Nonoperative Treatment Options for Knee Osteoarthritis

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2.1 Introduction and Scope

This chapter provides a compilation of the latest knowledge regarding nonoperative treatment of knee osteoarthritis. The aim is to provide an accessible reference for clinicians to establish a coordinated and effective management plan with maximum patient involvement. It is hoped that this reference can provide clear guidance in the selection of known treatment options and provide useful guidelines for both initial counselling and subsequent active management of the disease.

Currently, both clinicians and patients are bombarded with information available on the Internet and popular media regarding "miracle cures" and "cutting edge therapies" for the treatment of knee osteoarthritis. The top ten search results from google.com.au and facebook.com reveal a spectrum of quality with regard to available information (Fig. 2.1). Overall, the information from Google included a mixture of credible, useful information, as well as some outdated information. However, a considerable amount of results would be considered as misinformation combined with sponsored content, which can be difficult for lay readers to discern the inherent bias.

To address the volume of potentially misleading information available to both clinicians and patients, this chapter has been compiled from guidelines released by authoritative sources and updated with a comprehensive literature search of updated information, with emphasis on the

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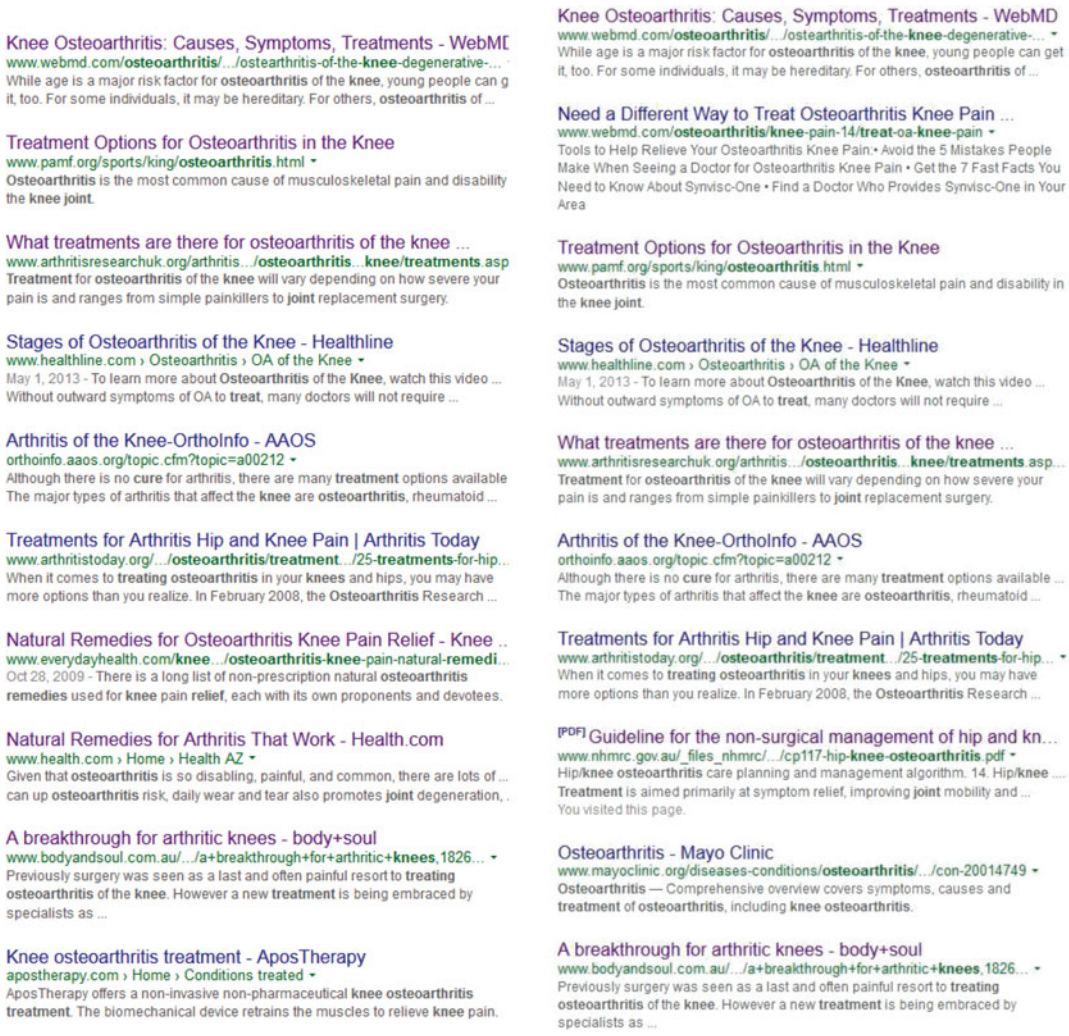

Fig. 2.1 First page of search results from google.com.au using the terms "treatments for knee osteoarthritis"

highest quality systematic reviews and meta-analyses of current evidence.

2.2 Authoritative Recommendations

The Osteoarthritis Research Society International (OARSI) recently released an evidence-based summary of recommended treatment options for knee osteoarthritis [1]. The options recommended are summarised in Fig. 2.2 and comprise a set of *core treatments,* suggested for the management of all types of osteoarthritis in all individuals, as well as treatment options specific to knee OA for individuals with and without serious comorbidities.

Similarly, the American Academy of Orthopaedic Surgeons (AAOS) has also released a 2nd edition of their clinical practice guidelines for first-line treatment of knee OA [2]. These recommendations are summarised in Table 2.1 and address a number of options not covered in the OARSI recommendations. However, the AAOS clinical practice guidelines are older (2013), and updated information has since become available for a number of recommendations.

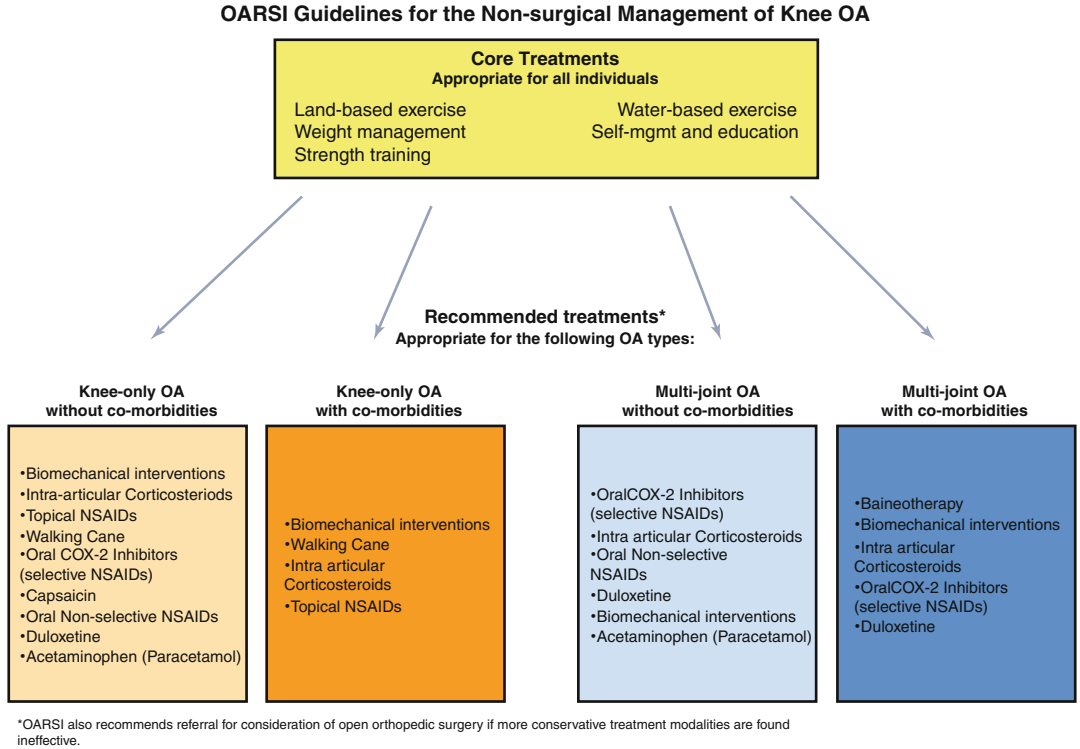

Fig. 2.2 OARSI guidelines for non-surgical management of knee OA [1]

Table 2.1 Summary of AAOS clinical practice guidelines for non-operative treatment of knee OA [2]

Treatment	Recommendation	Strength	Updated information
1. Self-management; strengthening; low-impact aerobic exercise; neuromuscular education; physical activity	Recommended	Strong	Yes
2. Weight loss BMI > 25	Suggested	Moderate	No change
3. (a) Acupuncture	Unable to recommend	Inconclusive	None available
(b) Physical agents (electrotherapy)	Unable to recommend	Inconclusive	No change
(c) Manual therapy	Unable to recommend	Inconclusive	Yes
4. Valgus-directing knee brace	Unable to recommend	Inconclusive	Yes
5. Lateral wedge insoles	Unable to recommend	Moderate	Yes
6. Glucosamine or chondroitin	Cannot be recommend	Strong	Yes
7. (a) NSAIDS or tramadol	Recommended	Strong	No change
(b) Acetaminophen	Unable to recommend	Inconclusive	Yes
8. Intra-articular corticosteroids	Unable to recommend	Inconclusive	Yes
9. Hyaluronic Acid	Cannot recommend	Strong	Yes

2.2.1 Core Treatments

2.2.1.1 Exercise

Exercise is any targeted, prescribed or organised activity where participation occurs with the aim of improving strength, endurance, range of motion or aerobic capacity [1]. Exercise to treat knee OA can be based on land or in water, and reductions in pain and improvements in function are well established. The OARSI guidelines are

based on a systematic review and a meta-analysis of randomised controlled trials, with a good overall quality of the evidence. The average size of the effect for land-based exercise on pain reduction ranges from small to moderate. Similarly, water-based exercise also provides beneficial effects on pain and function, although the expected size of the effect has yet to be established. A more recent systematic review [3] of high-quality evidence reported that land-based exercise provided a moderate short-term (up to 6 months post-treatment) reduction in pain and improved physical function.

2.2.1.2 Strength Training

Exercise that specifically targets the ability of muscles to generate force, known as strength training, has been singled out in the OARSI recommendations as a key modality to reduce pain and improve physical function for knee OA. In particular, targeting the quadriceps and other lower-limb muscle groups should be considered as a key treatment option. Strength training can take a variety of forms, but recent evidence has been based on exercises conducted on land in group or individual sessions, and training combined with mobilisation is considered most effective.

2.2.1.3 Weight Loss

Being overweight or obese is a significant risk factor for knee osteoarthritis in older adults [4, 5]. Weight loss is particularly important for individuals diagnosed with knee OA who are also considered overweight or obese. Although a programme involving diet modification with exercise is considered most effective, a moderate reduction in weight (5 % of bodyweight) over a 20-week period provides small to moderate reductions in pain and improves physical function [1]. These recommendations are based on good-quality evidence from a systematic review and meta-analysis of randomised controlled trials. A more recent systematic review [6] suggests that weight reduction with combined diet modification and exercise is effective for pain relief and functional improvements even in elderly individuals (70 + years). Involvement of a dietitian and/or an exercise physiologist may be helpful in achieving these goals.

2.2.1.4 Self-Management and Education Programmes

Self-management programmes are distinct from patient education as they encourage people diagnosed with chronic disease to actively participate in the treatment of their condition [7]. The OARSI guidelines [1] suggest that self-management and education programmes can provide a small amount of pain reduction based on good-quality evidence stemming from a systematic review and a meta-analysis of randomised controlled trials. However, a more recent systematic review [7] found that the available evidence was of low to moderate quality but confirmed that such programmes provide no or small benefits up to 21 months after treatment. Importantly, this review reported that self-management programmes do not compare favourably to attention control methods or usual care.

2.2.1.5 Biomechanical Interventions

Treatment of knee OA should focus on the mechanical behaviour of the affected knee at any stage of disease progression but particularly at initial diagnosis in those with early signs [8]. Interventions designed to adjust knee and lower-limb loading during locomotion vary considerably. However, the OARSI guidelines focus on foot orthoses or shoe inserts or valgus knee braces. Foot orthoses alter the mechanical alignment of the lower leg by enhancing the valgus correction of the calcaneus, while braces apply an opposing valgus force to attenuate load on the medial knee compartment [9]. The proposed benefits of these interventions include pain reduction, reduced analgesic dosage, improved physical function, stiffness and potentially slowing disease progression. A more recent systematic review and meta-analysis [10] of valgus bracing reported a moderate to high effect on the knee adduction moment, which has been associated with disease progression [11], although the quality of current evidence remains fair.

2.2.2 Treatments Specifically for Knee Osteoarthritis

2.2.2.1 Intra-articular Injection of Corticosteroids

Corticosteroids mimic naturally occurring hormones that are anti-inflammatory in function. Common agents used to treat knee OA include betamethasone, methylprednisolone and triamcinolone which are injected directly into the joint space. The expected benefits of these injections are short-term pain relief, improved physical function and reduced joint inflammation. The current OARSI guidelines [1] suggest that corticosteroids are effective in providing short-term pain relief but are likely not appropriate for longer-term pain management. A more recent systematic review using network meta-analysis confirmed the effectiveness of corticosteroids in pain relief but reported a lack of effectiveness for improving joint function and stiffness. An earlier systematic review reported that the clinical response to injection may vary and can be predicted based on demographic and clinical factors [12].

2.2.2.2 Non-steroidal Anti-inflammatory Drugs (NSAIDs)

These medications have an anti-inflammatory effect and can be applied topically on the affected joint or taken orally. Oral NSAIDs are separated into Cox-2 inhibitors or non-selective options, and there is a risk of adverse events with extended use, despite moderate effects on pain. Cox-2 medications are felt to have a safer side effect profile than non-selective medications. Although the overall effect size of topical NSAIDs remains unknown, they are considered safer and better tolerated than oral NSAIDs. While oral NSAIDs are usually quite effective in pain management, their potential side effect profile makes them more suited to occasional rather than regular use, and caution should be employed in patients with any history of peptic ulceration and renal disease in particular.

2.2.2.3 Capsaicin

Capsaicin is a capsicum extract with anti-inflammatory properties which is applied topically. Although it has potential to reduce joint inflammation, reduce pain and increase function, based on good-quality evidence (systematic review and meta-analysis of randomised controlled trials), its effects range from small to moderate for reducing pain and improving function compared to placebo.

2.2.2.4 Duloxetine

Duloxetine is a serotonin-norepinephrine reuptake inhibitor and is usually prescribed as an antidepressant. Although there is fair evidence available based on systematic reviews and randomised trials, the size of its effect on knee pain remains unavailable; however, it has been reported to significantly decrease pain and improve physical function in knee OA.

2.2.2.5 Acetaminophen

Also known as paracetamol, this is commonly prescribed for a wide spectrum of pain, including knee OA. Good-quality evidence suggests that it has a small to moderate effect for pain and function, while a more recent review [12] suggests that its effects are small for pain relief. This is a medication than can be used regularly due to the relatively safe side effect profile and is probably more effective if used regularly.

2.3 Additional Treatment Options

2.3.1 Psychological Therapies

An individual's mental health is associated with the severity of their knee OA pain and risk of pain flares [13], with depression in particular associated with self-reported pain levels [14]. Psychological therapies have demonstrated efficacy in reducing pain, disability, depression and anxiety. Cognitive behavioural therapy is the most common approach reported in the literature and is typically delivered either in-person in group or individual sessions or via the Internet. Recent systematic reviews of low-quality evidence have reported small to moderate effects on

pain using traditional therapy methods [15] or by Internet delivery [16] in adults experiencing chronic pain for reasons other than headache but not specific to knee OA. However, there is potential in the future for psychological therapies to provide some benefit to individuals experiencing pain related to knee OA with little risk of adverse side effects.

2.3.2 Chondroitin

Chondroitin is a nutritional supplement containing chondroitin sulphate which is normally found in articular cartilage, and its loss is potentially associated with the progression of osteoarthritis in the knee. Supplementing chondroitin orally is thought to possibly provide pain reduction and may modify the disease process. Recent systematic reviews are favourable for its ability to achieve these effects with one review of low-quality evidence [17] reporting an overall 10 % reduction in pain compared to placebo, while another review of moderate-quality evidence concluded that chondroitin significantly reduced cartilage loss in OA knees compared to placebo [18]. Although these results should probably be treated with caution, considering its non-invasive nature and low risk of negative side effects, chondroitin could be considered a treatment option, particularly for early stage knee osteoarthritis.

2.3.3 Glucosamine

Glucosamine is an aminosaccharide naturally occurring in the body and is a principal substrate in the synthesis of proteoglycan, a key component of articular cartilage. Glucosamine therapy is provided as a nutritional supplement available without prescription. A recent systematic review of low-quality evidence [18] suggested that glucosamine sulphate is moderately effective at reducing pain associated with knee OA, while a second recent review of moderate-quality evidence [19] also indicated a significant reduction of cartilage loss compared to placebo for glucosamine sulphate, but not for glucosamine hydrochloride. Glucosamine sulphate provides a potential non-invasive treatment option, with a good safety profile for clinicians and patients to reduce pain and possibly slow the progression of cartilage loss and could be considered a possible option for early stage knee osteoarthritis treatment. As with chondroitin, although there are some studies showing positive results with glucosamine, the overall review of literature pertaining to these products would suggest that the evidence for clinical efficacy is modest, and therefore they cannot be strongly recommended for routine use.

2.3.4 Viscosupplementation

Refers to the intra-articular injection of hyaluronic acid, which is a main component of synovial fluid. Its proposed benefits include pain reduction, improved physical function and a low-risk of harm, with a particular emphasis on short-term improvement in pain post-injection. The current OARSI and AAOS guidelines are either unable to recommend viscosupplementation as a treatment option or indicate uncertain appropriateness. However, recent systematic reviews [12, 20] of low- to moderate-quality evidence reported moderate to large effects on pain relief, although variability in the clinical response was identified as a limiting factor [20]. A more recent review [21] of meta-analyses with low- to high-quality studies reported that intra-articular injection of hyaluronic acid improved function for up 6 months after treatment and was a viable option for patients with early stage knee osteoarthritis. Many of these more favourable studies should be interpreted with caution as they have been sponsored studies, and when the non-independent studies are excluded, the benefit would seem questionable.

2.3.5 Autologous Concentrated Plasma (ACP) or Platelet-Rich Plasma (PRP)

Platelet-derived growth factors regulate some processes in tissue repair. Currently, these factors

are derived from a patient's own blood sample and injected directly into the joint space after appropriate preparation. The scientific literature presently suffers from a lack of consensus on the clinical efficacy of these treatments. One systematic review [22] of eight articles with low- to moderate-quality evidence concluded that PRP efficacy remains uncertain. However, a systematic review and meta-analysis [23] of moderate-quality evidence indicated that PRP provides effective pain relief at least 6 months post-injection. In addition, a review of three meta-analyses of low- to high-quality evidence [24] found that PRP injections improved pain and function as early as 2 months after treatment with peak improvement at 6 months, with symptomatic relief for up to 12months. These authors concluded that particularly those with mild to moderate osteoarthritic changes in the knee should consider this as a treatment option.

2.3.6 Gait Modification

The first-line approaches for early knee osteoarthritis should target the loading patterns around the knee during common daily activities [8]. Although biomechanical interventions should be an important part of OA treatment, the current OARSI guidelines only recommend the use of foot orthoses or valgus braces. However, the loads imposed on the knee during walking can also vary with different walking strategies. One systematic review [25] of low- to moderate-quality evidence suggested that the knee adduction moment, a key loading parameter in the progression of knee OA, can be reduced by increasing a person's step width or hip internal rotation, increasing their trunk lean or by encouraging an inward (medial) knee thrust or inward foot weight transfer.

A more recent review [26] of low- to moderate-quality evidence also reported that reductions in knee adduction moment could be achieved by altering foot progression angle (toe-in or toe-out), shortening stride length, leaning the trunk to one side or encouraging an inward thrust of the knee during weight bearing. Gait retraining offers a low-cost and low-risk option for intervention in knee osteoarthritis; however, modifications that are suitable for each individual may take time to identify due to the natural variation of gait patterns and will require a concerted effort on the part of both clinician and patient. Clinicians and patients should also be prepared to manage the potential for gait modification to shift load to other joints, particularly in patients with joints other than the knee affected by osteoarthritis or significant comorbidities.

2.3.7 Stem Cell Therapy

Stem cells are theoretically capable of differentiating into a range of specialised cells, with particular emphasis in therapeutic applications for osteoarthritis for their capacity to regenerate cartilage. For stem cell therapy, cells can be derived from mesenchyme (bone marrow), adipose tissue, the patient's own synovium or allogenic umbilical cord material. Unfortunately, despite its theoretical potential, the evidence of clinical efficacy remains weak, with a recent clinical review [27] of low- to moderate-quality evidence highlighting the lack of in vivo data for these therapies. At this time, stem cell therapy cannot be recommended as a viable treatment option for knee osteoarthritis, but is certainly an appropriate area for ongoing clinical research to better define the treatment and its role in OA.

2.4 Recommended Treatment Strategy for Knee OA

A limitation of the current guidelines and authoritative evidence is the lack of integration between treatment modalities and guidance for the clinician in regard to the optimal approach for any given patient. Although considerable amounts of research are required to address this gap with high-quality evidence, evidence-based recommendations have been released by the European Union League Against Rheumatism (EULAR) [28] for non-pharmacological management of knee OA, with a framework for applying many of

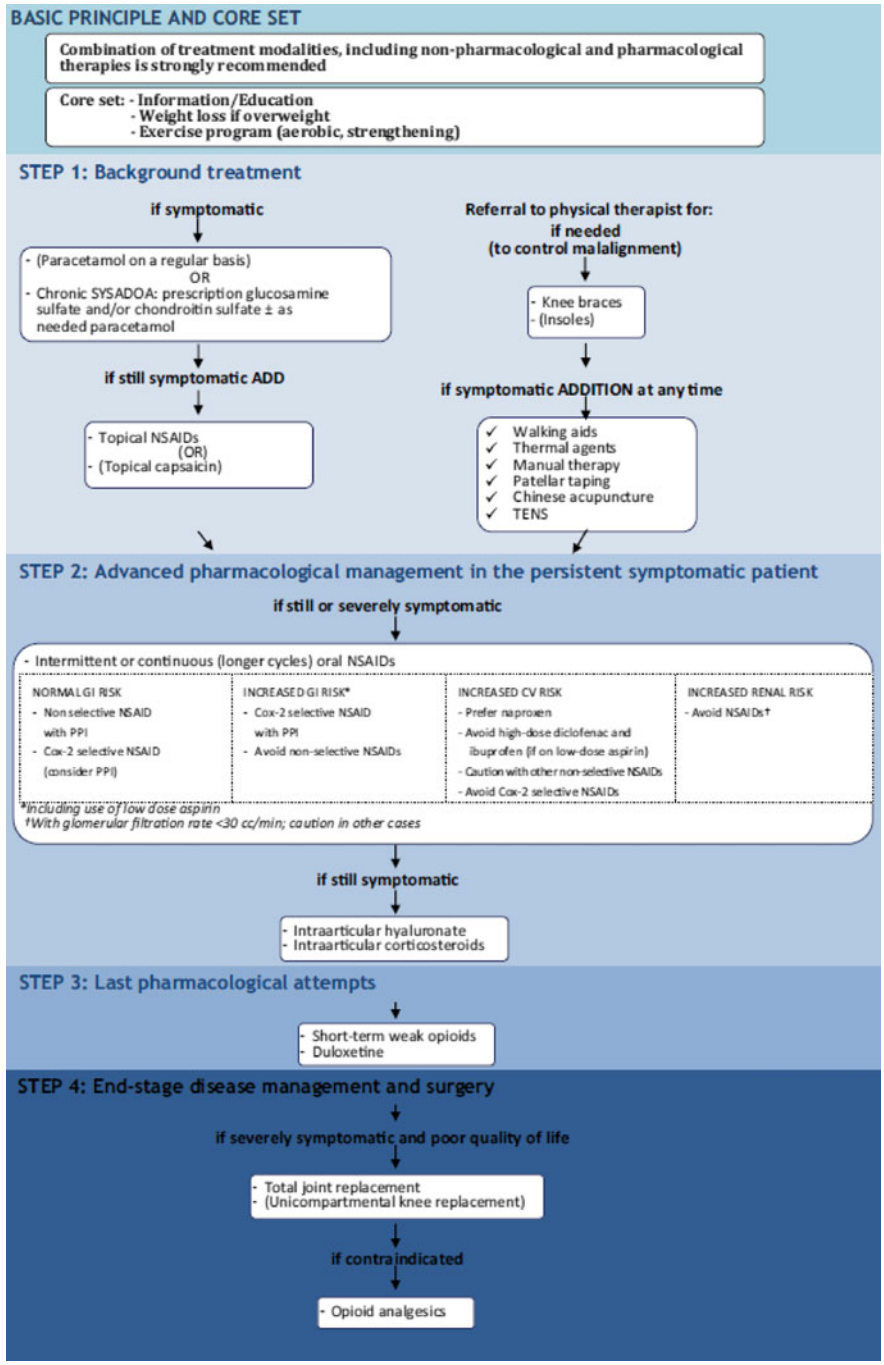

Fig. 2.3 Proposed treatment algorithm for knee osteoarthritis [29]

the treatment options covered in this chapter. Other recent attempts to develop treatment algorithms for knee OA have been presented (Fig. 2.3) [29]. A limitation of the model illustrated in Fig. 2.3 is its linear nature between diagnosis and disease progression to end-stage intervention. In the early stages of the disease, it is likely that the clinician and the patient may move through a

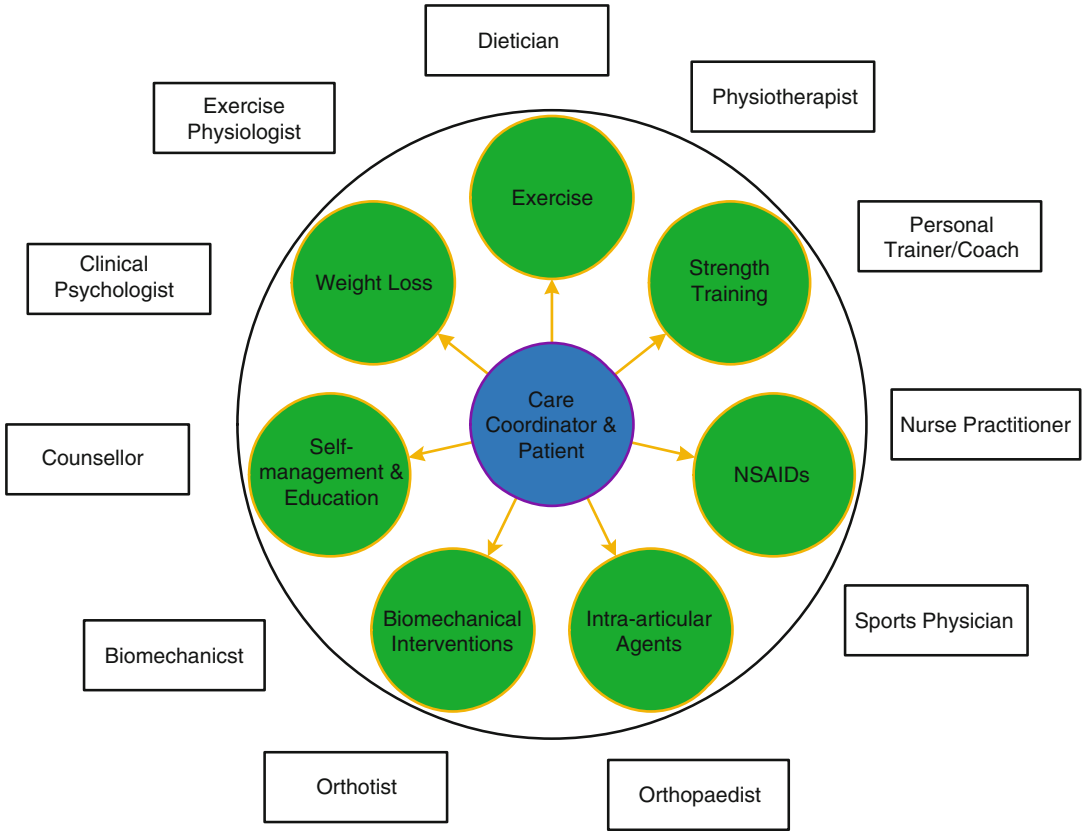

Fig. 2.4 Proposed model of coordinated care for non-operative treatment of knee osteoarthritis

range of modalities in a circular manner as the severity of pain and functional disability varies.

An ongoing difficulty that the clinician faces in managing OA non-operatively is initially convincing patients of the value of the multidisciplinary approach and subsequently providing a coordinated programme that ensures patients get the appropriate treatment from each of the modalities in a clear and well-managed fashion. For patients, this requires a clear explanation of the problem and the proposed solutions and sufficient education so that the treatment pathway and goals are clear to the patient. Written and Web-based resources can be provided for the patient and a clear timetable for treatment including regular assessments to evaluate progress and modify programs accordingly. A central coordinator such as a nurse practitioner who has a good relationship with the patient and can help coordinate treatment, advise and provide regular feedback is central to the success of this type of program.

Therefore, based on the literature summarised in this chapter, a coordinated-care model is recommended with specialists engaged to apply specific treatment modalities where appropriate. A key emphasis of this approach is coordinated care and ongoing feedback from the patient regarding the care plan and effects of specific treatments with a close working relationship between the care coordinator, the patient and specialists (Fig. 2.4). The care coordinator should be an appropriately qualified health professional such as a nurse or general practitioner, and the key traits of a successful coordinator are a basic understanding of the mechanisms of each treatment option and an ability to establish and maintain an interpersonal relationship with the patient.

The care coordinator should be actively involved in determining the key treatment

priorities with a thorough needs analysis, including assessment of symptoms and disability using standardised and validated instruments. From the patient clinical profile, a patient-specific model of care should be established in collaboration with the patient that targets the priority symptoms with the safest and least invasive modalities in the first instance, with focus on the core treatment options (Fig. 2.4). The care coordinator should aim to perform a thorough reassessment of the patient's condition at appropriate milestones, such as conclusion of supervised therapy. Positive feedback to the patient regarding the effectiveness of the program improves compliance and likelihood of sustaining ongoing improvement.

2.5 Summary and Conclusions

Historically knee osteoarthritis has been thought to have very limited treatment options, but clinicians and patients in the present day have many options to relieve symptoms and restore function reasonably quickly and safely. Many of the regularly promoted options have questionable clinical efficacy and safety, and it can be difficult to separate valid evidence from advertising to determine the most appropriate options with information publicly available, particularly through popular Web search engines. For this reason, this chapter has highlighted a series of core non-surgical treatment options based on the highest quality consensus recommendations from authoritative sources. In addition, a series of options have been identified that could provide viable treatments, with evidence of clinical efficacy that has been established since publication of the consensus recommendations. Given the limited surgical options, particularly for younger patients, establishing and maintaining optimal non-surgical treatment is critical for these patients and is an area that all health professionals managing these patients should be familiar with.

The onset and progression of knee osteoarthritis is a multifactorial and complex process, which can be targeted by a dynamic and adaptive mix of treatment options for symptom relief in the early stages of the disease. In light of this, this chapter has also presented some recommendations for how patient care should be arranged in a coordinated manner with a close working relationship between a care coordinator and the patient, with a mix of specialists providing specific treatment input where appropriate. Although the recommendations for non-surgical management of knee osteoarthritis will continue to rapidly evolve, this chapter provides a basis for clinicians and patients to have an informed discussion on current treatment options for optimising non-surgical management of knee OA. This should always predate any discussion of surgical management and hopefully if applied effectively, will allow appropriate deferment of surgical management until absolutely necessary.

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