
Physical therapy for patients with knee and hip osteoarthritis: supervised, active treatment is current best practice

S.T. Skou^{1,2}, E.M. Roos¹

¹Research Unit for Musculoskeletal Function and Physiotherapy, Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark;

²Department of Physiotherapy and Occupational Therapy, Næstved-Slagelse-Ringsted Hospitals, Region Zealand, Slagelse, Denmark.

Søren T. Skou, PT, PhD

Ewa M. Roos, PT, PhD

Please address correspondence and reprint requests to:

Dr Søren Thorgaard Skou,
Research Unit for Musculoskeletal Function and Physiotherapy,
Department of Sports Science
and Clinical Biomechanics,
University of Southern Denmark,
55 Campusvej,
DK-5230 Odense M, Denmark.

E-mail: stskou@health.sdu.dk

Received and accepted on September 6, 2019.

Clin Exp Rheumatol 2019; 37 (Suppl. 120): S112-S117.

© Copyright CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2019.

Key words: osteoarthritis, knee, hip, physical therapy, exercise

Funding: S.T. Skou is currently funded by a grant from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement no. 801790). The funders did not have any role in this study other than to provide funding.

Competing interests: see page 115.

ABSTRACT

Most patients with knee and hip osteoarthritis (OA) should be treated in primary care by non-surgical treatments. Building on substantial evidence from randomised trials, exercise therapy and education, typically delivered by physical therapists, are core first line treatments universally recommended in treatment guidelines for OA alongside weight loss, if needed. Exercise therapy provides at least as effective pain relief as pharmacological pain medications, without serious adverse effects; furthermore, the treatment effect from exercise therapy is similar, irrespective of baseline pain intensity and radiographic OA severity. Exercise therapy should be individualised to the preferences and needs of the individual patient, but at least 12 supervised sessions, 2 sessions per week, are required initially to obtain sufficient clinical benefit. Structured patient education concerning OA and its treatment options, including self-management, is important to retain motivation and adherence to an exercise programme and thereby maintain the effects over the long-term. If treatment effects from exercise therapy and patient education are insufficient, the physical therapist can deliver supplementary interventions that include knee orthoses and manual treatment.

Introduction

Joint pain and functional disability are cardinal symptoms of knee and hip osteoarthritis (OA) (1, 2). It is often implied that these symptoms are due to structural damage, which must be 'fixed' and not treated with non-surgical approaches (3, 4). By contrast, contemporary evidence demonstrates that OA is a 'whole person condition' in which different biopsychosocial factors that modulate inflammatory processes as well as behavioural responses which trigger pain and disability interact to af-

fect a person's joint health (5, 6). This viewpoint highlights the key role of active, non-surgical treatments in the management of OA.

In many, but not all, health care systems, exercise therapy is typically delivered by physical therapists. In this article, we focus on knee and hip OA, as evidence concerning treatment of OA in other peripheral joints remains limited. It is likely that the physical therapy treatment paradigm for OA in those joints will shift as new evidence emerges. We use the phrase "knee and hip OA" throughout this manuscript to refer to patients suffering from OA of the knee, of the hip, or of both the knee and hip.

Physical therapy as treatment of knee and hip OA

Exercise, patient education and weight loss [at a Body Mass Index (BMI) of 25 or higher] comprise first-line treatment recommended in treatment guidelines for knee and hip OA. If patient education and exercise therapy are unsuccessful to improve pain and function, the physical therapist may offer supplementary treatments such as knee orthoses and manual treatment (7-10). Also, a supplementary pain-relieving treatment such as acupuncture sometimes is included initially as an additional alternative to oral pharmacological pain relievers, to facilitate starting an exercise programme, although evidence remains inconclusive concerning its effectiveness (Fig. 1) (11, 12). Weight loss is rarely offered by the physical therapist and therefore will not be described in detail in this article. However, it should be noted that even modest weight loss of 5% appears to have a significant impact on symptoms (13); therefore, weight loss is an important part of the treatment plan for overweight, and especially obese patients.

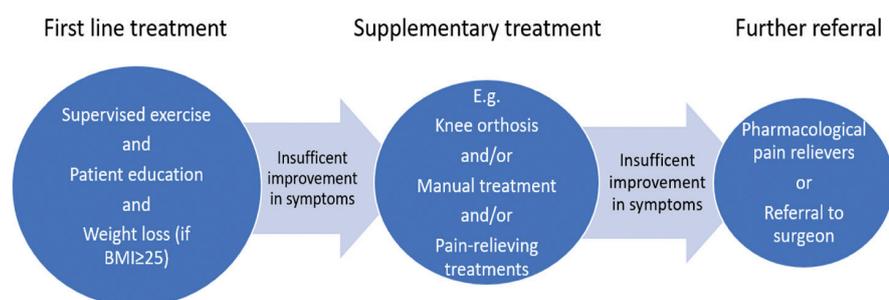


Fig. 1. The universally recommended treatment approach to hip and knee osteoarthritis. The sizes of the blue ovals indicate that fewer patients would need supplementary treatment and even fewer would need further referral.

First-line treatment

Exercise therapy

Exercise therapy is the most important non-surgical treatment of knee and hip OA, not only because of the positive effect on joint symptoms (14–16), but also because evidence highlights that exercise and physical activity help prevent at least 35 chronic conditions (17) and improve symptoms in at least 26 chronic conditions (18). Up to two out of three patients with knee and hip OA have one or more comorbidities, including hypertension, type 2 diabetes and depression (19), and therefore exercise and physical activity are crucial for maintaining good general health and well-being in patients with OA (16).

Over the last 25 years, more than 54 randomised controlled trials evaluating the effect of exercise therapy in knee OA patients (14) and more than 12 trials evaluating the effect of exercise therapy in hip OA patients (15) have been reported. The conclusion is unquestionable: pain and physical function are improved significantly following a supervised exercise intervention in patients with knee and hip OA (14, 15). Based on existing evidence, exercise therapy appears to have a larger effect on both pain (effect size of 0.49 vs. 0.38) and function (effect size of 0.52 vs. 0.38) in knee OA patients compared with hip OA patients. Although the treatment effect is slightly smaller (20), water-based exercise may offer a viable alternative, if the patient is unable to perform land-based exercises, due to, for example, intolerable symptoms from loading the joint and/or severe obesity.

• Exercise therapy as a painkiller in OA irrespective of radiographic severity

The effects of exercise therapy and physical therapy in general are not associated with radiographic severity of knee OA (21, 22) or the degree of pain (21) that the patients experienced before the treatment. The modern diagnosis of OA is based on clinical findings without necessarily including radiographic evidence (2), and the x-ray findings generally do not change the initial clinical management of the patient (23). In patients with moderate to severe knee or hip OA awaiting total joint replacement, 95% of one-hour twice weekly weight-bearing exercise sessions were performed with no more than acceptable pain (36). Therefore, the clinician plays an important role in explaining to the patient that OA severity has no clinical impact on the potential effect he or she may expect from the exercise programme.

Strikingly, exercise therapy appears more effective and safer for relief of pain than the traditional pharmacological pain relievers offered today. On a group level, exercise therapy has at least the same pain-relieving effect as NSAIDs and 2–3 times as large effect as acetaminophen in patients with knee OA (21, 24, 25). At the same time, exercise therapy is associated with only mild side effects such as muscle soreness and temporary pain flares (26), whereas pharmacological pain relievers may be associated with a considerable risk of side effects including on the stomach, liver and cardiovascular system (27–29).

Patients with severe pain that prevents

them from participating in an exercise therapy programme may benefit from supplementary pharmacological pain relievers, in consultation with their general practitioner (30, 31). Once the patient's symptoms decrease as a result of the exercise therapy, the patient may stop or reduce the intake of pharmacological pain relievers. According to recent guidelines, topical NSAIDs are preferred over oral pharmacological pain relievers in most patients due to a better safety profile, and acetaminophen (paracetamol) is not recommended due to the absence of clinical effects compared to placebo (25).

It is good to inform patients that pain flares are to be expected with frequent daily activities such as repeated chair stands (32) and when starting to exercise (33). This is not a sign of danger to the cartilage (34, 35), but rather a sign of exposing the body to a new or repeated activity and similar to what all people (even who do not have any arthritis) would experience when starting any new activities. In patients with knee and hip OA who start exercising twice weekly, pain flares decrease with number of exercise sessions and are gone for most patients after about 5–6 weeks (33). Remarkably, also in patients with severe knee and hip OA awaiting total joint replacement, 95% of pre-operative exercise sessions can be performed with acceptable pain, *i.e.* temporary increase of pain intensity to no more than 5 on a 0–10 scale (36).

• Individualisation and exercise dose are important to increase the clinical effects

Unfortunately, existing studies have applied a number of different exercise programmes that are not detailed enough to be incorporated into clinical practice (37). If the exercise programmes for knee OA are grouped into three subgroups, aerobic, resistance, and performance exercise, effects are similar for these three subgroups (21). This does not mean that the all patients should be offered the same exercise programme. On the contrary, individualisation might further increase treatment effects, as an increasing number of studies have shown that effects of

exercise may vary considerably based on individual patient characteristics (38-40). For instance, it appears that patients with varus thrust may benefit more from a neuromuscular exercise programme, whereas patients with a BMI of 30 or more may benefit more from quadriceps strengthening (38) (Figure 2 presents examples of neuromuscular exercises).

Supervision and exercise dose are essential elements and may have a large impact on the effect of exercise therapy. An element sometimes forgotten is a need for progression of the exercise programme. When patients respond to exercise and improve their muscle strength and function, the exercises should be made more difficult to ensure further gains in muscle function. That is one reason why supervision is needed, as individual adjustments will maximise benefits of the programme. Another reason is to coach and reassure the patient if pain flares are experienced. Pain during exercise and exercise-induced pain flares are common, especially in the early phase of a programme (33), and an individualised and progressive exercise plan is essential to optimise results (41). Furthermore, patient preferences is important to consider to ensure long-term motivation and adherence (16).

It is not yet possible to present any strong specific exercise dose recommendations. However, it appears that a minimum of 12 supervised sessions is more effective compared to fewer than 12 sessions among knee OA patients (21). Also, studies on knee OA that follow the recommendations from the American College of Sports Medicine (ACSM) regarding strength training (41) provide superior outcomes compared to exercise interventions that do not follow these recommendations (42). In hip OA, the same importance has not been established for number of supervised sessions; however, pain and physical function appear to improve more if the exercise intervention follows the ACSM criteria for strength training (43).

More research is needed to develop an optimal, individualised exercise protocol. Until then, the existing evidence



Fig. 2. Examples of neuromuscular exercises for patients with knee and hip osteoarthritis (Photo: Jørn Ungstrup; GLA:D®).

Table I. Eight exercise recommendations for knee and hip OA.

Number	Recommendation
1	Offer the patient supervised, progressive aerobic, resistance or performance exercise tailored to the patient's needs, preferences and characteristics.
2	Consider water-based exercises if the patient is unable to perform land-based exercises, especially during the initial part of the programme.
5	After an adjustment period, and if symptoms allow it, consider three weekly sessions to increase the effect.
6	Offer patient education to improve compliance and long-term effects.
7	Consider follow-up sessions after the programme to improve compliance and long-term effects.
8	Consider supplementary treatment such as knee orthoses and manual treatment if the intervention shows no effect.

should be applied as summarised in Table I. Some countries already have evidence-based national individualised knee and hip OA programmes consisting of education and exercise supervised by certified physical therapists, *e.g.* GLA:D® which is available in Denmark, Canada, Australia, China and Switzerland (44, 45). For more information and results, please visit glaid.dk; gladcanada.ca; gladaustralia.com.au and gladswitzerland.ch.

• *The combined effect of exercise therapy and other treatment modalities*

Exercise therapy combined with patient education appears more effective than exercise therapy or patient education alone in patients with knee OA (46), and combined treatment is also recommended for hip OA patients based on the existing evidence (25, 47). A combined treatment plan consisting of exercise and weight loss also is more effective in improving pain and physical function in overweight knee OA patients than either exercise and weight loss alone (48).

Two recent parallel randomised controlled trials investigated the effect of a tailored 12-week treatment plan consisting of neuromuscular exercise, patient education, weight loss, pharmacological pain relievers (if indicated), and insoles for knee OA patients (31, 49). One study found that on a group level, the tailored treatment plan was more effective in improving pain and function than leaflets with information and treatment advice (49). The other study investigated the effectiveness of total knee replacement followed by the tailored treatment plan compared with the tailored treatment plan alone. On a group level, the total knee replacement group had improvement in pain and function that was twice as large as the tailored treatment plan only group. However, the tailored treatment plan group also experienced clinically relevant improvements in pain and function, allowing for 3 out of 4 to postpone surgery for one year (31), and 2 out of 3 at two years (50). Contrary to the total knee replacement group, patients following the tailored treatment plan had no knee-related serious adverse events (31).

A study performed in hip OA patients found that the combination of exercise therapy and patient education could reduce total hip replacement by 44% as compared to those patients who received patient education alone (51). Based on the presented evidence, exercise combined with other non-surgical treatments is effective and can postpone surgery for a large number of OA patients. If a patient ultimately decides to request a total knee or hip replacement, having participated in a preceding exercise programme will help lead to faster postoperative recovery (52).

Patient education

The effect measured immediately after a supervised exercise programme is favorable, but diminishes over time (14, 15), most likely explained by low adherence to the exercise regime and lifestyle changes (16, 53). Patient education alone may have only a small effect on pain and function (25); however, patient education that is combined with follow-up sessions after the completion of the programme (54), may be key to increasing self-efficacy and retaining motivation and adherence to an exercise programme and thus maintaining benefit in OA patients (16, 55). Patient education should include information about causes, risk factors and disease mechanisms, the importance of physical activity and consequences of inactivity, effective and ineffective treatments and coping strategies and a self-help guide to help patients successfully manage their disease (16). This information will support the patient in understanding how to manage pain and exercise-induced pain flares and motivate him or her to life-long exercise and physical activity.

Supplementary treatment

Several physical therapeutic treatments beyond exercise and education are available to patients suffering from knee or hip OA who desire and need further therapy. Some of these treatments have not been analysed in formal clinical trials or other clinical research, which must be kept in mind before they are offered as part of the treatment plan. The most widely-used supplementary

treatments are described in more detail below. In agreement with clinical guidelines, supplementary treatments should never be offered as a stand-alone treatments, but always combined with exercise therapy, patient education and weight loss (if relevant).

Manual treatment in the form of joint mobilisation and manipulation appears to provide moderate benefit for pain and function in knee OA patients (7), and can be considered in the treatment of hip OA based on previous studies (8, 9). However, the quality of existing studies on knee and hip OA is poor, and the added effect of manual treatment in addition to exercise therapy is uncertain (56, 57). Therefore, firm conclusions concerning this type of treatment remain a subject for further clinical research.

Unloader braces for knee OA that shift load from the medial compartment appear to result in small-to-moderate improvements in pain and function in patients with medial knee OA (10). However, the effect size was small compared to a control group that used a neutral knee brace, neoprene knee sleeve, or shoe insert (10). Importantly, compliance ranged from 45% to 100%, and up to 25% of patients reported complications with brace use, including poor fit, swelling and skin irritation (10), highlighting the importance of individual adaptation of the fit of the brace if needed and supervision of usage, in order to optimise the potential for clinical effects.

Another study has investigated the efficacy of lateral wedge insoles as a treatment for pain in medial knee OA and found no significant effect compared with a neutral insole (58), probably because custom orthotic insoles require individual adjustments or are helpful only to certain subgroups of OA patients. The effect of insoles, shoes and knee braces on lateral and patellofemoral compartment knee OA has not been sufficiently investigated to make specific recommendations (59).

A recent Cochrane review concluded that there is little or no effect of acupuncture compared with placebo acupuncture on hip OA (11). By contrast, another recent review found a small

effect of acupuncture compared with placebo acupuncture on knee OA symptoms (12), while the additional effects from acupuncture beyond exercise are questionable (12). There remains insufficient evidence to conclude whether or not acupuncture is an effective treatment for OA.

Other passive treatment approaches such as massage, neuromuscular electrical stimulation, transcutaneous electrical nerve stimulation (TENS), ultrasound and laser cannot be recommended as part of the treatment plan, based on the absence of high-quality supportive evidence (25, 47, 57).

Acknowledgement

The authors would like to thank Mette Dideriksen, MSc, for her support preparing the manuscript.

Competing interests

E.M. Roos is deputy editor of Osteoarthritis and Cartilage, the developer of the Knee injury and Osteoarthritis Outcome Score (KOOS) and several other freely available patient-reported outcome measures, and co-founder of Good Life with Osteoarthritis in Denmark (GLA:D®), a not-for profit initiative hosted at University of Southern Denmark aimed at implementing clinical guidelines for osteoarthritis in clinical practice.

S.T. Skou is associate editor of the Journal of Orthopaedic & Sports Physical Therapy, has received grants from The Lundbeck Foundation, personal fees from Munksgaard, all of which are outside the submitted work. He is co-founder of GLA:D®.

The authors affirm that they have no financial affiliation (including research funding) or involvement with any commercial organisation that has a direct financial interest in any matter included in this manuscript, except as disclosed in an attachment and cited in the manuscript.

References

1. ALTMAN RD, HOCHBERG M, MURPHY WA JR, WOLFE F, LEQUESNE M: Atlas of individual radiographic features in osteoarthritis. *Osteoarthritis Cartilage* 1995; (Suppl. A): 3-70.
2. ZHANG W, DOHERTY M, PEAT G *et al.*: EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis. *Ann Rheum Dis* 2010; 69: 483-89.
3. DARLOW B, BROWN M, THOMPSON B *et al.*: Living with osteoarthritis is a balancing act: an exploration of patients' beliefs about knee pain. *BMC Rheumatology* 2018; 2: 15.

4. BUNZLI S, O'BRIEN P, AYTON D *et al.*: Misconceptions and the acceptance of evidence-based nonsurgical interventions for knee osteoarthritis. A qualitative study. *Clin Orthop Relat Res* 2019; 477: 1975-83.
5. KITTELSON AJ, GEORGE SZ, MALUF KS, STEVENS-LAPSLEY JE: Future directions in painful knee osteoarthritis: harnessing complexity in a heterogeneous population. *Phys Ther* 2014; 94: 422-32.
6. HUNTER DJ: Osteoarthritis: time for us all to shift the needle. *Rheumatology (Oxford)* 2018; 57 (Suppl. 4): iv1-iv2.
7. XU Q, CHEN B, WANG Y *et al.*: The effectiveness of manual therapy for relieving pain, stiffness, and dysfunction in knee osteoarthritis: a systematic review and meta-analysis. *Pain Physician* 2017; 20: 229-43.
8. POULSEN E, HARTVIGSEN J, CHRISTENSEN HW, ROOS EM, VACH W, OVERGAARD S: Patient education with or without manual therapy compared to a control group in patients with osteoarthritis of the hip. A proof-of-principle three-arm parallel group randomized clinical trial. *Osteoarthritis Cartilage* 2013; 21: 1494-503.
9. ABBOTT JH, ROBERTSON MC, CHAPPLE C *et al.*: Manual therapy, exercise therapy, or both, in addition to usual care, for osteoarthritis of the hip or knee: a randomized controlled trial. 1: clinical effectiveness. *Osteoarthritis Cartilage* 2013; 21: 525-34.
10. MOYER RF, BIRMINGHAM TB, BRYANT DM, GIFFIN JR, MARRIOTT KA, LEITCH KM: Valgus bracing for knee osteoarthritis: a meta-analysis of randomized trials. *Arthritis Care Res* 2015; 67: 9.
11. MANHEIMER E, CHENG K, WIELAND LS *et al.*: Acupuncture for hip osteoarthritis. *Cochrane Database Syst Rev* 2018; 5: Cd013010.
12. VICKERS AJ, VERTOSICK EA, LEWTH G *et al.*: Acupuncture for chronic pain: update of an individual patient data meta-analysis. *J Pain* 2018; 19: 455-74.
13. CHRISTENSEN R, BARTELS EM, ASTRUP A, BLIDDAL H: Effect of weight reduction in obese patients diagnosed with knee osteoarthritis: a systematic review and meta-analysis. *Ann Rheum Dis* 2007; 66: 433-39.
14. FRANSEN M, MCCONNELL S, HARMER AR, VAN DER ESCH M, SIMIC M, BENNELL KL: Exercise for osteoarthritis of the knee. *Cochrane Database Syst Rev* 2015; 1:CD004376.
15. FRANSEN M, MCCONNELL S, HERNANDEZ-MOLINA G, REICHENBACH S: Exercise for osteoarthritis of the hip. *Cochrane Database Syst Rev* 2014; 4:Cd007912.
16. SKOU ST, PEDERSEN BK, ABBOTT JH, PATTERSON B, BARTON C: Physical activity and exercise therapy benefit more than just symptoms and impairments in people with hip and knee osteoarthritis. *J Orthop Sports Phys Ther* 2018; 48: 439-47.
17. BOOTH FW, ROBERTS CK, LAYE MJ: Lack of exercise is a major cause of chronic diseases. *Comprehensive Physiology* 2012; 2: 1143-211.
18. PEDERSEN BK, SALTIN B: Exercise as medicine – evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scand J Med Sci Sports* 2015; 25 (Suppl. 3): 1-72.
19. WESSELING J, WELSING PM, BIERMAZEINSTRAS SM *et al.*: Impact of self-reported comorbidity on physical and mental health status in early symptomatic osteoarthritis: the CHECK (Cohort Hip and Cohort Knee) study. *Rheumatology (Oxford)* 2013; 52: 180-88.
20. BARTELS EM, JUHL CB, CHRISTENSEN R *et al.*: Aquatic exercise for the treatment of knee and hip osteoarthritis. *Cochrane Database Syst Rev* 2016; 3: CD005523.
21. JUHL C, CHRISTENSEN R, ROOS EM, ZHANG W, LUND H: Impact of exercise type and dose on pain and disability in knee osteoarthritis: A systematic review and meta-regression analysis of randomized controlled trials. *Arthritis Rheumatol* 2014; 66: 622-36.
22. SKOU ST, DEROSCHE CA, ANDERSEN MM, RATHLEFF MS, SIMONSEN O: Nonoperative treatment improves pain irrespective of radiographic severity – a cohort study of 1,414 patients with knee osteoarthritis. *Acta Orthop* 2015; 86: 1-6.
23. SKOU ST, THOMSEN H, SIMONSEN OH: The value of routine radiography in patients with knee osteoarthritis consulting primary health care: a study of agreement. *Eur J Gen Pract* 2014; 20: 10-16.
24. HENRIKSEN M, HANSEN JB, KLOKKER L, BLIDDAL H, CHRISTENSEN R: Comparable effects of exercise and analgesics for pain secondary to knee osteoarthritis: a meta-analysis of trials included in Cochrane systematic reviews. *J Comp Eff Res* 2016; 5: 417-31.
25. BANNURU RR, OSANI MC, VAYSBROT EE *et al.*: OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis Cartilage* 2019 Jul 3 [Epub ahead of print].
26. QUICKE JG, FOSTER NE, THOMAS MJ, HOLDEN MA: Is long-term physical activity safe for older adults with knee pain?: a systematic review. *Osteoarthritis Cartilage* 2015; 23: 1445-56.
27. BANNURU RRDU, MCALINDON TE: Reassessing the role of acetaminophen in osteoarthritis: systematic review and metaanalysis. *Osteoarthritis Cartilage* 2010; 18 (Suppl. 2): 250.
28. CRAIG DG, BATES CM, DAVIDSON JS, MARTIN KG, HAYES PC, SIMPSON KJ: Staggered overdose pattern and delay to hospital presentation are associated with adverse outcomes following paracetamol-induced hepatotoxicity. *Br J Clin Pharmacol* 2012; 73: 285-94.
29. CHOU R, MCDONAGH MS, NAKAMOTO E, GRIFFIN J: Analgesics for Osteoarthritis: An Update of the 2006 Comparative Effectiveness Review (Internet). In: vol. Report No.: 11(12)-EHC076-EF. ROCKVILLE (MD): Agency for Healthcare Research and Quality, US; 2011.
30. VAN TUNEN JA, VAN DER LEEDEN M, BOS WH *et al.*: Optimization of analgesics for greater exercise therapy participation among patients with knee osteoarthritis and severe pain: a feasibility study. *Arthritis Care Res* 2016; 68: 332-40.
31. SKOU ST, ROOS EM, LAURSEN MB *et al.*: A randomized, controlled trial of total knee replacement. *New Engl J Med* 2015; 373: 1597-606.
32. SKOU ST, GRØNNE DT, ROOS EM: Prevalence, severity and correlates of pain flares in response to a repeated sit to stand activity: A cross-sectional study of 14,902 patients with knee and hip osteoarthritis in primary care. *J Orthop Sports Phys Ther* 2019 Sep 6 [Epub ahead of print].
33. SANDAL LF, ROOS EM, BOGESVANG SJ, THORLUND JB: Pain trajectory and exercise-induced pain flares during 8 weeks of neuromuscular exercise in individuals with knee and hip pain. *Osteoarthritis Cartilage* 2016; 24: 589-92.
34. BRICCA A, STRUGLICS A, LARSSON S, STEULTJENS M, JUHL CB, ROOS EM: Impact of exercise therapy on molecular biomarkers related to cartilage and inflammation in people at risk of, or with established, knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. *Arthritis Care Res (Hoboken)* 2018 Oct 15 [Epub ahead of print].
35. BRICCA A, JUHL CB, STEULTJENS M, WIRTH W, ROOS EM: Impact of exercise on articular cartilage in people at risk of, or with established, knee osteoarthritis: a systematic review of randomised controlled trials. *Br J Sports Med* 2019; 53: 940-47.
36. AGEBERG E, LINK A, ROOS EM: Feasibility of neuromuscular training in patients with severe hip or knee OA: the individualized goal-based NEMEX-TJR training program. *BMC musculoskeletal disorders* 2010; 11: 126.
37. BARTHOLDY C, WARMING S, NIELSEN SM, CHRISTENSEN R, HENRIKSEN M: Replicability of recommended exercise interventions for knee osteoarthritis: a descriptive systematic review of current clinical guidelines and recommendations. *Osteoarthritis Cartilage* 2017; 25 (Suppl. 1): 2.
38. BENNELL KL, DOBSON F, ROOS EM *et al.*: The influence of biomechanical characteristics on pain and function outcomes from exercise in medial knee osteoarthritis and varus malalignment: exploratory analyses from a randomised controlled trial. *Arthritis Care Res* 2015; 67: 1281-88.
39. KNOOP J, VAN DER LEEDEN M, ROORDA LD *et al.*: Knee joint stabilization therapy in patients with osteoarthritis of the knee and knee instability: Subgroup analyses in a randomized, controlled trial. *J Rehabil Med* 2014; 46: 703-7.
40. LIM BW, HINMAN RS, WRIGLEY TV, SHARMA L, BENNELL KL: Does knee malalignment mediate the effects of quadriceps strengthening on knee adduction moment, pain, and function in medial knee osteoarthritis? A randomized controlled trial. *Arthritis Rheum* 2008; 59: 943-51.
41. GARBER CE, BLISSMER B, DESCHENES MR *et al.*: American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc* 2011; 43: 1334-59.
42. BARTHOLDY C, JUHL C, CHRISTENSEN R, LUND H, ZHANG W, HENRIKSEN M: The role

- of muscle strengthening in exercise therapy for knee osteoarthritis: A systematic review and meta-regression analysis of randomized trials. *Semin Arthritis Rheum* 2017; 47: 9-21.
43. MOSENG T, DAGFINRUD H, SMEDSLUND G, OSTERAS N: The importance of dose in land-based supervised exercise for people with hip osteoarthritis. A systematic review and meta-analysis. *Osteoarthritis Cartilage* 2017; 25: 1563-76.
 44. SKOU ST, ROOS EM: Good Life with osteoarthritis in Denmark (GLA:D): evidence-based education and supervised neuromuscular exercise delivered by certified physiotherapists nationwide. *BMC Musculoskeletal Disord* 2017; 18: 72.
 45. ROOS EM, BARTON CJ, DAVIS AM *et al.*: GLA: D to have a high-value option for patients with knee and hip arthritis across four continents: Good Life with osteoarthritis from Denmark. *Br J Sports Med* 2018; 52: 1544-45.
 46. BENNELL KL, AHAMED Y, JULL G *et al.*: Physical therapist-delivered pain coping skills training and exercise for knee osteoarthritis: randomized controlled trial. *Arthritis Care Res (Hoboken)* 2016; 68: 590-602.
 47. FERNANDES L, HAGEN KB, BIJLSMA JW *et al.*: EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. *Ann Rheum Dis* 2013; 72: 1125-35.
 48. MESSIER SP, MIHALKO SL, LEGAULT C *et al.*: Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. *JAMA* 2013; 310: 1263-73.
 49. SKOU ST, RASMUSSEN S, LAURSEN MB *et al.*: The efficacy of 12 weeks non-surgical treatment for patients not eligible for total knee replacement: a randomized controlled trial with 1-year follow-up. *Osteoarthritis Cartilage* 2015; 23: 1465-75.
 50. SKOU ST, ROOS EM, LAURSEN MB *et al.*: Total knee replacement and non-surgical treatment of knee osteoarthritis: 2-year outcome from two parallel randomized controlled trials. *Osteoarthritis Cartilage* 2018; 26: 1170-80.
 51. SVEGE I, NORDSLETTEN L, FERNANDES L, RISBERG MA: Exercise therapy may postpone total hip replacement surgery in patients with hip osteoarthritis: a long-term follow-up of a randomised trial. *Ann Rheum Dis* 2015; 74: 164-69.
 52. WANG L, LEE M, ZHANG Z, MOODIE J, CHENG D, MARTIN J: Does preoperative rehabilitation for patients planning to undergo joint replacement surgery improve outcomes? A systematic review and meta-analysis of randomised controlled trials. *BMJ Open* 2016; 6: e009857.
 53. RODDY E, ZHANG W, DOHERTY M *et al.*: Evidence-based recommendations for the role of exercise in the management of osteoarthritis of the hip or knee--the MOVE consensus. *Rheumatology (Oxford)* 2005; 44: 67-73.
 54. NICOLSON PJ, BENNELL KL, DOBSON FL, VAN GINCKEL A, HOLDEN MA, HINMAN RS: Interventions to increase adherence to therapeutic exercise in older adults with low back pain and/or hip/knee osteoarthritis: a systematic review and meta-analysis. *Br J Sports Med* 2017; 51: 791-99.
 55. GAY C, CHABAUDA A, GUILLEY E, COUDEYRE E: Educating patients about the benefits of physical activity and exercise for their hip and knee osteoarthritis. Systematic literature review. *Ann Phys Rehabil Med* 2016; 59: 174-83.
 56. FITZGERALD GK, FRITZ JM, CHILDS JD *et al.*: Exercise, manual therapy, and use of booster sessions in physical therapy for knee osteoarthritis: a multi-center, factorial randomized clinical trial. *Osteoarthritis Cartilage* 2016; 24: 1340-49.
 57. NEWBERRY SJ, FITZGERALD J, SOOHOO NF *et al.*: Treatment of Osteoarthritis of the Knee: An Update Review. In: *AHRQ Comparative Effectiveness Reviews*. ROCKVILLE (MD): Agency for Healthcare Research and Quality (US); 2017.
 58. PARKES MJ, MARICAR N, LUNT M *et al.*: Lateral wedge insoles as a conservative treatment for pain in patients with medial knee osteoarthritis: a meta-analysis. *JAMA* 2013; 310: 722-30.
 59. HENRIKSEN M, SKOU ST: Bandager til knælidelser. *Ugeskr Laeger* 2017; 179.