Update on the Role of Muscle in the Genesis and Management of Knee Osteoarthritis

Kim L. Bennell, BAppSci(physio), PhD[a,*], Tim V. Wrigley, BSc, MSc[a], Michael A. Hunt, PT, PhD[b], Boon-Whatt Lim, MSc, PhD[c], Rana S. Hinman, BPhysio, PhD[a]

KEYWORDS

• Muscle • Knee • Osteoarthritis • Proprioception • Strength • Rehabilitation • Exercise

KEY POINTS

- Deficits in muscle function, including muscle strength, activation, and proprioception, are found in people with knee osteoarthritis.
- Stronger quadriceps muscle may reduce the risk of knee osteoarthritis onset but the role of muscle strength in influencing disease progression is conflicting.
- Exercise can improve deficits in muscle function.
- Improvement in muscle function, especially strength, is associated with reduced pain and improved function in people with knee osteoarthritis.

INTRODUCTION

The muscles of the lower limb, particularly the quadriceps, play an important role in the genesis and management of knee osteoarthritis (OA). At the knee, muscles function to produce movement but also to absorb limb loading and provide dynamic joint stability. Muscle weakness has been identified as a potential risk factor for disease development due to increased joint loading. In addition, the presence of OA has a negative impact on the integrity of the structure and function of muscles, potentially further affecting the disease process.

Research has provided a rationale for the use of muscle rehabilitation as part of the overall treatment regimen for knee OA to reduce symptoms, increase function, and possibly protect against disease onset or progression. A detailed understanding of

[a] Department of Physiotherapy, Centre for Health, Exercise and Sports Medicine, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, 200 Berkeley Street, Parkville, Victoria 3010, Australia; [b] Department of Physical Therapy, University of British Columbia, Vancouver, Canada; [c] School of Sports, Health and Leisure, Republic Polytechnic, Singapore
* Corresponding author.
E-mail address: k.bennell@unimelb.edu.au

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the role of muscles in knee OA can, therefore, aid in the implementation of effective rehabilitation strategies and form the basis of primary prevention strategies against disease development.

This review, updated from 1 published in 2008,[1] outlines the influence of muscle activity on knee joint loading, describes the deficits in muscle function observed in people with knee OA, and summarizes available evidence pertaining to the role of muscle in the development and progression of knee OA. The review also focuses on whether muscle deficits can be modified in knee OA and whether improvements in muscle function lead to improved symptoms and joint structure. The review concludes with a discussion of exercise prescription for muscle rehabilitation in knee OA.

INFLUENCE OF MUSCLE ACTIVITY ON KNEE JOINT LOADING

Because knee OA is believed to be due to joint loading acting within the context of systemic and local susceptibility, it is important to understand the influence of muscle activity on knee joint load. To achieve equilibrium of motion and joint stability, all external forces acting on a joint must be counteracted by internal forces equal in magnitude, but opposite in direction. External knee joint loading experienced during human movement is primarily derived from the ground reaction forces and inertial properties of the lower limb, resulting in a total tibiofemoral joint force approaching 3 times body weight.[2,3] The individual contributions of internal structures such as muscles, ligaments, subchondral bone, and cartilage varies, and is highly influenced by the anatomic arrangement of each structure and their capacity to absorb load.

Of particular interest to the pathogenesis of knee OA is the ability to counteract the external adduction moment applied about the knee as this moment is suggested to influence disease initiation,[4] disease severity,[5] and disease progression.[6,7] Part of the reason why so much work has been done with this measure is that it is easy to obtain via three-dimensional gait analysis. Measures that may better reflect true medial compartment load are under development but have yet to be related to OA disease in the same way as the external adduction moment has been. There may be circumstances in which other moments (such as the sagittal flexor-extensor moment) need to be take into account as well,[8] but the extent to which this might be routinely important is somewhat unclear.

The external adduction moment, present throughout much of the stance phase of gait, results from the ground reaction force passing medial to the knee joint center of rotation.[9] It affects the load distribution between the medial and lateral tibiofemoral joint compartments and it has been used as a proxy for medial tibiofemoral joint load,[10,11] where most knee OA occurs. The external adduction moment not only compresses the tibiofemoral joint medially but distracts the joint laterally.[11] Thus, contributions from lateral and medial structures are required to maintain joint stability internally. Dynamic stability of the knee depends on the load-sharing characteristics of many passive soft tissues and active muscle forces.[11] Although in vivo data quantifying the relative contributions of knee joint structures in generating internal forces do not exist, many biomechanical modeling studies provide estimations of these forces.

Schipplein and Andriacchi[11] were among the first to evaluate passive soft tissue and active muscle contributions to dynamic knee stability during walking. They found that activation of the quadriceps muscles in isolation was insufficient to balance the external adduction moment and that cocontraction from the hamstrings and/or tension in lateral soft tissues was required to produce an internal abduction moment to maintain dynamic equilibrium in the frontal plane. This requirement for active muscle contributions to internal abduction moment generation has been supported by subsequent

studies examining isometric loading.[12,13] Buchanan and Lloyd[13] reported individual activation patterns of many lower-limb muscles during static loads in the frontal plane. Muscles active during the production of internal abduction forces included sartorius, gracilis, quadriceps (primarily rectus femoris), long head of biceps femoris, and lateral gastrocnemius. Shelburne and colleagues[2] showed in a biomechanical modeling study that, although these muscles are capable of producing internal abduction moments isometrically, much of the contribution to the total abduction moment during normal gait came from the quadriceps (early stance) and gastrocnemius (late stance). These muscles were able to generate a sufficient internal abduction moment to counteract the external adduction moment, despite small frontal plane muscle moment arms. Recent work in healthy young individuals has suggested that muscles that do not span the knee can also contribute to compressive tibiofemoral joint forces along with those muscles that do span the joint (**Fig. 1**).[14] This general principle has been known for some time but has yet to be studied specifically in knees with OA.

These findings indicate that for a given external load, muscles are capable of generating enough force to produce most of the internal balancing load. However, there is still a requirement of other soft tissue structures such as ligaments to sustain load. Muscle force generation is of particular interest to clinicians given that it can be consciously controlled by the individual and improved with training. Improving the load-bearing capacities of lower-limb muscles through strength training and muscle rehabilitation programs may protect against soft tissue damage resulting from excessive load.

It is unclear, however, if the increase in the total joint reaction force occurring with muscle contraction may actually accelerate the degeneration of articular cartilage, rather than prevent it. Although muscle activity, particularly cocontraction of the quadriceps and hamstrings, may balance the external adduction moment and improve the dynamic stability of the knee joint during walking by limiting lateral condylar liftoff and shearing in the transverse plane, axial compression due to the muscles' line of pull

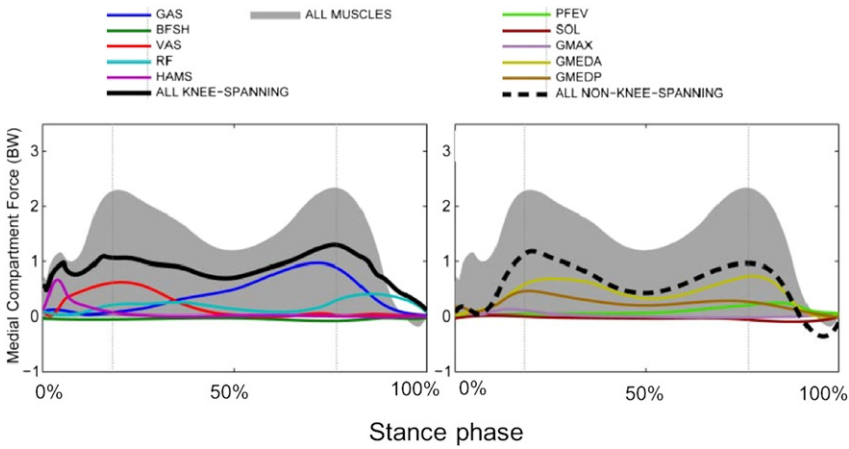

Fig. 1. Contributions of selected knee-spanning and non–knee-spanning muscles to the medial knee compartment force (compressive forces are positive). The first vertical gray line represents contralateral toe off and the second gray line represent contralateral heel strike. BFSH, biceps femoris; GAS, gastrocnemius; GEMEDA, anterior portion of gluteus medius; GMAX, gluteus maximus; GMEDP, posterior portion of gluteus medius; HAMS, medial hamstrings; PFEV, plantar flexor evertor; RF, rectus femoris; SOL, soleus; VAS, vastii. (*From* Sritharan P, Lin YC, Pandy MG. Muscles that do not cross the knee contribute to the knee adduction moment and tibiofemoral compartment loading during gait. J Orthop Res 2012;30(10):1586–95; with permission.)

may place the cartilage in an environment of excessive and prolonged load. Alterations in muscle activation in association with OA are discussed in the following section but it is apparent that further research into the effects of muscle cocontraction on the health of articular cartilage in the tibiofemoral joint is needed.

Muscle activation patterns influence not only the overall magnitude of the knee joint load but also the rate of loading. Coordinated timing of appropriate muscles during the weight-acceptance phase of gait ensures proper attenuation of axial compressive or impact loads suggested to be associated with the onset of knee OA.[15,16] Specifically, it is thought that adequate eccentric loading of the quadriceps during this phase of the gait cycle allows for a safe and controlled descent of the center of mass and protection against high impact loads. Mikesky and colleagues[17] reported a significant increase in the rate of loading during gait in a group of sedentary women compared with those who actively participated in strength training. However, faster walking speed seems to be more important in the generation of higher impact forces in OA than quadriceps muscle strength.[18] Consistent with what is known about the deleterious effects of high impact loading on cartilage degeneration from animal studies[19] and previous reports of the association between rate of loading and presence of knee pain,[20] it has been suggested that impact forces and loading rate may contribute to the development and/or progression of knee OA. However, no longitudinal studies have investigated this, and cross-sectional studies so far have not found a difference in impact forces between patients with OA and healthy controls.[21]

The hip muscles responsible for stabilizing the pelvis on the weight-bearing lower limbs during walking may also play a role in knee OA by altering knee loads. People with insufficient stance limb hip abductor strength to control the pelvis can exhibit a contralateral pelvic drop, the Trendelenburg sign.[22] This drop theoretically shifts the body's center of mass away from the stance limb toward the swing limb, thereby increasing the distance between the ground reaction force vector and the knee joint center of rotation, and hence increasing the knee adduction moment. It also increases the external hip adduction moment which, given such a patient's weak hip abductors, is not sustainable. Therefore, patients often adopt compensatory trunk lean back to the affected side, reducing the load on both the knee and the hip muscles.

Lower hip adduction moments consistent with these patterns have been found in studies using gait analysis in patients with more severe and progressive knee OA,[23,24] as has increased trunk lean to the affected side.[25,26] The hip adductor muscles may also assist in resisting the knee adduction moment particularly in a varus malaligned knee. By virtue of their attachment to the distal medial femoral condyle, the adductors theoretically could eccentrically restrain the tendency of the femur to move into further varus during the stance phase of gait.[27]

DEFICITS IN MUSCLE FUNCTION IN KNEE OA

Given the role of muscles in influencing knee joint load and knee stability, an understanding of deficits in muscle function associated with knee OA is important. Most studies of muscle function in knee OA have concerned muscle strength. However, other aspects of muscle function are also affected by the OA disease process, including activation patterns and proprioceptive acuity. Understanding how muscle function is impaired can assist clinicians in prescribing more effective rehabilitation programs.

Strength

Muscle weakness is a well-accepted impairment in knee OA (see Bennell and colleagues[28] for an in-depth review). However, assessment of strength is not

straightforward and has not always been well conducted in OA studies. Clinical methods may not be as sophisticated as research methods, but should follow similar principles. The ability to generate muscle force is a function of muscle cross-sectional area and the ability to recruit and fire descending alpha motor neurons to muscle fibers at sufficient frequencies.[29,30] That force then acts in conjunction with the muscle's moment arm to generate a torque or moment about a particular joint.[29,30]

Ideally, strength should be measured to reflect this muscle-generated torque. Torque is thus measured as the product of the force (in Newtons) exerted at the point of attachment of a force-measuring transducer to the limb, and the distance (in meters) of that attachment from the axis of rotation of the joint in question; thus strength is reported in units of Newton meters (N m). Strength varies with body size (which affects muscle size and the moment arm length), in patients with OA as in athletes.[31,32] In some studies on OA, the investigators have failed to normalize the torque measurements for differences in body size (most logically body mass in kilograms).

Results of studies that have correctly measured strength as torque, and normalized for body mass differences (ie, N m/kg) show that patients with knee OA are 20% to 40% weaker in relative quadriceps strength than healthy controls.[33–39] Although other lower-limb muscles in knee OA have received less attention, strength of the hip muscles also seems to be reduced with 1 study reporting strength deficits ranging from 16% (hip extensors) to 27% (hip external rotators) compared with controls.[40]

There are several contributors to muscle weakness in individuals with knee OA. Pain, anxiety, motivation, effusion, muscle atrophy, and aberrant joint mechanics can all contribute to a loss of measurable strength. Some of the weakness in relation to body size seen in OA is likely caused by the obesity that is also commonly present, as the proportion of total body mass made up of force-generating muscle is by definition reduced. Primary deficits in muscle strength may be associated with muscle fiber atrophy (ie, loss of muscle cross-sectional area), reduced ability to activate muscle fibers, or both.

There are few studies investigating muscle atrophy in OA. Ikeda and colleagues[41] found that quadriceps cross-sectional area was significantly reduced by an average of 12% in women with incident radiological OA without symptoms, compared with women matched for age and body mass with no signs of OA. In later stage disease, more obvious signs of actual muscle fiber atrophy have been reported.[42,43] In patients before knee replacement, Pettersen and colleagues[44] found quadriceps lean muscle cross-sectional area to be 12% lower in the affected limb compared with the contralateral lateral side. Thus, it seems likely that at least some of any strength loss in OA is caused by loss of muscle cross-sectional area.

When muscle atrophy cannot explain the full extent of muscle weakness, inhibition in the ability to activate muscle is implicated. Detection of inhibition is primarily a research tool, whereby an electrical stimulus over the muscle is applied during a maximal contraction to determine whether the patient's voluntary activation is less than maximal. Overall, there is a large variation in the results of studies assessing the extent of maximal voluntary muscle activation typically possible in OA. For example, 1 study[45] found that patients before high tibial osteotomy had an average quadriceps activation of 71% (ie, 29% inhibited), with a range of 41% to 86%. Pettersen and colleagues[44] found that inhibition explained most of the strength variance in end-stage knee OA. Despite some variation in research findings, the literature overall does show that patients with OA commonly exhibit impaired activation compared with healthy controls, as was the conclusion of a recent meta-analysis of published studies.[46] This analysis also concluded that there was some evidence for activation deficits in the unaffected opposite limb.

The causes of muscle inhibition in knee OA are likely to be multifactorial. Pain is commonly presumed to be a major source of inhibition in the ability to voluntarily activate muscle surrounding arthritic joints.[47] Pain relief via local anesthetic injection resulted in an 11% to 12% increase in percentage activation of the quadriceps in people with knee OA,[48] confirming that at least some of the reduced voluntary activation observed in knee OA is caused by the presence of pain inhibition. Joint effusion on its own has also been found to be a potent inhibitor of maximal muscle activation in non-OA studies, even at low levels that might otherwise not be deemed clinically important (see Wrigley[49] for review of classic work in this area). Effusion is often associated with OA and associated pain.[50] Experimentally induced knee joint effusion has previously been found to generate pathologic gait changes.[51] Recently, Rutherford and colleagues[52] found that 17 medial patients with OA who presented with clinical knee joint effusions (bulge test) actually showed increased quadriceps activation and hamstring duration during gait compared with 18 patients without effusion. The patients also demonstrated greater stance flexion and a reduced external knee extensor moment. There were no differences in walking speed or pain between the groups. This supports the notion that effusions should be addressed in patients with OA, as they may be a barrier to rehabilitation and function.

Knowledge of the sources of muscle weakness in a patient is important, as it will determine how restoration of muscle strength might be approached therapeutically. If the deficit is primarily due to atrophy, then a pure muscle-strengthening approach should be taken. Alternatively, if the deficit is primarily in the ability to activate an essentially normal muscle, then attention might be directed toward removing the inhibitory sources that prevent sufficient activation (such as pain and effusion), and retraining the patient to activate their muscles fully.

Muscle Activation Patterns

In recent years, there has been increasing interest in the patterns of muscle activation associated with knee OA. As muscles are often the major contributors to joint loading,[53] their inefficient activation during walking and other functional tasks could be implicated in disease progression. It seems that some patients with OA are able to activate their knee muscles in a way that is most efficient for dealing with the commonly increased joint loading, especially of the medial compartment during gait, while satisfying the other requirements for weight support and propulsion. However, other patients adopt a less efficient strategy that involves activating many muscles in a less specific fashion that may increase overall joint loading.

Several cross-sectional studies have noted differences in muscle activation patterns comparing people with knee OA of varying disease severity to age-matched controls.[54–61] Using surface electromyography (EMG), Hubley-Kozey and colleagues[56] found that patients with moderate OA biased the activation of quadriceps and hamstrings toward the lateral components of these muscle groups in early stance, compared with healthy controls. Schmitt and Rudolph[57] found that patients with mild to severe medial tibiofemoral joint OA showed increased activation of lateral hamstrings and gastrocnemius before foot contact and increased cocontraction of the lateral quadriceps and gastrocnemius as well as medial quadriceps and hamstrings during weight acceptance.

Astephen and colleagues[58] found that patients with severe tibiofemoral OA could be distinguished from healthy controls by increased medial and lateral hamstring activity during stance; they were also different from those with moderate OA in terms of higher medial gastrocnemius activity in swing and early stance phases, but lower activity during late stance. In patients with a range of OA severity, Childs and colleagues[59]

found that muscles were activated for longer durations in the period just before and during stance compared with healthy age-matched and gender-matched controls. Heiden and colleagues[60] found that cocontraction biased more toward lateral knee muscles increased with higher external knee adduction moments; this suggests that this pattern of muscle activation is directly linked to resisting associated increases in medial compartment loading. Thus, it seems that, as the disease progresses, a less specific and efficient activation of a greater number of knee muscles may become more apparent.

All the alterations in activation patterns in knee OA described in the literature are not necessarily consistent, and part of the variability may relate to methodological issues particularly in EMG measurement and analysis.[28] Nevertheless, it seems that muscle activation patterns do differ in people with knee OA and may be influenced by the stage of OA disease and aspects of the disease process. For example, a recent study found that, in people with knee OA, those with a joint effusion had greater overall quadriceps activation and prolonged hamstring activation during midstance compared with those without a joint effusion.[52] Whether these differences reflect the increasing difficulty in activating muscles efficiently for ambulation in the face of pain, effusion, and deteriorating joint mechanics, and/or are involved in disease progression itself, needs to be clarified. There is also little evidence that such patterns can be altered; nor is it clear what would constitute a desirable alteration.

Proprioception

Knee joint proprioception is important for the coordinated activity of surrounding muscles to protect against excessive movements, stabilize during static postures, and coordinate movement.[62] Proprioceptive afferent information from mechanoreceptors, particularly in muscles but also in ligaments, capsule, menisci, and skin, contributes at the spinal level to arthrokinetic and muscular reflexes, which play a large part in dynamic joint stability.[63] The information is also conveyed to supraspinal centers where it is integral to motor learning and the ongoing programming of complex movements. Abnormal proprioception could predispose to musculoskeletal lesions by altering the control of movement leading to abnormal stresses on tissues.[64] Alternatively, a pathologic condition, effusion, and pain may impair proprioceptive information,[65–67] possibly further compounding functional deficits.

Proprioception is typically measured in OA studies as conscious perception of joint position sense using accuracy of reproduction or threshold of movement detection tests. However, proprioception during normal function rarely requires conscious perception. Furthermore, just because a patient perceives proprioceptive information (consciously or unconsciously) does not mean that it is efficiently used by the nervous system to modulate movement.[28] Measurements of knee position sense and knee motion sense are not well correlated and as such seem to indicate different aspects of knee proprioception and probably stimulate different receptors.[62]

Most studies have found deficits in knee joint proprioception in patients with knee OA compared with similarly aged asymptomatic individuals.[68–72] A recent study also showed consistent differences in knee proprioception between groups with and without knee OA across all knee movement directions (varus, valgus, flexion, and extension) suggesting a global, rather than a direction-specific, reduction in sensation in patients with knee OA.[73] In addition to impaired proprioception at the affected knee joint, there is also evidence of proprioceptive deficits at other nonaffected sites including the contralateral knee[74] and the elbow.[75] This has led to suggestions that OA may be associated with a generalized defect in proprioception. The topic of proprioception in knee OA has recently been reviewed by Knoop and colleagues.[62]

EVIDENCE FOR A RELATIONSHIP BETWEEN MUSCLE FUNCTION AND OA ONSET AND PROGRESSION

As previously described, muscles influence knee joint loading, and impairments in muscle function have been observed in people with knee OA. This section (summary in **Table 1**) discusses the longitudinal cohort studies and randomized controlled trials (RCTs) that link impaired muscle function to the development and progression of knee OA. These studies have focused primarily on muscle strength with a limited number investigating proprioception. The RCTs that investigate the effects of strengthening exercise (as distinct from strength per se) on structural outcomes are discussed in a following section.

Disease Onset

There is some evidence to suggest that quadriceps weakness precedes the onset of knee OA and hence could increase the risk of disease development, particularly in women. The first longitudinal study to investigate this issue more than a decade ago demonstrated 15% to 18% lower baseline isokinetic quadriceps strength (adjusted for body and muscle mass) in women who went on to develop incident radiographic knee OA than in women who did not develop OA.[76] This was not seen in men nor was there a relationship between hamstring strength and OA onset in either sex. Although the study had some methodological issues, including lack of adjusting for potential covariates, these results were subsequently confirmed in a larger longitudinal cohort study involving 3081 adults.[77] In this study, higher isokinetic quadriceps strength (relative to body mass) was associated with a 55% to 64% reduced risk of developing knee or hip OA (self-reported) in women with similar, albeit nonsignificant, results in men (~25% less risk). Support for a link between quadriceps strength and disease onset also comes from a study on a group of 94 people aged 35 to 54 years with chronic knee pain but normal radiographs at baseline, in which the maximal number of one-legged rises, a functional measure that can indicate quadriceps strength, predicted radiographic knee OA 5 years later.[78]

More recent data from the large Multicenter Osteoarthritis Study (MOST) published in several papers have provided further insights into the relationship between muscle strength and OA development.[79–82] In 1 study, absolute isokinetic knee extensor and flexor strength was adjusted for age, body mass index, hip bone density, surgical history, pain, and physical activity score in multivariate models, and related to the onset of symptomatic and radiographic OA 30 months later.[80] Compared with the

Table 1
Summary of findings of the relationship between muscle function and knee OA onset and progression

Disease Onset	Disease Progression
Quadriceps muscle weakness may increase risk of symptomatic knee OA particularly in women	Conflicting evidence but higher strength may be related to slower progression in women and at the patellofemoral joint
Hamstring muscle weakness does not seem to be related	Strengthening exercise for the quadriceps and hip muscles does not alter knee adduction moment
Knee joint proprioception does not seem to be related to either radiographic or symptomatic onset	Weaker quadriceps, hamstrings, and hip abductor muscles as well as poorer knee joint proprioception are related to greater functional decline

lowest tertile, the highest tertile of adjusted isokinetic knee extensor strength protected against development of incident symptomatic tibiofemoral or patellofemoral OA in both sexes. However, neither adjusted knee extensor strength nor the hamstring to quadriceps ratio was predictive of incident radiographic tibiofemoral OA. This suggests that, in this cohort at least, quadriceps muscle weakness may play a greater role in OA symptom development than structural changes per se. These results were confirmed using knee extensor specific strength (knee extensor torque divided by total thigh muscle mass).[82] This study also found that absolute total thigh muscle mass, as measured by dual energy x-ray absorptiometry, was not related to OA incidence.[82] This might be interpreted as implicating other sources of weakness than reduced contractile material (such as the inhibition discussed earlier). However, it would be interesting to further explore adjustment for the expected effects of body size on a volumetric quantity such as absolute muscle mass.

People who have sustained a knee joint injury, particularly a tear of the anterior cruciate ligament (ACL) or meniscus, are at an increased risk of developing knee OA compared with those with uninjured knees.[83,84] Whether subsequent muscle weakness further predisposes these individuals to developing knee OA has only been investigated in 1 longitudinal study to date.[85] In this study, concentric quadriceps muscle function measured using isokinetic dynamometry (60°/s, 5-repetition total work divided by body mass) at 6, 12, and 24 months following patellar tendon ACL reconstruction was not associated with the development of radiographic or symptomatic radiographic knee OA 10 to 15 years later. Further research is needed to determine the role of muscle function in influencing knee joint health in this patient population.

The link between knee proprioception and OA disease onset has been investigated in 2 recent large longitudinal studies using data from MOST.[81,86] Active knee joint position sense measured without weight bearing at baseline was not significantly associated with incident radiographic or symptomatic knee OA[81] or with the new onset of frequent knee pain[86] over a 30-month follow-up. Although it was hypothesized that sensorimotor factors may interact to mediate OA risk, the combination of high absolute isokinetic knee extensor strength and better knee joint position sense did not protect against development of knee OA.[81] These findings suggest that proprioception, at least as assessed by knee joint position sense, does not predict the onset of either radiographic or symptomatic knee OA.

Disease Progression

Although it seems that quadriceps muscle strength is related to OA disease onset, the longitudinal evidence to suggest that stronger muscles can protect against OA progression in those with established disease is conflicting. Most studies used isokinetic dynamometry to assess concentric quadriceps strength (albeit at various speeds) and different methods and grading systems to assess disease progression.

The earliest study, published in 1999, found that the mean absolute quadriceps strength of women with progressive OA (defined as worsening of the Kellgren and Lawrence grade over 2.5 years) was about 9% lower than those with radiographically stable OA.[87] However, this strength difference between the groups was not statistically significant, which could be due to the small number of participants (17 out of 82) exhibiting radiographic progression. Strength relative to body mass did not differ between progressors and nonprogressors. The use of nonstandardized conventional radiographs for evaluating progression could also reduce the potential of this study to detect structural progression. Nevertheless, in support of this nonsignificant finding, a larger more recent study involving 265 individuals and using the supposedly more

sensitive technique of magnetic resonance imaging (MRI) to assess tibiofemoral cartilage loss over 30 months also failed to find an effect of relative isokinetic quadriceps strength on disease progression.[88] Conversely, a study using data from MOST showed that women in the lowest tertile of relative isokinetic quadriceps strength (normalized for height and weight) had an increased risk of tibiofemoral joint space narrowing over 30 months (odds ratio 1.69, 95% confidence interval 1.26, 2.28) compared with women in the highest strength tertile.[89] These results suggest that in women, but not men, quadriceps weakness may be a risk factor for structural deterioration in those who already have knee OA. A differential gender result also concurs with previous findings for incident symptomatic knee OA in MOST. Segal and Glass[90] postulated that this gender difference may relate to the strength capacity of women being closer to a threshold for risk, whereas greater absolute strength in men provides greater reserve such that a loss of strength is insufficient to lead to greater risk of progression.

Muscle strength may have differential effects depending on the joint involved. Greater isokinetic quadriceps strength (60°/s) relative to body mass has been found to protect against cartilage degeneration in the lateral aspect of the patellofemoral joint.[88] The findings were supported by another study showing a similar trend in women but not men, although that study used absolute isokinetic strength (60°/s) not strength relative to body size (eg, body mass).[89] Quadriceps weakness could alter patellar tracking and walking biomechanics, which could lead to disproportionate compressive forces across the patellofemoral joint.

It has been proposed that the local mechanical environment may also influence the relationship between strength and disease progression. A study by Sharma and colleagues[91] found that greater absolute quadriceps peak torque (at 120°/s) at baseline increased the risk of tibiofemoral joint disease progression in individuals with malaligned knees (defined as >5° deviation from the mechanical axis) or high-laxity knees (defined as >6.75° varus valgus deviation), but not in those who had neutral alignment or low-laxity knees. The investigators suggested that the inability of malaligned knees to evenly distribute muscle forces could result in focal stress, and the increase in muscle contraction to stabilize lax knees could lead to higher joint reaction forces. The inferred clinical implication of these results, espoused in an editorial that accompanied this study, was that quadriceps strengthening, the cornerstone of exercise therapy in OA, might actually be detrimental in those people with knee OA and malalignment or laxity.[92] However, a more recent study in 265 elderly individuals[88] has not supported the results of Sharma and colleagues.[91] In this study, there was no relationship between the relative isokinetic quadriceps strength (60°/s) at baseline and loss of medial tibiofemoral joint cartilage using MRI in those with or without knee malalignment.[88] As longitudinal studies assess relationships and cannot directly assess causality, clinical trials are needed to definitively investigate the effects of strengthening exercise on structural outcomes at different joint compartments, in different sexes, and in the presence of different mechanical factors.

Although the quadriceps muscle has been the major focus, there has also been interest in the role of the hip abductors. It has been suggested that stronger hip abductors may be associated with a reduced risk of knee OA progression in the ipsilateral knee. In an 18-month study of 57 patients with mild to moderate unilateral knee OA, every additional unit of normalized internal hip abductor moment during gait was associated with a 43% reduction in the risk of ipsilateral medial knee OA progression.[23] Although hip abductor strength was not measured, the investigators suggested that the internal hip abduction moment might be primarily related to abductor muscle strength. Mundermann and colleagues[24] reported higher peak internal hip abduction

moments during gait in individuals with mild to moderate knee OA compared with those with severe OA, further suggesting a protective effect of hip abduction strength against knee OA progression.

Some studies have used the external knee adduction moment during gait to examine the indirect effects of muscle strengthening on OA disease progression,[93–98] by virtue of the moment's association with both medial compartment loading[10,99] and structural disease progression.[6,7] Of the 6 studies, only 2 found an effect of exercise in reducing the knee adduction moment; both were uncontrolled pilot studies.[97,98] In 1 study, an 8-week, supervised, lower-limb strength and neuromuscular control exercises program including functional strengthening was evaluated in 13 patients with early knee OA.[98] The investigators found that the peak knee adduction moment during gait was not significantly altered at completion of the exercise program but there was a 14% reduction in the adduction moment measured during a one-leg rise. However, the clinical relevance of small changes in loading only during a one-leg rise task is unknown. The other study of 6 patients found that a 4-week strengthening program involving the hip and other lower-limb muscles led to an average 9% reduction in the peak knee adduction moment during walking even though strength gains were not found.[97]

In contrast to these pilot studies, several larger RCTs[93–96,98] and an uncontrolled study of 40 people[96] have failed to find changes in the knee adduction moment with strengthening programs targeting the quadriceps and hip muscles, despite strength gains and symptomatic improvements. In 1 study, 107 participants were stratified according to knee malalignment (more varus or more neutral) and randomized into either a 12-week, supervised, home-based, quadriceps strengthening group or a control group with no intervention. Quadriceps strengthening did not significantly alter the adduction moment in people with more malaligned or more neutral knees.[94] In another recent RCT, a 12-week hip muscle-strengthening program did not affect the knee adduction moment in 89 people with medial knee OA.[93] These results were further confirmed by a study involving 54 women randomized into a 6-month high-intensity progressive resistance training program or sham exercise.[95] In summary, the evidence currently suggests that muscle-strengthening exercise does not alter the knee adduction moment in people with knee OA.

Limited longitudinal data do not support a link between proprioception and progression of knee OA in those with established disease.[86] From MOST, active joint position sense was not associated with radiographic worsening over 30 months in 2440 people with mild disease.[86] It is not known whether proprioceptive deficits become more important risk factors in later stage disease when greater impairments in the sensorimotor system are found.

Although the role of muscle function on structural disease development and progression has received most of the attention in the literature, its effects on functional progression are less well known. Sharma and colleagues[100] conducted a 3-year longitudinal cohort study investigating factors contributing to poor physical functioning in 257 patients with knee OA. They found that in addition to factors such as age, reduced absolute quadriceps and hamstrings strength and poor proprioceptive acuity (measured as joint position sense) increased the likelihood of poor physical functioning as measured by the time to perform 5 repetitions of rising and sitting in a chair. Similarly, in a cohort of more than 2000 individuals, those with worse proprioceptive acuity (measured as active non–weight-bearing joint position sense) at baseline had slightly greater worsening of WOMAC (Western Ontario and McMaster Universities) pain scores (0.47 on a 20-point scale) and physical function scores (by 1.5 points on a 0- to 68-point scale) compared with those with the best proprioceptive acuity

(for pain $P = .05$; for physical function $P = .02$) over 30 months.[86] Lastly, a longitudinal cohort study found that reductions in hip abductor strength were related to poorer functional outcomes more than 3 years in people with knee OA.[101] Taken together, these findings suggest that impaired muscle function is related to greater pain and declines in physical in those with knee OA.

CAN MUSCLE DEFICITS BE MODIFIED IN KNEE OA?

Given that numerous deficits in muscle function are associated with knee OA, it is important for health professionals to understand which deficits may be amenable to change with intervention (**Table 2**). An appreciation of which treatment strategies are most effective at improving muscle function will allow clinicians to tailor treatment to the nature of the presenting muscle deficit for each individual with knee OA.

Muscle Strength

Extensive research indicates that muscle strength can be improved with an appropriately targeted strengthening program.[102] A large systematic review assessed the effectiveness of isolated resistance training in people with knee OA.[103] Fourteen RCTs were identified that measured parameters of muscle strength and compared the effects of isolated resistance training to a non-exercising control group. In general, muscle strength improved significantly with resistance training (mean improvement of 17.4%, range 10.5% decrease to 49.5% increase), with 9 out of 14 studies reporting significant strength gains. Relative effect sizes for strength outcomes ranged from -0.04 to 1.52, with an average of 0.38, indicating small to moderate effects of resistance training in this patient group. Whereas/although the most research has targeted strength training to the quadriceps muscle, strength gains have also been observed with targeted training for the hamstrings and hip musculature.[93,104–107] Strength gains are apparent with both supervised clinic-based programs and home exercise regimes,[103,108–110] although it is presently not clear which mode of delivery is superior for achieving strength gains as this has not been directly evaluated. The magnitude of strength gain achieved with resistance training varies according to the intensity of training (resistance applied as well as frequency), patient adherence and the specificity of training, which probably explains the variation in strength change observed

Table 2
Summary of interventions that have been investigated in the literature and may potentially affect deficits in muscle function

Muscle Deficit	Interventions
Weakness	Strengthening exercise EMG biofeedback
Atrophy	Strengthening exercise
Muscle inhibition	Exercise generally including quadriceps strengthening Transcutaneous electrical nerve stimulation Cryotherapy
Altered activation patterns	Unloading knee brace Stochastic resonance electrical stimulation with knee sleeve
Proprioceptive deficits	Proprioceptive exercise Whole-body vibration Knee bandaging Knee bracing

in the systematic review by Lange and colleagues.[103,108–110] More research is needed to establish dose-response relationships with respect to resistance training for people with knee OA.

There has been interest in whether modalities such as EMG biofeedback or whole-body vibration platforms can assist in augmenting strength gains achieved with exercise in people with knee OA. A recent systematic review to determine the magnitude of the treatment effect for EMG biofeedback on quadriceps strength compared with that of placebo and traditional exercise interventions in both healthy and pathologic populations found the strongest effect in knee OA populations.[111] However, more definitive evidence is needed to confirm the benefits. With regards to vibration, there is limited research in knee OA with conflicting results. Segal and colleagues[112] recently found that in women with risk factors for knee OA, the addition of vibration to a twice-weekly lower-limb exercise program did not result in significantly greater improvements in lower-limb strength or power than did performance of the exercise program without vibration. In another small RCT, knee muscle strength gains were significantly increased compared with control.[113] A recent systematic review on whole-body vibration programs in older populations in general concluded that the effects do not seem to be greater than those achieved with conventional exercise alone.[114]

Muscle Atrophy and Activation

Increases in muscle strength with resistance training are probably only partly explained by muscle hypertrophy, and research is required to investigate the relative contributions of neural adaptation and muscle hypertrophy to the strength increases observed.

One study evaluated the effects of isokinetic training on the cross-sectional area of the quadriceps and hamstrings in people with bilateral knee OA.[115] Significant within-group increases in cross-sectional area were observed for both muscle groups with both a concentric and a combined concentric-eccentric training program.

Some studies have demonstrated improvements in voluntary activation of the quadriceps following an exercise regime, usually including quadriceps strengthening exercise.[110,116] Mean within-group increases in activation ranging from 5 to 14% have been reported. Other treatment modalities that have been shown to influence motor neuron pool excitability in healthy subjects with experimentally effused knee joints include transcutaneous electrical nerve stimulation (TENS) and cryotherapy.[117] Pietrosimone and colleagues[118] randomly allocated participants with knee OA to receive either 45 minutes of TENS, 20 minutes of focal knee joint cooling with ice bags or control intervention (sitting quietly for 20 minutes) and evaluated the effect of treatment on the quadriceps central activation ratio. Application of TENS resulted in a significantly higher percent change in activation ratio scores compared with control at 20 min, 30 min, and 45 min. Focal knee joint cooling resulted in significantly higher percent change activation ratio scores compared with the control group at 20 min only. No significant differences in percent change for the central activation ratio were found between the TENS and the focal knee joint cooling group. The same investigators also showed that the addition of TENS to an exercise program increases quadriceps activation beyond that observed with exercise alone.[119] These studies provide evidence that modalities such as TENS and cryotherapy may be useful for increasing muscle activation in people with knee OA, at least in the quadriceps.

Scopaz and colleagues[120] evaluated whether pre-treatment magnitude of quadriceps activation predicted the change in quadriceps strength with exercise therapy in knee OA. The investigators hypothesized that people with lower magnitudes of muscle activation would have smaller gains in strength following exercise, when compared

with those with higher magnitudes activation. Although correlations demonstrated that baseline quadriceps activation was positively associated with absolute isometric quadriceps strength at both baseline and 2-month follow-up, the level of relative quadriceps activation at baseline did not predict post-exercise absolute quadriceps strength when data were controlled for baseline absolute strength and type of exercise therapy. This data would suggest that factors other than baseline voluntary quadriceps activation may be more important in determining response to strengthening exercise. However, Pietrosimone and Saliba[121] did recently show that changes in voluntary activation predicted 47% of the change in quadriceps strength in a group of patients with OA undergoing 4 weeks of supervised resistance training. Thus improvement in voluntary activation was linked to improvement in strength. This would suggest that deficits in activation could be investigated and targeted as part of OA rehabilitation.

Although impairments in muscle activation *patterns* during gait are associated with knee OA (see earlier), there currently seem to be no studies evaluating whether exercise can change this specific impairment in people with OA, probably because it is not clear what constitutes an optimal or desirable muscle activation pattern in these people. However a recent study has shown that application of a new therapy, stochastic resonance electrical stimulation combined with a neoprene knee sleeve, significantly decreased the ratio of vastus lateralis to lateral hamstring activity during walking.[122] Similarly, a study in people with medial knee OA found that a valgus producing knee brace significantly reduced the cocontraction of both the vastus lateralis-lateral hamstrings and vastus medialis-medial hamstrings.[123] Thus, it is possible to alter muscle activation patterns but whether this translates into clinical or structural benefits is not yet known.

Proprioception

Although many treatment strategies are postulated to improve proprioception, relatively few intervention studies in knee OA evaluate proprioception in their assessment of treatment efficacy. There is some evidence that impairment in proprioceptive acuity associated with knee OA may be enhanced with exercise training more so with exercise that specifically targets the proprioceptive system. One novel program involves a computer game, where seated participants control movement of a snake on the computer screen by stepping on 4 foot pedals in multiple directions at increasing speeds.[124–126] In addition to training the proprioceptive system, task performance involves some resistance applied to the foot. This program has been evaluated alongside strength training and a no-exercise control in RCTs conducted by the same group of investigators,[124–126] although it is not clear if the data reported in each paper were collected from 3 separate cohorts of people with knee OA or a single group. Within-group analyses demonstrated significant improvements in absolute error in knee angle repositioning from baseline to follow-up in the proprioceptive training group in all 3 studies (changes approximating 2–3° in magnitude). No change was evident within the no exercise control group[127] or within the group undergoing seated concentric & eccentric quadriceps training.[125] Another RCT, which evaluated the additive effect of a sensorimotor training program using sling suspension to routine physical therapy,[128] found that the program resulted in improved knee repositioning compared with physical therapy without the sensorimotor component (mean change $1.9^\circ \pm 1.7$). In contrast, another randomized study demonstrated that the addition of kinesthesia and balance exercises to a routine strengthening program did not offer any additional improvement in proprioceptive acuity than a strengthening program alone.[129]

The effects of whole-body vibration on proprioceptive function have been investigated in knee OA. An RCT compared whole-body vibration on a stable platform to

whole-body vibration on a balance board to a non-treated control group.[113] Movement detection threshold was significantly improved in the vibrating balance board group compared with controls and there was a tendency for the vibrating stable platform group to perform better than the controls. It is not clear from this study whether improvement in proprioception was caused by/because of the whole-body vibration or simply an effect of the training on the balance board.

There is some evidence to suggest that knee bandaging or bracing can improve proprioception in knee OA,[69,130] but findings are inconsistent across the literature.[131] Neither taping,[132] stimulating massage,[133] magnetic knee wraps[134] nor stochastic resonance electric stimulation[135] seem to have an effect/affect on proprioception in people with knee OA. Thus it seems that some but not all treatments show promise for enhancing proprioceptive acuity in knee OA. However reported mean changes are generally quite small and it is unclear if such changes are clinically relevant or indeed, merely within the realm of measurement error.

DO IMPROVEMENTS IN MUSCLE FUNCTION LEAD TO IMPROVED SYMPTOMS AND JOINT STRUCTURE IN KNEE OA?

There is ample evidence demonstrating that muscle-strengthening exercises result in improvements in pain, physical function and quality of life in people with knee OA.[102,136] Again, the most research has focused on quadriceps strengthening programs. A systematic review of exercise that pooled data from the strengthening studies noted small to moderate effect sizes for both pain (pooled effect size 0.32, range 0.23–0.42) and physical function (pooled effect size 0.32, range 0.23–0.41) following quadriceps strengthening.[136] These findings are supported by the most recent systematic review of strengthening exercise for knee OA, conducted by Lange and colleagues.[103] Although the investigators did not pool data across trials, they reported that 56% (10 out of 18) of studies found significant decreases in pain with strengthening exercise and physical disability significantly improved in 79% (11 out of 14) of studies.

Whereas/although the improvements observed in pain and physical function following strengthening programs are often attributed to improvements in muscle strength, studies generally do not correlate changes in muscle function with clinical improvements following intervention. Indeed, most clinical trials of exercise do not include measures of muscle function in their test battery. The systematic review by Lange and colleagues[103] found only 2 studies that evaluated such relationships. They reported positive associations between increased muscle strength and walking self-efficacy,[108] reduced pain,[137] improved function[108,137] and total WOMAC score.[137] Thus, although the evidence is limited, it is likely that increases in muscle strength are at least partially responsible for improvements in pain or function with exercise.

Improvements in clinical state with strengthening exercise are generally not maintained once the patient stops exercising. This was clearly demonstrated in a study by van Baar and colleagues,[138] who evaluated the long-term effectiveness of a multifaceted exercise program that included muscle strengthening in hip and knee OA. Participants were evaluated 6 months after completion of the 3-month exercise program. Although exercise was associated with reductions in pain and observed disability at 3 months,[106] these improvements had disappeared 6 months later.[138] This may partially be due to the gradual loss of improvement in muscle function once exercise has ceased (**Fig. 2**). Thus, for ongoing improvements in pain and function, and to maintain increases in muscle strength, long-term involvement in exercise is necessary.

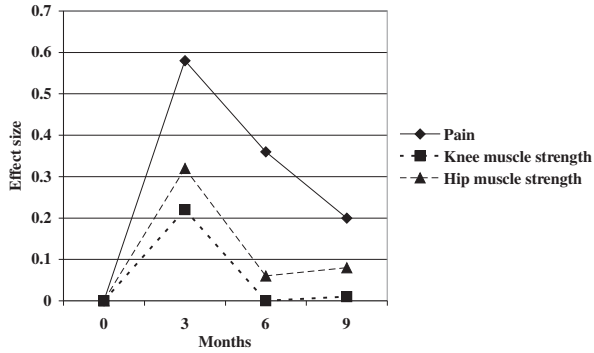

Fig. 2. Decline in effect size of muscle strength with exercise over time, as reported by van Baar and colleagues,[138] and its correlation with change in pain.

Compared with effects on symptoms, there are few RCTs evaluating whether improvements in muscle function have any discernable effect on joint structure in knee OA.[104,139,140] All these studies used radiographs to measure changes in joint structure and only 1 included a measure of joint structure as the primary outcome.[140] In this 30-month clinical trial, 105 people with knee OA were randomized to a strength-training group, with an emphasis on the quadriceps and hamstrings, or to a control range-of-motion exercise group.[140] The exercise programs were performed 3 times per week with supervision progressively withdrawn over the course of the study. The results showed a nonsignificant trend for a greater percentage of people in the control group (28%) to show an increase in grade of joint space narrowing on radiographs compared with the strength-training group (18%, $P = .09$) (**Fig. 3**). It is likely that this trial was underpowered to detect statistically significant differences in structural outcomes across groups, which may explain the nonsignificant findings of this study. Although the data suggest that it may be possible to slow structural joint deterioration over time with exercise, these results need to be interpreted cautiously given the low adherence to exercises, the high drop out rate, and the fact that the

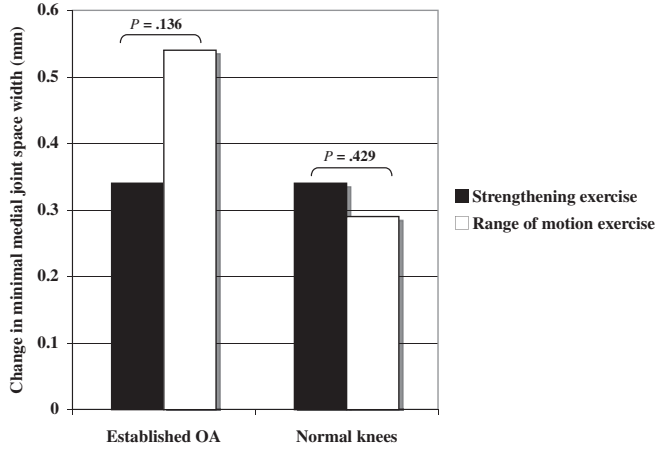

Fig. 3. Change in joint space width over 30 months with exercise as reported by Mikesky and colleagues,[140] relative to baseline disease state and according to treatment group.

strengthening groups actually lost, rather than gained, lower-extremity muscle strength over the 30-month trial. Trends in data from this study suggest that lower-limb strength training may play a role in slowing deterioration over time in established knee OA, but further large-scale studies using more sensitive imaging techniques (such as MRI) are needed.

Two other studies that included disease progression as a secondary outcome failed to find a significant effect of 18 months of exercise that included strength training in knee OA.[104,139] In 1 study, the exercise program comprised quadriceps, hamstrings, and calf strength training as well as moderate intensity walking 3 days per week[139]; the other study involved only strength training.[104] It has been proposed that the intensities or loads (% repetition maximum) used in OA exercise studies are well below those recommended for strength training in older individuals[141] and that long-duration, high-intensity strength training may be needed for structural effects. Given that knee malalignment increases the risk of structural progression over time,[142] exercise studies should also account for the severity of malalignment in data analysis so that the independent effects of exercise on disease progression can be elucidated. Further longer-term studies are needed before conclusions can be made on whether strengthening exercise can modify structural disease.

EXERCISE PRESCRIPTION FOR MUSCLE REHABILITATION

Muscle rehabilitation is an important component in the clinical management of knee OA and advocated for all patients with OA by clinical guidelines,[143] including the most recent (2012) from the American College of Rheumatology.[144] Given the muscle dysfunction (weakness, reduced proprioception) common in those with knee OA, restoration or improvement of muscle function is a key objective in the treatment of these individuals. Furthermore, because muscle dysfunction may have negative consequences on the loading environment within the knee joint, it is essential to include muscle rehabilitation exercises within the overall clinical management of knee OA to produce beneficial long-term outcomes. This section discusses practical aspects related to exercise prescription for patients and reviews current evidence about the best mode of delivery, type of exercise, and dosage (**Box 1**).

Mode of Delivery

Exercise may be delivered via individual treatments, supervised group classes, or performed at home; each has its own advantages and disadvantages. Advantages of

Box 1
Summary of exercise prescription for muscle rehabilitation in knee OA

- Refer to health professional for appropriate exercise prescription
- Supervised group or individual treatments are superior to independent home exercise for pain reduction
- Supplement home exercise with initial group exercise
- Exercise handouts or audiovisual material alone are ineffective
- Target quadriceps, hamstrings, and hip abductors for strengthening
- Minimize compressive joint forces
- Utilize a combined program of strengthening, flexibility, and functional exercises
- Use strategies to maximize long-term patient adherence to exercise

group-based exercise programs include the social aspects of group therapy and the ability to minimize the resources and costs to deliver the intervention. Disadvantages include difficulty in tailoring exercise to individual patients and the need to coordinate the schedules of multiple patients. Home exercise entails little financial outlay and provides the patient with greater flexibility regarding timing of the exercise session. However, there is a lack of supervision and often a lack of suitable equipment.

A recent Cochrane review compared the effect sizes of different exercise delivery modes in knee OA.[145] Results indicated that home-based exercise programs produced smaller effects on pain and physical function than individual supervised treatments or group-based interventions. However, these differences were not statistically significant. One potential explanation for the lack of statistical difference was that some of the home-based exercise programs also included visits from health care professionals. The review found that the magnitude of the treatment effect was significantly related to the number of supervised visits with a health care professional; 12 or more supervised sessions gave superior outcomes compared with less than 12 sessions. Thus, although home-based exercises may be the most feasible for some individuals with knee OA, it seems that supplementing home exercises with an initial class-based program supervised by a physiotherapist can lead to greater improvements in pain and locomotor function with home exercises in the longer term.[146] Economic analyses demonstrate that the additional cost of the group exercise classes can be offset by reductions in resource use elsewhere in the health care system.[147] Thus, exercise class supplementation represents a cost-effective method of maximizing the benefits of a home exercise program.

These findings indicate that some form of supervision from a qualified health care professional is needed to optimize outcomes. A minimalist approach whereby patients are simply given a pamphlet or audiovisual material outlining a standardized exercise program has not been found to be beneficial. In a large study, this exercise approach delivered by rheumatologists yielded similar clinical outcomes to usual care after 6 months.[148] Numerous factors likely contributed to the ineffectiveness of exercise in this study. Patients were poorly adherent and an unsupervised standardized exercise program and dosage was used, which may have been ineffective for such a heterogeneous patient group. Although a videotape demonstration of the exercises was provided, it would seem that technology is no substitute for personal demonstration and tuition in correct exercise technique. It is possible that many patients were performing the exercises incorrectly, further reducing their effectiveness.

Type of Program

Quadriceps strengthening has formed the cornerstone of traditional OA exercise therapy. Previous research into muscle dysfunction in people with knee OA has focused primarily on the quadriceps. Muscle-strengthening exercises may be performed in a variety of modes including isometric, isotonic, or isokinetic; the latter 2 may be concentric and/or eccentric. They may also be performed in an open kinetic or closed kinetic chain manner. Open kinetic chain exercises at the knee are non–weight bearing whereas closed kinetic chain exercises are typically weight bearing involving multiple joints and are believed to be more functional. However, the important issue for OA is keeping compressive joint forces as low as possible while still achieving an adequate muscle-strengthening stimulus. Thus, the advantages of functional closed kinetic chain exercises must be weighed against the potential disadvantages of increased joint loading. A meta-analysis published in 2009 identified 32 trials of exercise interventions for people with knee OA using a variety of modes including quadriceps strengthening, lower-limb muscle strengthening, combined strengthening

and aerobic exercise, and other (unspecified exercises focusing on lower-limb muscle strengthening or aerobic conditioning).[149] Although the simple quadriceps strengthening programs produced only marginal significance for both pain and function and the other programs provided no significant benefit for physical function, the results of this meta-analysis found no significant differences in pain or function outcomes based on the type of exercise. Thus, clinicians can prescribe the type of exercise that best suits the individual patient. It is also likely that the effectiveness of joint-specific strengthening is maximized when combined with general strength, flexibility, and functional exercises.

Factors that may influence the type of exercise prescribed include the magnitude of joint pain and muscle weakness, disease severity, as well as the coexistence of symptoms arising from the patellofemoral joint. Given that patellofemoral involvement is generally prevalent in combination with tibiofemoral OA,[150] strengthening may need to be performed in positions that minimize patellofemoral contact forces and knee loading, which could include exercises that are performed in lesser degrees of knee flexion or in non–weight-bearing situations. Regardless of the compartmental involvement, aquatic exercise may be a useful way to strengthen muscles while minimizing joint loading particularly in the obese or in those with more advanced disease or with greater abnormalities in the local mechanical environment. A clinical trial comparing 18 weeks of aquatic exercise or land-based exercise in 64 people with knee OA found similar improvements in pain and function.[151] This suggests that aquatic exercise is a suitable and effective alternative to land-based exercise that should be considered when prescribing exercise.

Muscle rehabilitation for knee OA has largely focused on strengthening exercises given the desire to improve overall muscle force production. However, given the known impairments in muscle activation patterns in those with knee OA (see earlier section), investigation into the role of exercises that target muscle timing and function rather than purely strength (termed neuromuscular retraining exercises) has received increased interest in recent years. Neuromuscular retraining exercises may be important in people with knee OA who report instability, the symptom of buckling, slipping or giving way of the knee during functional activities.[152] Preliminary evidence for the role of neuromuscular retraining for people with knee OA has been largely surmised from treatment of other patient populations such as those with ACL injury or after meniscal surgery. A large prospective cohort study (n = 100) following individuals for 15 years after an ACL tear and subsequent neuromuscular retraining and activity modification showed similar strength and functional performance as the uninjured limb.[153] However, research into the clinical effects of neuromuscular retraining exercises in people with knee OA is limited and most research has been limited by single case studies or pilot studies. A recent RCT of 183 people with knee OA examined the addition of neuromuscular retraining exercises (including agility and perturbation exercises) to a standard strengthening exercise program.[154] The study found that the additional exercises did not improve pain and function any more than the standard exercise program alone. Further research in this area should focus on the identification of potential subgroups that would benefit most from neuromuscular retraining exercises as well as the longer-term effects on knee joint loading and disease progression.

Dosage

The frequency, duration, and intensity of the exercise program may affect clinical outcomes but these have not been well studied in people with knee OA. Although a definitive dose-based response to exercise has been reported in people with OA as well as many other populations, there may be issues with maintaining good

adherence to programs with long durations. Most exercise guidelines would suggest a physiologic response can be attained with as little as 3 exercise sessions per week, and research into the effectiveness of exercise programs in individuals with knee OA have shown improvements after 8-week or 12-week programs.[155–157]

Although the notion of more is better is evident when determining the number of exercise sessions, the optimal intensity of resistance for a muscle-strengthening program for OA is unclear. High-intensity training (high resistance/load) might be expected to result in greater strength gains than low-intensity training and has been shown to be feasible in those with moderate to severe knee OA.[158] However, increased resistance during high-intensity exercise could potentially overload the joint and exacerbate symptoms such as pain, inflammation, and swelling. A study published in 2008 compared the effects of 8 weeks of high-intensity and low-intensity closed kinetic chain knee-strengthening exercise performed 3 times weekly in 102 people with knee OA.[159] High-intensity training was defined as 3 sets of 8 repetitions with an exercise weight set initially at 60% of 1 repetition maximum; low-intensity training was defined as 10 sets of 15 repetitions with an initial exercise weight of 10% of 1 repetition maximum. The results showed that both strengthening programs were beneficial for pain, function, walking time, and muscle strength. However, although not significantly different, the effect sizes were larger for high-resistance strength training. Similar findings have been reported recently by Foroughi and colleagues[95] who conducted an RCT on 54 women examining changes in biomechanical and clinical outcomes following a 6-month high-intensity (80% of 1 repetition maximum) muscle-strengthening intervention compared with a sham exercise program (similar exercises but with minimal resistance and no progression). Although muscle strength changes were significantly greater in the high-intensity group, no group differences were found in any measure of knee pain or function. Thus, it seems that with the exception of improved muscle strength, high-intensity resistance exercises do not provide greater clinical and biomechanical benefits than lower-resistance exercise interventions for people with knee OA. General guidelines for strength-training parameters in people with OA as developed by the American Geriatrics Society[160] and in older adults from the American College of Sports Medicine[161] are shown in **Table 3**. The choice of strength-training parameters depends on the patient's pain levels, tolerance, and functional level.

Enhancing Uptake of Exercise and Patient Adherence

Despite evidence of the benefits of exercise in OA and clinical guidelines recommending exercise,[143,144] it is clear that adherence to an exercise program is a major determinant of the longer-term benefits of exercise.[162] Thus, the challenge remains to increase the proportion of patients with knee OA who are exercising and to maintain active participation in their exercise program. Although there are many factors affecting the uptake of exercise in the OA population, 2 are of particular importance: (1) recommendation of exercise to patients by medical practitioners and appropriate referral to exercise professionals and (2) adherence of patients to prescribed exercise programs.

Exercise is under used by medical practitioners as a treatment strategy for OA.[163] For example, a recent Canadian survey evaluated the quality of care for people with OA.[164] The investigators found that only 25% of the people surveyed who required advice to exercise had actually seen a physiotherapist or attended a land-based or pool-based exercise program or had used fitness facilities over the past year. Furthermore, in a survey of 3000 French general practitioners, less than 15% reported that they would prescribe exercise for knee OA as a first-line therapeutic approach.[165]

Table 3
General guidelines for strength-training parameters developed by the American Geriatrics Society for people with OA and by the American College of Sports Medicine for healthy older adults. Dosage can be modified taking into account the individual's ability and pain levels

Exercise Type	Intensity	Volume	Frequency
American Geriatrics Society Recommendations for OA			
Isometric	Low-moderate: 40%–60% MVC	1–10 submaximal contractions/ muscle group; hold 1–6 s	Daily
Isotonic	Low: 40% 1 RM Moderate: 40%–60% 1 RM High: >60% 1 RM	10–15 repetitions 8–10 repetitions 6–8 repetitions	2–3/wk
American College of Sports Medicine Recommendations for older adults			
Isotonic	60%–80% of 1 RM	8–12 repetitions, 1–3 sets	2–3/wk

Abbreviations: 1 RM, 1 repetition maximum; MVC, maximum voluntary contraction.

Data from American Geriatrics Society Panel on Exercise and Osteoarthritis. Exercise prescription for older adults with osteoarthritis pain: consensus practice recommendations. J Am Geriatr Soc 2001;49:808–23; and American College of Sports Medicine. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. Med Sci Sports Exerc 2009:41(3);687–708.

A survey of patients with OA in Canada revealed that only one-third had been advised to use exercise for their condition,[166] however, 73% reported that they had tried exercise in the past. Given the large number of patients who chose to try exercise independently, it is possible that many failed to consult a professional regarding the most appropriate exercise. Given the known benefits of having therapist supervision during an exercise program (see earlier), it is imperative to identify ways to improve patient access to qualified health care professionals as well as inform clinicians of the benefits of exercise across the disease spectrum.

Patient adherence is a key factor in determining outcome from exercise therapy in patients with knee OA.[162,167] Although patient adherence to exercise is often good when commencing an exercise program, it typically declines over the longer term. Several factors can contribute to adherence rates for exercise programs in individuals with knee OA. Adherence is improved when patients receive attention from health professionals rather than a primarily home-based exercise program.[147] Psychosocial attributes of the individual also influence adherence. Better adherence with therapy has been found to be related to the perception of more severe knee symptoms, belief in the effectiveness of the intervention, and understanding of the pathogenesis of knee OA (those who are less adherent tend to believe that OA is part of the natural aging process or that it is simply a wear and tear disease).[168] Self-efficacy, or one's belief in one's own ability to perform tasks, is also associated with higher adherence and better outcome.[169]

Many strategies have been suggested to improve patient adherence when prescribing exercise interventions for those with knee OA.[170] Tailoring the exercise program to the unique requirements of the patient as well as ensuring availability of resources can be effective. Other methods suggested to improve adherence include monitoring via telephone contact[171] or self-reported diary,[172–174] graphic feedback on exercise goals and progress,[175] or lifestyle retraining.[172] Although monitoring from a health care professional is the preferred method of contact, patients can rely on their own social support network when an appropriate health care professional is unavailable.[172,176,177] In addition, self-monitoring via positive feedback loops based

Box 2
Strategies that may assist in improving adherence to exercise in people with OA

- Patient-centered and individually tailored exercise programs with respect to exercise capacity, pain levels, goals, and interests rather than standardized nonspecific programs
- Supervised exercise sessions rather than unsupervised where possible
- Supplement a home-based-program with group exercise
- Long-term monitoring/review by a health professional (phone, mail, or visits)
- Patient education regarding the importance and benefits of exercise
- Inclusion of spouse/family in the exercise program
- Self-monitoring by means of an exercise diary or pedometer
- Support from family and friends to incorporate exercise into lifestyle
- Intermittent booster or refresher exercise sessions with a health professional
- Ensure access to appropriate exercise resources and facilities

on level of physical function and attainment of goals may be useful for some patients. **Box 2** provides a summary of ways to improve adherence to exercise in people with knee OA.

Recently, integrated treatment combining both exercise and self-management strategies has been advocated for OA as a means of improving patient adherence as well as targeting physical and psychological factors associated with OA.[178] Traditionally, these interventions are usually delivered separately, and theoretically, the benefits of each strategy individually may be additive. In addition, although self-management programs for OA typically emphasize the importance of exercise for OA, most programs do not have an active exercise component. A recent cluster randomized trial evaluated the efficacy of an integrated rehabilitation program that included an individualized progressive exercise regime, education, and self-management strategies to alter behavior and dispel inappropriate health beliefs.[179] In this study involving 418 people with chronic knee pain, self-reported physical functioning was evaluated immediately after the 6-week intervention, as well as 6, 18, and 30 months later. Results showed that participants undergoing integrated rehabilitation (delivered by a physiotherapist either individually or in groups) had better functioning than those receiving only usual primary care after the intervention. Although improvements in function declined over time, the integrated program still resulted in better function and was more cost-effective than usual care at 30 months. Other strategies of combining exercise and psychological treatment such as pain coping skills training have been examined and show positive benefits of combined training either by a single practitioner or via discipline-specific health care professionals.[180,181] These approaches have the added advantage of directly addressing personal barriers to exercise adherence through practical examples unique to the individual embedded within the treatment program. More research in this area is needed to identify ways of optimizing the delivery of these combined treatments.

SUMMARY

Lower-limb muscles, particularly the quadriceps, influence knee joint load, a major contributor to knee OA. Impairments in muscle function including weakness, altered activation patterns, and proprioceptive deficits are commonly found in association

with knee OA. Furthermore, there is some evidence that muscle weakness may predispose to the onset and potentially the progression of knee OA. Exercise is a key component of conservative management of knee OA and has been found to be effective in symptom reduction. Whether exercise influences disease development and progression requires further research.

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