Clin Med*. 2024;13(11):3318.
12. Bjerre-Bastos JJ, Sejersen C, Nielsen HB, et al. The impact of weight-bearing exercise, non-weight-bearing exercise, and cardiovascular stress on biochemical markers of cartilage turnover in patients with mild to moderate knee osteoarthritis: a sequential, cross-over, clinical study. *Cartilage*. 2024:19476035241258170.
13. Cheng C, Wang J, Yang K, et al. Efficacy of hip abductors exercise training combined with repetitive transcranial magnetic stimulation on knee osteoarthritis: a randomized controlled trial. *Technol Health Care*. 2024 Jul 7.
14. O'Neil J, McEwen D, Del Bel MJ, et al. Assessment of the content reporting for therapeutic exercise interventions among existing randomized controlled trials on knee osteoarthritis. *Clin Rehabil*. 2018;32(7):980-984.
15. Grad R, Ebell MH. Top 20 research studies of 2023 for primary care physicians. *Am Fam Physician*. 2024;110(1):65-73.
16. Cheng HY, Liang CW, Lee YH, et al. Effects of the combination of various pharmacological treatments and exercise on knee osteoarthritis: a systematic review and network meta-analysis. *EFORT Open Rev*. 2024;9(7):668-675.
17. Lin CL, Chen HC, Huang MH, et al. Comparative efficacy of various exercise therapies and combined treatments on inflammatory biomarkers and morphological measures of skeletal muscle among older adults with knee osteoarthritis: a network meta-analysis. *Biomedicine*. 2024;12(7):1524.
18. van Middelkoop M, Schiphof D, Hattle M, et al. People with short symptom duration of knee osteoarthritis benefit more from exercise therapy than people with longer symptom duration: An individual participant data meta-analysis from the OA trial bank. *Osteoarthritis Cartilage*. 2024:S1063-4584(24)01313-X.
19. Ferreira RM, Martins PN, Gonçalves RS. Non-pharmacological and non-surgical interventions to manage patients with knee osteoarthritis: an umbrella review 5-year update. *Osteoarthritis Cartilage Open*. 2024;6(3):100497.
20. Hallett SA, Ono W, Ono N. The hypertrophic chondrocyte: to be or not to be. *Histol Histopathol*. 2021;36(10):1021-1036.
21. Eckstein F, Hudelmaier M, Putz R. The effects of exercise on human articular cartilage. *J Anat*. 2006;208(4):491-512.

22. Paukkonen K, Helminen HJ. Chondrocyte ultrastructure in exercise and experimental osteoarthritis. A stereologic morphometric study of articular cartilage of young rabbits using transmission electron microscopy. *Clin Orthop Relat Res.* 1987;(224):284.
23. Ivanochko NK, Gatti AA, Stratford PW, et al. Interactions of cumulative load with biomarkers of cartilage turnover predict knee cartilage change over 2 years: data from the osteoarthritis initiative. *Clin Rheumatol.* 2024;43(7):2317-2327.
24. Wu Y, Boer CG, Hofman A, Schiphof D, et al. Weight-bearing physical activity, lower-limb muscle mass, and risk of knee osteoarthritis. *JAMA Netw Open.* 2024;7(4):e248968.
25. Bahşi A, Altındağ Ö, Akaltun MS, et al. Comparison of the effects of isokinetic, isometric, and isotonic exercises on knee osteoarthritis using ultrasound. *Cureus.* 2022;14(8):e28324.
26. Marriott KA, Hall M, Maciukiewicz JM, et al. Are the effects of resistance exercise on pain and function in knee and hip osteoarthritis dependent on exercise volume, duration, and adherence? a systematic review and meta-analysis. *Arthritis Care Res.* 2024;76(6):821-830.
27. Jørgensen AEM, Schjerling P, DellaValle B, et al. Acute loading has minor influence on human articular cartilage gene expression and glycosaminoglycan composition in late-stage knee osteoarthritis: a randomised controlled trial. *Osteoarthritis Cartilage.* 2023;31(7):884-893.
28. Blazek AD, Nam J, Gupta R, et al. Exercise-driven metabolic pathways in healthy cartilage. *Osteoarthritis Cartilage.* 2016;24(7):1210-1222.
29. Coburn SL, Crossley KM, Kemp JL, et al. Is running good or bad for your knees? A systematic review and meta-analysis of cartilage morphology and composition changes in the tibiofemoral and patellofemoral joints. *Osteoarthritis Cartilage.* 2023;31(2):144-157.
30. Krauss I, Hein T, Steinhilber B, et al. A 12-week exercise program for patients with hip osteoarthritis has no influence on gait parameters: a secondary analysis of a randomized controlled trial. *Gait Posture.* 2020;78:6-12.
31. Kaiser JM, Bernard FC, Pucha K, et al. Mild exercise expedites joint clearance and slows joint degradation in a joint instability model of osteoarthritis in male rats. *Osteoarthritis Cartilage.* 2024;32(7):912-921.
32. Lee AC, Harvey WF, Han X, et al. Pain and functional trajectories in symptomatic knee osteoarthritis over up to 12 weeks of exercise exposure. *Osteoarthritis Cartilage.* 2018;26(4):501-512.
33. Sono T, Meyers CA, Miller D, et al. Overlapping features of rapidly progressive osteoarthritis and Charcot arthropathy. *J Orthop.* 2019 12;16(3):260-264.
34. Santos ACG, Caiado VDS, Moreira-Marconi E, et al. The influence of physical exercises on the flexibility of older individuals with knee osteoarthritis: a systematic review. *Iran J Public Health.* 2024;53(2):255-267.
35. Hollander JL: Joint problems in the elderly. *Post Grad Med.* 1988; 84:210-216.
36. Garg R, Krishna A, Daga R, et al. Is quadriceps-strengthening exercises (qse) in medial-compartment knee osteoarthritis with neutral and varus malalignment a paradox? - a risk-appraisal of strength-training on disease progression. *Malays Orthop J.* 2024;18(1):73-83.

37. Roos EM, Dahlberg L. Positive effects of moderate exercise on glycosaminoglycan content in knee cartilage: a four-month, randomized, controlled trial in patients at risk of osteoarthritis. *Arthritis Rheum.* 2005;52(11):3507-3514.
38. Dissanayaka TD, Deveza LA, Heller G, et al. Baseline knee osteoarthritis radiographic severity as a predictor of symptom response to diet and exercise program: a secondary analysis. *Int J Rheum Dis.* 2023;26(9):1722-1728.
39. Boeth H, MacMahon A, Poole AR, et al. Differences in biomarkers of cartilage matrix turnover and their changes over 2 years in adolescent and adult volleyball athletes. *J Exp Orthop.* 2017;4(1):7.
40. Thudium CS, Engström A, Bay-Jensen AC, et al. Cartilage tissue turnover increases with high- compared to low-intensity resistance training in patients with knee OA. *Arthritis Res Ther.* 2023;25(1):22.
41. Brown PS, Sorrels RB, Kovealeski TM, et al: Interdisciplinary approach to arthritis rehabilitation. *J Arkansas Med Soc.* 1988;84:474-476.
42. Lindh M. Increase of muscle strength from isometric quadriceps exercises at different knee angles. *Scand J Rehabil Med.* 1979;11:33-36.
43. Sale DG: Neural adaptation to resistance training. *Med Sc Sports Exerc* 1988;20:S135-S145.
44. Altman R, Asch E, Bloch G, et al : Development of criteria for the classification and reporting of osteoarthritis. *Arthritis Rheum.* 1986;8:1040-1049.
45. Burley CV, Casey AN, Jones MD, et al. Nonpharmacological approaches for pain and symptoms of depression in people with osteoarthritis: systematic review and meta-analyses. *Sci Rep.* 2023;13(1):15449.
46. Hislop AC, Collins NJ, Tucker K, et al. Does adding hip exercises to quadriceps exercises result in superior outcomes in pain, function and quality of life for people with knee osteoarthritis? A systematic review and meta-analysis. *Br J Sports Med.* 2020;54(5):263-271.
47. Hua J, Sun L, Teng Y. Effects of high-intensity strength training in adults with knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. *Am J Phys Med Rehabil.* 2023;102(4):292-299.
48. Kong H, Wang XQ, Zhang XA. Exercise for osteoarthritis: a literature review of pathology and mechanism. *Front Aging Neurosci.* 2022;14:854026.
49. Goh SL, Persson MSM, Stocks J, et al. Relative efficacy of different exercises for pain, function, performance and quality of life in knee and hip osteoarthritis: systematic review and network meta-analysis. *Sports Med.* 2019;49(5):743-761.
50. Zeng CY, Zhang ZR, Tang ZM, et al. Benefits and mechanisms of exercise training for knee osteoarthritis. *Front Physiol.* 2021;12:794062.
51. Koli J, Multanen J, Kujala UM, et al. Effects of exercise on patellar cartilage in women with mild knee osteoarthritis. *Med Sci Sports Exerc.* 2015;47(9):1767-1774.
52. Armagan O, Yilmazer S, Calisir C, et al. Comparison of the symptomatic and chondroprotective effects of glucosamine sulphate and exercise treatments in patients with knee osteoarthritis. *J Back Musculoskelet Rehabil.* 2015;28(2):287-293.

53. Munukka M, Waller B, Häkkinen A, et al. Effects of progressive aquatic resistance training on symptoms and quality of life in women with knee osteoarthritis: a secondary analysis. *Scand J Med Sci Sports*. 2020;30(6):1064-1072.
54. Rao A, Evans MF. Does a structured exercise program benefit elderly people with knee osteoarthritis? *Can Fam Physician*. 1998;44:283-284.
55. Kuş G, Tarakçı E, Razak, et al. Sensory-motor training versus resistance training in the treatment of knee osteoarthritis: a randomized controlled trial. *Clin Rehabil*. 2023;37(5):636-650.
56. Thompson AR, Christopherson Z, Marshall LM, et al. A pilot randomized controlled trial for aerobic and strengthening exercises on physical function and pain for hip osteoarthritis. *PM R*. 2020;12(3):229-237.
57. Marriott KA, Birmingham TB. Fundamentals of osteoarthritis. Rehabilitation: exercise, diet, biomechanics, and physical therapist-delivered interventions. *Osteoarthritis Cartilage*. 2023;31(10):1312-1326.
58. Ettinger WH Jr, Burns R, Messier SP, et al. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST). *JAMA*. 1997;277(1):25-31.
59. Hinman RS, Jones SE, Nelligan RK, et al. Absence of improvement with exercise in some patients with knee osteoarthritis: a qualitative study of responders and nonresponders. *Arthritis Care Res*. 2023;75(9):1925-1938.
60. Huang CC, Wang HH, Chen KC, et al. Effects of a dynamic combined training on impulse response for middle-aged and elderly patients with osteoporosis and knee osteoarthritis: a randomized control trial. *Aging Clin Exp Res*. 2021;33(1):115-123.
61. Ferreira GE, Robinson CC, Wiebusch M, et al. The effect of exercise therapy on knee adduction moment in individuals with knee osteoarthritis: a systematic review. *Clin Biomech* 2015;30(6):521-527.
62. Foroughi N, Smith RM, Lange AK, et al. Lower limb muscle strengthening does not change frontal plane moments in women with knee osteoarthritis: a randomized controlled trial. *Clin Biomech*. 2011;26(2):167-174.
63. Baker KR, Nelson ME, Felson DT, et al. The efficacy of home based progressive strength training in older adults with knee osteoarthritis: a randomized controlled trial. *J Rheumatol*. 2001;28(7):1655-1665.
64. Bruce-Brand RA, Walls RJ, Ong JC, et al. Effects of home-based resistance training and neuromuscular electrical stimulation in knee osteoarthritis: a randomized controlled trial. *BMC Musculoskelet Disord*. 2012;13:118. .
65. De Zwart AH, Dekker J, Roorda LD, et al. High-intensity versus low-intensity resistance training in patients with knee osteoarthritis: a randomized controlled trial. *Clin Rehabil*. 2022;36(7):952-967.
66. DeVita P, Aaboe J, Bartholdy C, et al. Quadriceps-strengthening exercise and quadriceps and knee biomechanics during walking in knee osteoarthritis: a two-centre randomized controlled trial. *Clin Biomech*. 2018;59:199-206.

67. Holm PM, Blankholm AD, Nielsen JL, et al. Effects of neuromuscular control and strengthening exercises on MRI-measured thigh tissue composition and muscle properties in people with knee osteoarthritis - an exploratory secondary analysis from a randomized controlled trial. *Semin Arthritis Rheum.* 2024;65:152390.
68. Huang L, Guo B, Xu F, et al. Effects of quadriceps functional exercise with isometric contraction in the treatment of knee osteoarthritis. *Int J Rheum Dis.* 2018;21(5):952-959.
69. Messier SP, Mihalko SL, Beavers DP, et al. Effect of high-intensity strength training on knee pain and knee joint compressive forces among adults with knee osteoarthritis: the START Randomized Clinical Trial. *JAMA.* 2021;325(7):646-657.
70. Oğuz R, Belviranlı M, Okudan N. Effects of exercise training alone and in combination with kinesio taping on pain, functionality, and biomarkers related to the cartilage metabolism in knee osteoarthritis. *Cartilage.* 2021;13(1):1791S-1800S.
71. Øiestad BE, Årøen A, Røtterud JH, et al. The efficacy of strength or aerobic exercise on quality of life and knee function in patients with knee osteoarthritis. a multi-arm randomized controlled trial with 1-year follow-up. *BMC Musculoskelet Disord.* 2023;24(1):714.
72. Vincent KR, Vasilopoulos T, Montero C, et al. Eccentric and concentric resistance exercise comparison for knee osteoarthritis. *Med Sci Sports Exerc.* 2019;51(10):1977-1986.
73. Yabroudi MA, Aldardour A, Nawasreh ZH, et al. Effects of the combination of pulsed electromagnetic field with progressive resistance exercise on knee osteoarthritis: a randomized controlled trial. *J Back Musculoskelet Rehabil.* 2024;37(1):55-65.
74. Husted RS, Troelsen A, Husted H, et al. Knee-extensor strength, symptoms, and need for surgery after two, four, or six exercise sessions/week using a home-based one-exercise program: a randomized dose-response trial of knee-extensor resistance exercise in patients eligible for knee replacement (the QUADX-1 trial). *Osteoarthritis Cartilage.* 2022;30(7):973-986.
75. Bricca A, Struglics A, Larsson S, et al. Impact of exercise therapy on molecular biomarkers related to cartilage and inflammation in individuals at risk of, or with established, knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. *Arthritis Care Res.* 2019;71(11):1504-1515.
76. Henriksen M, Runhaar J, Turkiewicz A, et al. Exercise for knee osteoarthritis pain: Association or causation? *Osteoarthritis Cartilage.* 2024;32(6):643-648.
77. Hansen S, Mikkelsen LR, Overgaard S, et al. Effectiveness of supervised resistance training for patients with hip osteoarthritis - a systematic review. *Dan Med J.* 020;67(6):A08190424.
78. Davis HC, Luc-Harkey BA, Seeley MK, et al. Sagittal plane walking biomechanics in individuals with knee osteoarthritis after quadriceps strengthening. *Osteoarthritis Cartilage.* 2019;27(5):771-780.
79. Felson DT. Risk factors for osteoarthritis: understanding joint vulnerability. *Clin Orthop Rel Res.* 2004;427:S16-21.
80. Mikesky AE, Mazzuca SA, Brandt KD, et al. Effects of strength training on the incidence and progression of knee osteoarthritis. *Arthritis Rheum.* 2006;55(5):690-596.
81. Pires DPC, Monte FAD, Monteiro LF, et al. Updates in the treatment of knee osteoarthritis. *Rev Bras Ortop (Sao Paulo).* 2024;59(3):e337-e348.

82. Pazit L, Jeremy D, Nancy B, et al. Safety and feasibility of high speed resistance training with and without balance exercises for knee osteoarthritis: a pilot randomised controlled trial. *Phys Ther Sport*. 2018;34:154-163.
83. Suzuki Y, Iijima H, Tashiro Y, et al. Home exercise therapy to improve muscle strength and joint flexibility effectively treats pre-radiographic knee OA in community-dwelling elderly: a randomized controlled trial. *Clin Rheumatol*. 2019;38(1):133-141.
84. Nery M, Natour J, Jennings F, et al. Effects of a progressive resistance exercise program in patients with hand osteoarthritis: a randomized, controlled trial with a blinded assessor. *Clin Rehabil*. 2021;35(12):1757-1767.
85. Zhu S, Qu W, He C. Evaluation and management of knee osteoarthritis. *J Evid Based Med*. 2024 Jul 4.
86. Mao Y, Qiu B, Wang W, et al. Efficacy of home-based exercise in the treatment of pain and disability at the hip and knee in patients with osteoarthritis: a systematic review and meta-analysis. *BMC Musculoskelet Disord*. 2024;25(1):499.
87. Xu T, Zhang B, Fang D. The effect of resistance training on patients with knee osteoarthritis: a systematic review and meta-analysis. *Res Sports Med*. 2024:1-19.
88. Du X, Fan R, Kong J. What improvements do general exercise training and traditional Chinese exercises have on knee osteoarthritis? A narrative review based on biological mechanisms and clinical efficacy. *Front Med*. 2024;11:1395375.
89. Somaiya KJ, Samal S, Boob MA. Physiotherapeutic intervention techniques for knee osteoarthritis: a systematic review. *Cureus*. 2024;16(3):e56817.
90. Deng X, Xu H, Hao X, et al. Effect of moderate exercise on osteoarthritis. *EFORT Open Rev*. 2023;8(3):148-161.
91. Maly MR, Marriott KA, Chopp-Hurley JN. Osteoarthritis year in review 2019: rehabilitation and outcomes. *Osteoarthritis Cartilage*. 2020;28(3):249-266.
92. Helmark IC, Mikkelsen UR, Børglum J, et al. Exercise increases interleukin-10 levels both intraarticularly and peri-synovially in patients with knee osteoarthritis: a randomized controlled trial. *Arthritis Res Ther*. 2010;12(4):R126.
93. Holden MA, Metcalf B, Lawford BJ, et al. Recommendations for the delivery of therapeutic exercise for people with knee and/or hip osteoarthritis. An international consensus study from the OARSI Rehabilitation Discussion Group. *Osteoarthritis Cartilage*. 2023;31(3):386-396.
94. Vincent TL, Wann AKT. Mechanoadaptation: articular cartilage through thick and thin. *J Physiol*. 2019;597(5):1271-1281.
95. Roos EM, Grønne DT, Thorlund JB, et al. Knee and hip osteoarthritis are more alike than different in baseline characteristics and outcomes: a longitudinal study of 32,599 patients participating in supervised education and exercise therapy. *Osteoarthritis Cartilage*. 2022;30(5):681-688.
96. Heikkinen R, Waller B, Munukka M et al. Impact or no impact for women with mild knee osteoarthritis: a Bayesian meta-analysis of two randomized controlled trials with contrasting interventions. *Arthritis Care Res*. 2022;74(7):1133-1141.
97. Lim J, Lee J, Park S, et al. Change in femoral cartilage cross-sectional area after aerobic and resistance exercise. *Int J Sports Med*. 2024;45(9):705-711.

98. Thomas DT, R S, Prabhakar AJ, Dineshbhai PV, et al. Hip abductor strengthening in patients diagnosed with knee osteoarthritis - a systematic review and meta-analysis. *BMC Musculoskeletal Disord.* 2022;23(1):622.
99. Thoma LM, McNally MP, Chaudhari AM, et al. Differential knee joint loading patterns during gait for individuals with tibiofemoral and patellofemoral articular cartilage defects in the knee. *Osteoarthritis Cartilage.* 2017;25(7):1046-1054.
100. Raposo F, Ramos M, Lúcia Cruz A. Effects of exercise on knee osteoarthritis: a systematic review. *Musculoskeletal Care.* 2021;19(4):399-435.
101. Nguyen C, Lefèvre-Colau MM, Poiraudéau S, et al. Rehabilitation (exercise and strength training) and osteoarthritis: A critical narrative review. *Ann Phys Rehabil Med.* 2016;59(3):190-195.
102. Knoop J, Dekker J, van der Leeden M, et al. Is the severity of knee osteoarthritis on magnetic resonance imaging associated with outcome of exercise therapy? *Arthritis Care Res.* 2014;66(1):63-68.
103. Hart HF, Patterson BE, Crossley KM, et al. May the force be with you: understanding how patellofemoral joint reaction force compares across different activities and physical interventions-a systematic review and meta-analysis. *Br J Sports Med.* 2022;56(9):521-530.
104. Teirlinck CH, Verhagen AP, Reijneveld EAE, et al. Responders to exercise therapy in patients with osteoarthritis of the hip: a systematic review and meta-analysis. *Int J Environ Res Public Health.* 2020;17(20):7380.
105. Dainese P, DE Mits S, Wittoek R, et al. Neuropathic-like pain in knee osteoarthritis: exploring differences in knee loading and inflammation. A cross-sectional study. *Eur J Phys Rehabil Med.* 2024;60(1):62-73.
106. Cottmeyer DF, Hoang BH, Lyle MA, et al. Can exercise interventions reduce external knee adduction moment during gait? A systematic review and meta-analysis. *Clin Biomech.* 2023;109:106064.
107. Regnaud JP, Lefevre-Colau MM, Trinquart L, et al. High-intensity versus low-intensity physical activity or exercise in people with hip or knee osteoarthritis. *Cochrane Database Syst Rev.* 2015;2015(10):CD010203.
108. Alfieri FM, Lima ARS, Salgueiro MMHAO, et al. Efficacy of an exercise program combined with lifestyle education in patients with knee osteoarthritis. *Acta Reumatol Port.* 2020;45(3):201-206.
109. Yuenyongviwat V, Duangmanee S, Iamthanaporn K, et al. Effect of hip abductor strengthening exercises in knee osteoarthritis: a randomized controlled trial. *BMC Musculoskeletal Disord.* 2020;21(1):284.
110. Bennell KL, Nelligan RK, Kimp AJ, et al. What type of exercise is most effective for people with knee osteoarthritis and co-morbid obesity?: the TARGET randomized controlled trial. *Osteoarthritis Cartilage.* 2020;28(6):755-765.