

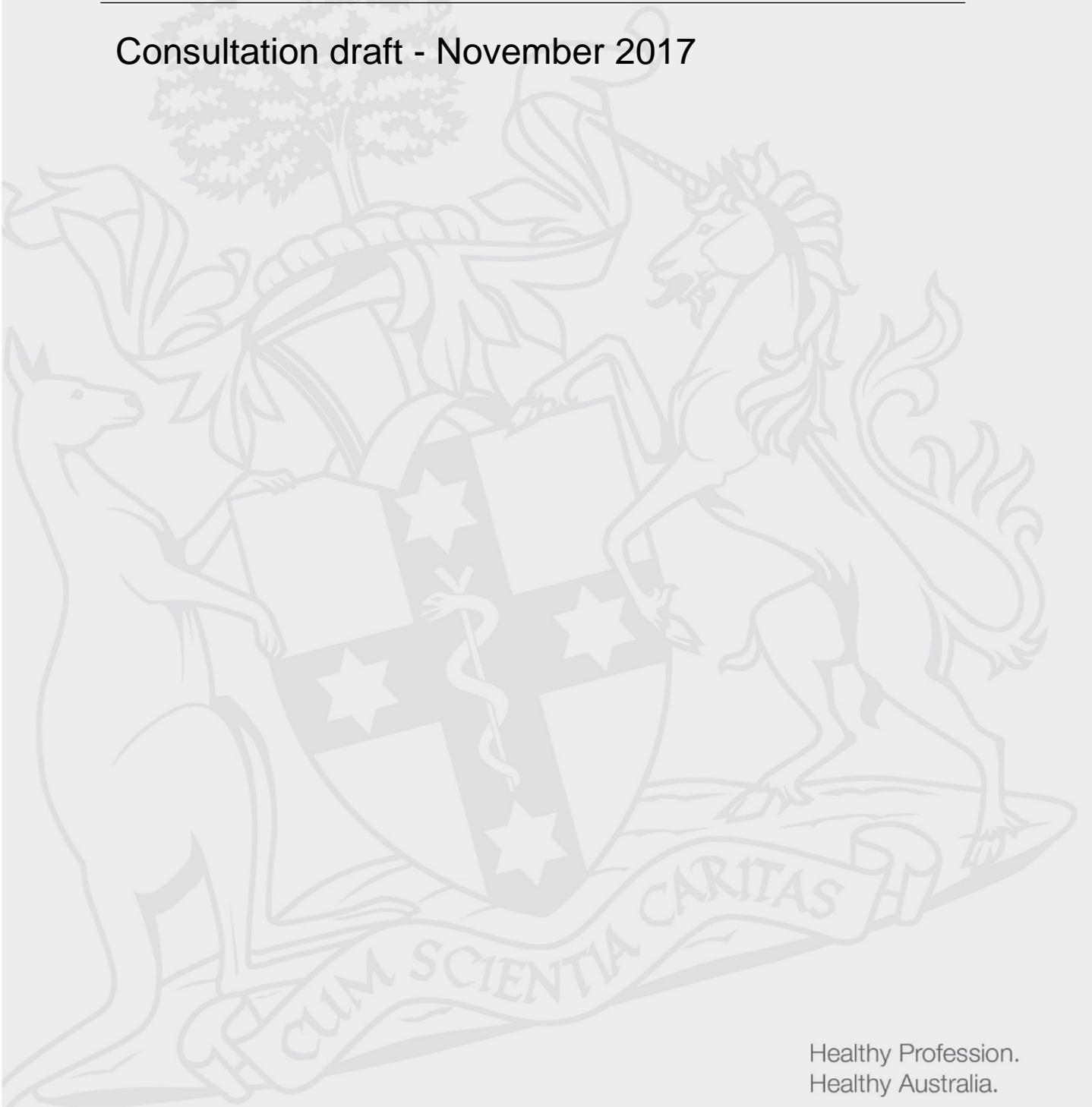


RACGP

Royal Australian College of General Practitioners

Guideline for the management of knee and hip osteoarthritis

Consultation draft - November 2017



Healthy Profession.
Healthy Australia.

Foreword, Acknowledgements, Acronyms

To be completed

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Conflicts of interest

This publication has been produced in accordance with the rules and processes outlined in the RACGP Conflict of Interest (COI) Policy. The RACGP COI Policy is available at www.racgp.org.au/support/policies/organisational

Conflict of interest disclosures are available in Appendix 6 of the Technical document.

Working Group members completed a conflict of interests register before commencement of guideline development. Any additional conflicts of interest were declared at the start of all meetings and appropriately recorded. If a member declared a conflict in relation to a specific intervention (with the exception of conducting research), the member did not participate in the discussion or decision-making for the intervention.

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Plain language summary

Osteoarthritis (OA) is a chronic disease and the most common form of chronic arthritis. It is characterised by joint pain, stiffness, swelling and most commonly affects the hands, knees and hips. OA occurs most commonly in people over the age of 55. Common risk factors include injury, weight and increasing age. With increasing age and obesity, the number of Australians suffering from OA is expected to rise from 2.2 million in 2015 to almost 3.1 million by 2030. There is no cure, but there are many treatments and approaches to managing the long-term symptoms of this disease. For someone with OA, their GP is often the first point of contact in the healthcare system. This guideline provides Australian GPs with advice and recommendations for the management of people with knee and or hip osteoarthritis and has a strong focus on non-surgical treatments to educate and improve the health of people with OA. Many of the recommendations are summarised below:

A healthy lifestyle

- Regular exercise is important for relieving pain in people with knee and hip OA. These include land-based activities such as yoga and walking and water-based activity such as hydrotherapy
- Weight management is important and is strongly recommended for people with knee and hip OA

Non-drug treatments

- Applying heat packs or hot water bottles can relieve muscle tension and soreness and improve blood flow. However, applying cold packs, or ice should not be offered.
- Footwear marketed for OA should not be offered however patients should avoid certain footwear such as high-heeled shoes
- There are different types of knee taping. Speak to your health professional about whether knee taping, such as patellar taping, would be helpful to for you.
- Using a cane or other devices such as a walker or crutches can help walking and assist movement in people with knee OA.
- Electromagnetic therapy (pulsed shortwave therapy) and transcutaneous electrical nerve stimulation (TENS) may be beneficial in some people with knee and/or hip OA.
- Acupuncture for people with knee and/or hip OA is not recommended as there are only small benefits and multiple visits can be expensive.
- Therapeutic ultrasound should not be offered
- Cognitive behavioural therapy (CBT) is recommended but any existing mental health conditions and patient choices must be considered.

Medication

- Paracetamol, and nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and aspirin are recommended for at low doses and short periods
- Pain relieving creams (topical NSAIDs) may be useful to manage pain
- Creams containing the extract of hot chilli peppers (capsaicin) are not recommended for managing pain
- Corticosteroid injections should be offered for short-term symptom relief for people with knee OA only
- Opioids, a class of prescription-only medication are not recommended
- Medications used in the treatment of osteoporosis, such as bisphosphonates and calcitonin are not recommended

Complementary and alternate therapies and nutraceuticals

- Speak to your health professional about herbal supplements such as avocado-soybean unsaponifiables, Indian frankincense (boswelia serrata extract), turmeric and pycnogenol. There is low and very low evidence benefits for pain and function.
- Glucosamine and chondroitin nutraceuticals should not be offered.
- Vitamin D should not be offered. Whilst it is relatively safe, there is little evidence of effectiveness.

We strongly recommend against surgery such as arthroscopic lavage and debridement, meniscectomy and cartilage repair for people with knee OA unless the person also has symptoms and signs of a “locked knee”.

Summary of the guideline

The Royal Australian College of General Practitioners (RACGP) first developed the Guidelines for the non-surgical management of hip and knee osteoarthritis in 2009. There has been substantial progress since in evaluating the effectiveness and safety of commonly used and new therapies for osteoarthritis (OA). The objective of the 2nd edition of these guidelines is to present the best available current scientific evidence for OA interventions other than joint replacement for the hip and knee.

Target population and audience

This guideline applies to all adult patients diagnosed with symptomatic OA of the hip and or knee up until referral for joint replacement. While this guideline is intended primarily for use in the primary care setting by general practitioners (GPs), consideration of the relevance of this guideline was also given to other health professionals who treat this condition. This is reflected in the multidisciplinary composition of the guideline development Working Group, including consumer representatives. Decisions are agreed upon by the entire Working Group.

Recommendations in this guideline

The RACGP has used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach to rate the quality of evidence and formulate strength of recommendations. Recommendations have been formulated using the GRADE evidence to decision framework considering: the quality of evidence, the balance between benefits and harms, values and preferences and resource use and other relevant considerations.

Strength of recommendations

<ul style="list-style-type: none">• Strong recommendation for the intervention• Strong recommendation against the intervention	The Working Group is very confident that the benefits of an intervention clearly outweigh the harms (or vice versa)
<ul style="list-style-type: none">• Conditional recommendation for the intervention• Conditional recommendation against the intervention	Denotes uncertainty over the balance of benefits and harms, such as when the evidence quality is low or very low, or when patient preferences or costs are expected to impact the decision, and as such refer to decisions where consideration of patient preferences is essential for decision making
<ul style="list-style-type: none">• Conditional (Neutral) recommendation	The Working Group cannot determine the direction of the recommendation

Recommendations are formulated using standardised wording, such as using the term ‘recommend offering’ for strong recommendations and ‘suggest offering’ for conditional or weak recommendations or other terminology such as “should” and “may”.

Quality of Evidence

The strength of recommendation is supported by a rating of the quality of the evidence as very low, low, moderate or high.

Each recommendation is supported with information explaining what the intervention is, the rationale for the recommendation and any associated harms. The intention is to provide sufficient information as to why the recommendation was made to enable a GP to discuss and recommend options with their patient. More information about the GRADE approach can be found within [2.4. Formulation of recommendations](#).

Algorithms

Accompanying algorithms have been developed from information in the guideline to provide guidance for the holistic assessment and diagnosis, non-surgical management and surgical management of symptomatic OA in adult patients. (Algorithms are also available as an accompanying document on the consultation page - *Holistic assessment and diagnosis of knee and hip OA – Draft algorithms 20 Nov 2017*).

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Summary of recommendations

3.1 Non-pharmacologic interventions

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Self-management education programs – knee and/or hip	<p>We are unable to recommend either for or against formal face-to-face self-management education programs for people with knee and/or hip OA.</p> <p>However, clinicians should provide information to enhance understanding about OA, its prognosis and its optimal management.</p>	conditional (neutral) recommendation	Very low
Cognitive behavioural therapy – knee and/or hip	<p>We suggest offering cognitive behavioural therapy for people with knee and/or hip OA.</p> <p>Clinicians should consider whether CBT is appropriate taking into account psychological co-morbidities and patient preference. They should be cognizant of issues related to cost and access. It is recommended that CBT is combined with exercise to improve outcomes.</p>	conditional for recommendation	Low (knee) Very low (hip)
Land-based exercise – knee	<p>We strongly recommend offering land-based exercise for all people with knee OA to improve pain and function regardless of their age, structural disease severity, functional status or pain levels.</p> <p>Exercise has also been found to be beneficial for other comorbidities and overall health. We strongly recommend muscle strengthening exercise, walking and Tai Chi. We suggest offering stationary cycling and/or hatha yoga. Clinicians should prescribe an individualised exercise program taking into account the person's preference, capability and the availability of resources and local facilities. Dosage should be progressed and realistic goals set.</p> <p>Attention should be paid to strategies to optimise adherence. Referral to an exercise professional to assist with exercise prescription and to provide supervision may be appropriate for some patients.</p>	<p>strong for recommendation (all land based, muscle-strengthening, walking, Tai Chi)</p> <p>conditional for recommendation (stationary cycling, Hatha yoga)</p>	<p>Low (land-based, Tai Chi)</p> <p>Very low (Hatha yoga, stationary cycling, walking, muscle strengthening)</p>
Land-based exercise - hip	<p>We strongly recommend offering land-based exercise for all people with hip OA to improve pain and function regardless of their age, structural disease severity, functional status or pain levels.</p> <p>Exercise has also been found to be beneficial for other comorbidities and overall health. However, we are unable to specifically recommend either for or against different types of land-based exercise at this stage. Clinicians should prescribe an individualised progressive exercise program taking into account the person's preference, capability and the availability of local facilities. The clinician should monitor the patient's response to the exercise program</p>	<p>strong for recommendation (when combining all studies of land-based exercise)</p> <p>conditional (neutral) for recommending one type of land based exercise over another (muscle strengthening, walking, stationary cycling, Tai Chi, hatha yoga)</p>	<p>Moderate (land-based)</p> <p>Very low (hatha yoga, Tai Chi, stationary cycling, walking, muscle strengthening)</p>

Intervention	Recommendation	Strength of recommendation	Quality of evidence
	and could try a different form of land-based exercise if improvements are not evident. Attention should be paid to strategies to optimise adherence. Referral to an exercise professional to assist with exercise prescription and provide supervision may be useful for some patients.		
Aquatic exercise/hydrotherapy – knee and/or hip	We suggest offering aquatic exercise/hydrotherapy for people with knee and/or hip OA. This will depend upon personal preference and the availability of local facilities.	conditional for recommendation	Low
Manual therapy (massage, mobilisation, manipulation) – knee and/or hip	We suggest offering a short course of manual therapy for people with knee and/or hip OA. This should be considered only as an adjunctive treatment to enable engagement with active management strategies and only for short term management, cognisant of issues related to cost and access.	conditional for recommendation	Low (massage) Very low (mobilisation and manipulation)
Weight management – knee and/or hip	We strongly recommend weight management for people with knee and/or hip OA. For those who are overweight or obese, a minimum weight loss target of 7.5% of body weight is recommended. Weight loss should be combined with exercise for greater benefits. For people of healthy body weight, education about the importance of maintaining healthy body weight is essential.	strong for recommendation (weight management) conditional for recommendation (combination weight management plus exercise)	Very low
Heat therapy – knee and/or hip	We suggest offering local heat therapy (e.g. hot packs) as a self-management strategy for people with knee and/or hip OA. This should be considered only as an adjunctive treatment.	conditional for recommendation	Very low
Cold therapy – knee and/or hip	We suggest not offering local cold application (e.g. ice packs) for people with knee and/or hip OA.	conditional against recommendation	Very low
Knee braces	We are unable to recommend either for or against the use of varus unloading/re-alignment braces for people with lateral tibiofemoral compartment knee OA. We suggest not offering valgus unloading/re-alignment braces for people with medial compartment tibiofemoral knee OA. We suggest not offering realigning patellofemoral braces for patellofemoral OA.	conditional (neutral) recommendation (varus unloading/re-alignment braces) conditional against recommendation (valgus unloading/re-alignment braces) conditional against recommendation (re-aligning patellofemoral braces)	Very low (varus unloading/re-alignment) Low (valgus unloading/re-alignment braces) Very low (realigning patellofemoral braces) braces - no RCT data)
Shoe orthotics (medial and lateral wedge insoles – knee, shock absorbing insoles and arch supports - knee and hip)	We are unable to recommend either for or against the use of medial wedged insoles for people with lateral tibiofemoral OA and valgus deformity. We suggest not offering lateral wedge insoles for people with medial tibiofemoral knee OA.	conditional (neutral) recommendation (medial wedge insoles for lateral tibiofemoral OA) conditional against recommendation (lateral wedge insoles)	Very low (medial, lateral wedged insoles) Very low (shock absorbing insoles, arch support - no RCT data)

Intervention	Recommendation	Strength of recommendation	Quality of evidence
	We are unable to recommend either for or against the use of shock absorbing insoles or arch supports	conditional (neutral) recommendation (shock absorbing insoles, arch supports)	Very low (all hip orthotics - no RCT data)
Footwear - knee	We suggest not offering unloading shoes, minimalist footwear or rocker-sole shoes for people with symptomatic knee OA. However, clinicians may consider advising patients to wear footwear with shock-absorbing properties and to avoid high heeled shoes.	conditional against recommendation	Very low (unloading shoes, minimalist footwear) Low (rocker sole shoes)
Taping – knee and hip	We are unable to recommend either for or against the use of patellar taping for people with knee OA. We suggest not offering kinesio taping for people with knee and/or hip OA.	conditional (neutral) recommendation (patellar taping) conditional against recommendation (kinesio taping)	Very low
Assistive walking device – knee and/or hip	We suggest offering an assistive walking device such as a cane for people with knee and/or hip OA, depending on a person's preference and capability.	conditional for recommendation	Low (knee) Very low (hip)
Pulsed electromagnetic/shortwave therapy – knee and/or hip OA	We do not recommend either for or against electromagnetic/shortwave therapy for people with knee and/or hip OA.	conditional (neutral) recommendation	Low (knee) Very low (hip)
Other electrotherapy – knee and/or hip (shockwave, interferential, laser)	We suggest not offering electrotherapy modalities of shockwave, interferential or laser for people with knee and/or hip OA.	conditional against recommendation	Low (laser) Very low (shock wave, interferential, laser-hip)
Transcutaneous electrical nerve stimulation (TENS) – knee and/or hip	We suggest offering transcutaneous electrical nerve stimulation (TENS) that can be used at home for people with knee and/or hip OA. Clinicians need to provide sufficient instructions on self-use and consider individual accessibility and affordability.	conditional for recommendation	Very low
Therapeutic ultrasound – knee and/or hip OA	We suggest not offering therapeutic ultrasound for people with knee and/or hip OA.	conditional against recommendation	Moderate (knee) Low (hip)
Acupuncture – knee and/or hip	We suggest not offering acupuncture for people with knee and/or hip OA.	conditional against recommendation	Low (knee) Very low (hip)

3.2 Pharmacologic interventions

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Paracetamol – knee and/or hip	We are unable to recommend either for or against the use of paracetamol for people with knee and/or hip OA. It might be reasonable to trial paracetamol for a short period and then discontinue use if it is not effective. Clinicians also need to monitor and capture adverse events that may be associated with its use.	conditional (neutral) recommendation	Very low
Oral Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) including cyclooxygenase-2 (COX-2) inhibitors – knee and/or hip	We suggest offering oral NSAIDs for people with knee and/or hip OA. It might be reasonable to trial oral NSAIDs at the lowest effective dose for a short period and then discontinue use if it is not effective. Clinicians also need to inform patients about, monitor and capture adverse events, especially gastrointestinal, renal and cardiovascular, that may be associated with its use.	conditional for recommendation	Moderate
Oral opioids – knee and/or hip	We do not recommend offering oral opioids for people with knee and/or hip OA.	strong against recommendation	Low (knee) Very low (hip)
Topical NSAIDs – knee and/or hip	We are unable to recommend either for or against the use of topical NSAIDs for people with knee and/or hip OA. It might be reasonable to trial topical NSAIDs for a short period and then discontinue use if not effective. Clinicians also need to monitor and capture the adverse effects along with its use.	conditional (neutral) recommendation	Moderate
Transdermal opioids – knee and/or hip	We do not recommend offering transdermal opioids for people with knee and/or hip OA.	strong against recommendation	Low
Topical capsaicin – knee and/or hip	We suggest not offering topical capsaicin for people with knee and/or hip OA.	conditional against recommendation	Low
Duloxetine – knee and/or hip	We suggest offering duloxetine for people with knee and/or hip OA.	conditional for recommendation	Moderate (knee) Low (hip)
Doxycycline – knee and/or hip	We do not recommend offering doxycycline for people with knee and/or hip OA.	strong against recommendation	Low (knee) Very low (hip)
Bisphosphonates - knee	We suggest not offering bisphosphonates for people with knee and/or hip OA.	conditional against recommendation	Very low
Calcitonin – knee and/or hip	We suggest not offering calcitonin for people with knee and/or hip OA.	conditional against recommendation	Very low
Strontium ranelate –knee and/or hip	We do not recommend offering strontium ranelate for people with knee and/or hip OA.	strong against recommendation	Moderate
Interleukin-1 (IL-1) inhibitors – knee and/or hip	We do not recommend offering IL-1 inhibitors for people with knee and/or hip OA.	strong against recommendation	Low
Anti-nerve growth factor (anti-NGF) – knee and/or hip	We suggest not offering anti-NGF for people with knee and OA	conditional against recommendation	Moderate
Fibroblast growth factor (FGF) – knee and/or hip	We do not recommend offering FGF for people with knee and/or hip OA.	strong against recommendation	Very low
Colchicine – knee and/or hip	We suggest not offering colchicine for people with knee and/or hip OA.	conditional against recommendation	Very low

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Methotrexate – knee and/or hip	We suggest not offering methotrexate for people with knee and/or hip OA.	conditional against recommendation	Low
Corticosteroid injection – knee or hip	We suggest offering an intra-articular corticosteroid injection for people with knee OA for short term use. Clinicians need to be cautious of the potential harms of repeated use.	conditional for recommendation	Very low
Viscosupplementation injection – knee and/or hip	We suggest not offering viscosupplementation injection for people with knee OA. We do not recommend offering viscosupplementation injection for people with hip OA.	conditional against recommendation strong against recommendation	Low
Platelet-rich plasma injection – knee and/or hip	We are unable to recommend either for or against the use of platelet-rich plasma injection for people with knee and/or OA	conditional (neutral) recommendation	Very low
Stem cell therapy – knee and/or hip	We do not recommend offering stem cell therapy for people with knee OA	strong against recommendation	Very low
Dextrose prolotherapy – knee and/or hip	We suggest not offering dextrose prolotherapy for people with knee OA	conditional against recommendation	Low

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3.3 Herbal therapies, supplements and nutraceuticals

3.3.1 Herbal therapies

Intervention	Recommendation	Strength of recommendation	Quality of evidence
avocado-soybean unsaponifiables – knee and/or hip	We are unable to recommend for or against the use of avocado-soybean unsaponifiables for people with knee and/or hip OA.	conditional (neutral) recommendation	Very low
Boswellia serrata extract – knee and/or hip	We are unable to recommend for or against the use of boswellia serrata for people with knee and/or hip OA.	conditional (neutral) recommendation	Very low
Curcuma/curcuminoid – knee and/or hip	We are unable to recommend for or against the use of curcuma/curcuminoid for people with knee and/or hip OA.	conditional (neutral) recommendation	Low
Pycnogenol – knee and/or hip	We are unable to recommend either for or against the use of pycnogenol for people with knee and/or hip OA.	conditional (neutral) recommendation	Low (knee) Very low (hip)

3.3.2 Nutraceuticals

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Glucosamine – knee and/or hip	We suggest not offering glucosamine for people with knee and/or hip OA.	conditional against recommendation	Very low (knee) Low (hip)
Chondroitin – knee and/or hip	We suggest not offering chondroitin for people with knee and/or hip OA.	conditional against recommendation	Very low
Glucosamine and chondroitin in compound form – knee and/or hip	We suggest not offering glucosamine and chondroitin in compound form for people with knee and/or hip OA.	conditional against recommendation	Very low
Vitamin D – knee and/or hip	We suggest not offering vitamin D for people with knee and/or hip OA.	conditional against recommendation	Low (knee) Very low (hip)
Omega-3 fatty acids - knee and/or hip	We suggest not offering omega-3 fatty acids for people with knee and/or hip OA.	conditional against recommendation	Very low
Collagen – knee and/or hip	We are unable to recommend either for or against the use of collagen for people with knee and/or hip OA.	conditional (neutral) recommendation	Low (knee) Very low (hip)
Methylsulfonylmethane – knee and/or hip	We are unable to recommend either for or against the use of methylsulfonylmethane for people with knee and/or hip OA.	conditional (neutral) recommendation	Very low
Diacerein – knee and/or hip	We suggest not offering diacerein for people with knee and/or hip OA.	conditional against recommendation	Very low

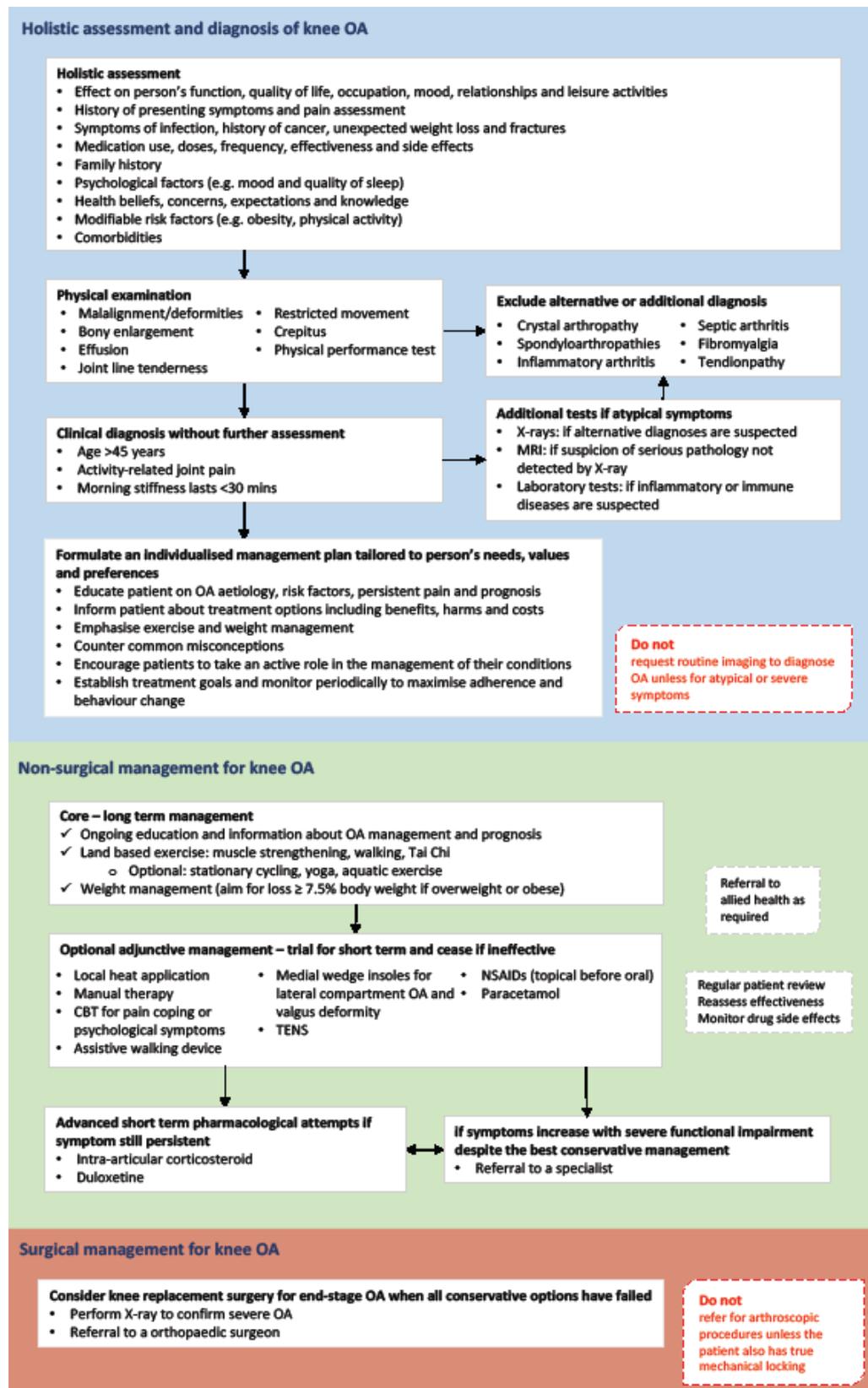
3.4 Surgical interventions

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Arthroscopic lavage and debridement, meniscectomy and cartilage repair – knee OA	We do not recommend offering arthroscopic, lavage and debridement, meniscectomy and cartilage repair for people with knee OA unless the person also has mechanical symptoms of a clinically locked knee as per Australian Knee Society Arthroscopy Position Statement.	strong against recommendation	Very low (lavage and debridement) Low (meniscectomy) Very low (cartilage repair)

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Algorithms

Holistic assessment and diagnosis of knee OA



Holistic assessment and diagnosis of hip OA

Holistic assessment and diagnosis of hip OA

Holistic assessment

- Effect on person's function, quality of life, occupation, mood, relationships and leisure activities
- History of presenting symptoms and pain assessment
- Symptoms of infection, history of cancer, unexpected weight loss and fractures
- Medication use, doses, frequency, effectiveness and side effects
- Family history
- Psychological factors (e.g. mood and quality of sleep)
- Health beliefs, concerns, expectations and knowledge
- Modifiable risk factors (e.g. obesity, physical activity)
- Comorbidities

Physical examination

- Malalignment/deformities
- Limited ROM (internal hip rotation, hip flexion)
- Pain on internal rotation and flexion
- Physical performance test

Exclude alternative or additional diagnosis

- Crystal arthropathy
- Spondyloarthropathies
- Inflammatory arthritis
- Septic arthritis
- Tendinopathy
- Osteonecrosis

Clinical diagnosis without further assessment

- Age >45 years
- Activity-related joint pain
- Morning stiffness lasts <30 mins

Additional tests if atypical symptoms

- X-rays: if alternative diagnoses are suspected
- MRI: if suspicion of serious pathology not detected by X-ray
- Laboratory tests: if inflammatory or immune diseases are suspected

Formulate an individualised management plan tailored to person's needs, values and preferences

- Educate patient on OA aetiology, risk factors, persistent pain and prognosis
- Inform patient about treatment options including benefits, harms and costs
- Emphasise exercise and weight management
- Counter common misconceptions
- Encourage patients to take an active role in the management of their conditions
- Establish treatment goals and monitor periodically to maximise adherence and behaviour change

Do not request routine imaging to diagnose OA unless for atypical or severe symptoms

Non-surgical management for hip OA

Core – long term management

- ✓ Ongoing education and information about OA management and prognosis
- ✓ Land based exercise
 - Optional exercise (muscle strengthening, walking, Tai Chi, stationary cycling, yoga, aquatic exercise)
- ✓ Weight management (aim for loss $\geq 7.5\%$ body weight if overweight or obese)

Referral to allied health as required

Optional adjunctive management – trial for short term and cease if ineffective

- Local heat application
- Manual therapy
- CBT for pain coping or psychological symptoms
- Assistive walking device
- TENS
- NSAIDs (topical before oral)
- Paracetamol

Regular patient review
Reassess effectiveness
Monitor side effects

Advanced short term pharmacological attempts if symptom still persistent

- Intra-articular corticosteroid (consider imaging-guided injection when required)
- Duloxetine

If symptoms increase with severe functional impairment despite the best conservative management

- Referral to a specialist

Surgical management for hip OA

Consider hip replacement surgery for end-stage OA when all conservative options have failed

- Perform X-ray to confirm severe OA
- Referral to a orthopaedic surgeon

Do not refer for arthroscopic procedures, unless the patient also has true mechanical locking

Abbreviations CBT, cognitive behavioural therapy; cardiovascular diseases; MSK, musculoskeletal; MRI, magnetic resonance imaging; NSAIDs, non-steroidal anti-inflammatory drugs; OA, osteoarthritis; ROM: range of motion; TENS, transcutaneous electrical nerve stimulation.

1. Background

1.1. Osteoarthritis

Osteoarthritis (OA) is a chronic disease that mostly affects the hands, knees and hips. The 2014–15 National Health Survey shows that 2.1 million Australians (9% of the population) at all ages have this condition.¹ For those over the age of 55, the prevalence of OA increases to over 60%.¹ With population ageing and increasing rates of obesity, the numbers of Australians suffering from OA is expected to increase from almost 2.2 million in 2015 to almost 3.1 million (12% of the population) by 2030.¹ Globally, hip and knee OA were ranked as the 11th highest contributor to global disability² and the most notable non-communicable disease with total disability-adjusted life-years (DALYs) rising by 35% between 1990 and 2015.³ OA is placing an increasing burden on individuals, societies and healthcare systems. Overall health expenditure on arthritis exceeds that of numerous other chronic conditions including coronary heart disease, diabetes, depression, stroke and asthma.⁴ Direct healthcare costs for OA were estimated to be over \$2.1 billion in 2015 and by the year 2030, these are forecast to exceed \$2.9 billion.⁵ Broader economic costs are estimated to be around \$22 billion annually.⁶

Whilst OA is a chronic condition which imposes significant burden in terms of years lived with disability, it has a much lesser impact on mortality, and is therefore often a secondary concern to treating health practitioners. Strategies for relieving pain, minimising disability and slowing disease progression, are key treatment goals of conservative, non-surgical management. Implementing conservative management strategies at a population level for people with OA could result in substantial cost savings for the Australian healthcare system. For example, the potential cost savings from avoiding or delaying knee replacements alone would be over \$233 million in 2030.⁵

For someone with OA, their general practitioner (GP) is often the first point of contact with the healthcare system. In 2015–16, OA was managed in 29 per 1,000 general practice encounters at all ages.⁶

1.2. Objectives

In 2009, the Royal Australian College of General Practitioners (RACGP) developed the *Guidelines for the non-surgical management of hip and knee osteoarthritis*,⁷ Substantial progress has since been made evaluating the effectiveness and safety of commonly used and new therapies for OA. The objective of this review is to present the most recent evidence for OA interventions other than joint replacement for the hip and knee and to inform the development of evidence-based recommendations for GPs working in the Australian healthcare setting.

The questions of specific interest to this literature review and guideline were:

1. What is the efficacy and safety of non-pharmacological (including 'complementary') interventions for adults with symptomatic knee or hip OA?

2. What is the efficacy and safety of pharmacological interventions for adults with symptomatic knee or hip OA?
3. What is the efficacy and safety of arthroscopic surgical procedures for adults with symptomatic knee or hip OA?

In developing and updating the guideline we also aimed to ensure:

- Recommendations were based on the best available evidence
- The content was practical, useful and appropriate for GPs.
- The accompanying treatment algorithm and summary of recommendations were updated.

A formal communication and implementation plan has been developed to promote the guidelines to general practice and key stakeholders. This plan aims to:

- Increase awareness and uptake of the guidelines
- Build awareness of project initiation and progress
- Seek support and buy-in from stakeholders
- Increase awareness of the new release and improve uptake.

1. 3. Scope and target population

This update of the 2009 RACGP guidelines:

- incorporates a review of the evidence of the safety and efficacy of new therapies for the management of hip and knee OA
- revisits established therapies in light of more recent evidence.

These guidelines will apply to all adult patients diagnosed with symptomatic OA of the hip or knee across the disease trajectory, and are intended primarily for use in the primary care setting by GPs to guide patient care. The recommendations are also relevant for other health professionals working in the management of patients with hip or knee OA in the community.

1. 4. Target audience

The primary target audience for the guidelines is Australian GPs in primary care settings in metropolitan, regional, rural and remote areas of Australia. Given the wide range of health professionals who treat this condition, consideration of the relevance of this guideline was also given to other health professionals. Additional target audiences include rheumatologists, orthopaedic surgeons, physiotherapists, sport and exercise medicine physicians, occupational therapists, osteopaths, pharmacists, podiatrists, pain physicians, psychologists, dietitians, chiropractors and nurses. This is reflected in the composition of the guideline development Working Group.

1. 5. Disadvantaged communities

Poor health outcomes are more frequent among individuals living in communities of low socioeconomic status (SES) who are more likely to be disadvantaged in receiving adequate healthcare. As seen with many other chronic conditions, areas of low SES have also been reported to have higher prevalence of OA. Social and economic circumstances including income, education, employment and social support impact the health of individuals in these areas, placing them at greater risk of poor health.⁸ Furthermore, evidence suggests that poor health, including high rates of arthritis may worsen poverty in low to middle income countries (LMICs) due to the inability of individuals to work and fulfil community roles.⁹

In providing quality healthcare, the needs and issues faced by disadvantaged groups, including Aboriginal and Torres Strait Islander peoples and Culturally and Linguistically Diverse (CALD) communities must be considered. In 2009-2010, people in lower socioeconomic households spent proportionately less on medical and healthcare than those in households with higher SES (3% in low compared to 5.1% in high of weekly equivalised expenditure).¹⁰ The Australian Institute of Health and Welfare (AIHW) reports Aboriginal and Torres Strait Islander peoples and CALD groups often lack access to nutritious and affordable food,^{11, 12} are less likely to engage in physical activity and have higher rates of overweight and obesity.^{8, 13}

Comparisons based on information from the 2004-2005 National Aboriginal and Torres Strait Islander Health Survey (NATSIHS) and the 2004-2005 National Health Survey¹⁴ demonstrate a higher prevalence of OA in Aboriginal and Torres Strait Islander peoples (12%) compared to non-Aboriginal and Torres Strait Islander peoples (8%). While no clear relationship has been established in Australia, it is highly likely other socioeconomically disadvantaged groups also experience a greater burden of OA.

In Australia, Aboriginal and Torres Strait Islander peoples with arthritis have fewer visits to GPs and other health professionals, so ensuring access to appropriate and specialised services is particularly important to reduce disparity gaps for Australians who live in rural and remote settings. In addition to good access to care, the provision of comprehensible resources in multiple languages for those with low literacy and low health literacy, relevant education materials and interpreter services when required will contribute to addressing the needs of socially disadvantaged groups.¹⁵ In both Aboriginal and Torres Strait Islander and CALD communities, connecting individuals to community based health programs has also been demonstrated to be effective.^{16, 17}

Barriers such as difficulties in communication and understanding cultural differences and coordinated planning for better service provision also need to be addressed. Appropriate assistance and consumer consultation also needs to be in place for these communities to ensure uptake of services provided.

1. 6. Assessment of the patient with hip or knee OA

1.6.1 Holistic assessment

An initial assessment of people with OA should be based upon a complete history and physical examination, including ascertaining the effect of OA on the person's function, quality of life, occupation, mood, sleep, relationships and leisure activities.¹⁸ OA is a multifaceted disease in which the structural evidence of joint damage frequently does not correlate with the presence and severity of joint pain and disability. A holistic assessment better facilitates a patient-professional partnership and collaborative care in which patients and healthcare professionals make shared decisions related to treatment to improve outcomes.¹⁹ Patient preferences for certain types of therapies should also be considered, as adherence to treatment recommendations and outcomes can be compromised if the care plan does not meet the patient's preferences and beliefs. Furthermore, people with OA are predominantly older adults and often have different personal priorities and aspirations, which may impact their treatment choices.

Patients with hip or knee OA should be asked about their knowledge of the disease and treatment alternatives, previous experiences with treatment and expectations of current treatment. The presence of misconceptions, such as that exercise will worsen OA, or that OA will inevitably get worse, may hamper the development of an appropriately tailored plan and limit the success of treatment, if not properly identified.

Key factors that should be considered as part of the holistic assessment:

- **Social factors:** impact on activities of daily living, relationships and quality of life; recreational and occupational activities
- **Health beliefs and concerns:** previous knowledge of OA; expectations of treatment; understanding of treatment options including benefits and harms
- **Psychological factors:** screen for depression; stresses in life; mood
- **Attitudes to physical activity and exercise:** concerns; participation restriction; beliefs
- **Pain assessment and other musculoskeletal pain:** self-help strategies; analgesics use, doses, frequency and side effects; current understanding about persistent pain
- **Presence of support:** concerns and expectations of carers; isolation issues
- **Influence of comorbidities:** interaction of two or more morbidities; falls risk
- **Modifiable risk factors:** overweight/obesity; joint alignment; and injury/buckling.

Whilst not every factor will be a concern for a person with hip or knee OA, some issues may warrant greater consideration depending on the patient's situation, their preferences and priorities. After taking into account these factors, a personalised package of care can be developed in collaboration with the patient.

1.6.2 Evaluation of treatment response

Periodic clinical assessments should be performed regularly at agreed intervals to assess the effects of treatment on symptoms, function, and status, as well as to quantify objective changes in metrics related to interventions such as weight and muscle strength. Assessing the patient periodically enables regular coaching and the reinforcement of the action plan. This also allows for monitoring of treatment effectiveness, side effects, and alterations to the management plan according to the outcome.

Diagnosis and evaluation of treatment response in OA is primarily based on clinical assessment and there is no established role for laboratory or imaging tests in assessing disease activity/status in clinical practice. As a result, these are not required for OA diagnosis or disease monitoring (See Section [1.7.1 Clinical diagnosis](#) and Section [1.7.2 Limited role for imaging](#)).

There are a variety of clinical tools aimed at evaluating the clinical status and patient-reported outcomes in OA that are mainly used in clinical research. A few commonly used instruments for assessing self-reported pain and function include the Numeric Pain Rating Scale (NPRS), Visual Analog Scale (VAS) for Pain,²⁰ Western Ontario and McMaster Universities (WOMAC) questionnaire,²¹ the Knee Injury and Osteoarthritis Outcome Score (KOOS),²² and the Hip Disability and Osteoarthritis Outcome Score (HOOS).²³ In addition, the 30-s chair-stand test, 40 m fast-paced walk test, stair-climb test, timed up-and-go test and 6-min walk test were recommended as complementary tests to patient report measures. The first three were recommended by the Osteoarthritis Research Society International (OARSI) advisory group as the minimal core set of performance-based tests for hip or knee OA.²⁴

1.7. Diagnosis of hip and knee OA

1.7.1 Clinical diagnosis

The diagnosis of knee or hip OA can be made based on the background risk (the population prevalence of knee or hip OA); the patient's risk factors for OA (eg. age, gender, body mass index (BMI), occupation); their symptoms (persistent knee/hip pain, brief morning stiffness and functional limitation) and an adequate physical examination (crepitus, restricted movement and bony enlargement). Plain radiographs are not needed but could be considered for atypical presentations.²⁵

A typical knee OA diagnosis can be made without requiring further investigations if a person is aged 45 years or older, has activity-related joint pain, morning stiffness lasts less than 30 minutes,¹⁸ crepitus on active motion, bony enlargement and no detectable warmth.^{26, 27} Additional features that may be present include deformity (fixed flexion and/or varus – less commonly valgus for knee); instability; peri-articular or joint-line tenderness and pain on patellofemoral compression.²⁸ Similar to knee OA, hip OA can be diagnosed by clinical features alone according to American College of Rheumatology (ACR) criteria.²⁹ Early physical signs of OA in the hip include restriction of internal rotation and abduction of the affected hip, with pain occurring at the end of the range of motion.²⁹

Be aware that atypical features, such as a history of trauma, prolonged morning joint-related stiffness, rapid worsening of symptoms or the presence of a swollen hot joint, may indicate alternative or additional diagnoses. Consideration of concerning clinical features (eg severe local inflammation, erythema, progressive pain unrelated to usage), suggesting tumour, septic arthritis, crystal arthritis, other inflammatory arthritides (for example, rheumatoid arthritis), osteonecrosis, fracture or serious bony pathology, is required during the clinical examination and if detected should be referred to an appropriate provider. Involvement of other joints may suggest a wide range of alternative diagnoses.

In clinical practice, laboratory tests (eg rheumatoid factor, erythrocyte sedimentation rate, synovial fluid aspirate for crystal confirmation, and C-reactive protein) would be requested to confirm or exclude coexistent inflammatory disease (eg calcium pyrophosphate crystal deposition, gout, rheumatoid arthritis) in patients with suggestive symptoms or signs. However, laboratory tests on blood, urine or synovial fluid are not needed as a diagnosis of OA can be readily made in their absence. If a palpable effusion is present, synovial fluid should be aspirated and analysed to exclude inflammatory disease and to identify urate and calcium pyrophosphate crystals. OA synovial fluid is typically non-inflammatory with <2000 leucocytes/mm³; if specifically sought, basic calcium phosphate crystals are often present.²⁸

1.7.2 Limited role for imaging

In atypical presentations, imaging might be considered when diagnoses other than OA are suspected. Imaging can also be helpful when the clinical diagnosis is uncertain. Imaging for OA follow-up is recommended only if unexpected rapid progression of symptoms or change in clinical characteristics need to be confirmed such as increasing severity of OA.^{18, 25} However, it has been noted that many structural abnormalities seen on imaging are very common in older populations³⁰ and these should be considered in the appropriate clinical context. There is a lack of co-occurrence of the radiographic changes and symptoms of OA.³¹ In patients with frequent hip pain, only 15.6% showed evidence of radiographic OA (Kellgren-Lawrence grade 3 or 4).³² Studies have shown that 15 to 81% of patients with radiographic OA have knee pain.³¹ In addition, the accuracy of the association between symptoms and radiographic OA could be affected by the extent of radiographic view, definitions of pain measurements, study group and other potential confounders.³³⁻³⁵ If imaging is required, conventional (plain) radiography should be used before other modalities. Soft tissues are best imaged by ultrasound or magnetic resonance imaging (MRI) and bone by computed tomography or MRI. Consideration of radiographic views is important for optimising detection of OA features; in particular, for the knee, weight-bearing and patellofemoral views²⁵ are recommended. A full history, clinical examination and anteroposterior X-ray of the affected hip should be the first-line choice of imaging to diagnose the cause of hip pain, but MRI has a definite role in excluding or confirming differential diagnoses, such as osteonecrosis, avascular necrosis and insufficiency fracture. However, due to the absence of strong evidence supporting the additional impact on the certainty of diagnosis using imaging, the systematic use of imaging in the diagnostic process was not recommended in cases with typical clinical presentation.²⁵

Key messages regarding imaging in OA:

- Imaging is not needed but could be considered for atypical presentations.
- Radiographic changes and meniscal tears are an almost universal finding in people with OA and are typically just age-related abnormalities and not related to symptoms.^{36, 37}
- Serious underlying pathologies are unlikely to be missed even if people with a clinical diagnosis of OA have no routine imaging.¹⁸

1. 8. Formulating a management plan

OA management should include a holistic assessment considering the global needs of the patient.¹⁸ Patient preferences for certain types of therapies should be assessed, as adherence and outcomes may be compromised if the care plan does not match the patient's preferences and beliefs.

Broadly, OA management goals are to minimise pain, optimise function and participation, and to educate the consumer. Given the modest effects for individual treatment approaches, a combination of therapeutic approaches is commonly used. Clinicians should also aim to target modifiable risk factors (such as obesity, strength, malalignment, depression).

The principles of chronic disease management apply to the care of patients with OA and are based on the following: care should be continuous, tailored to patients according to individual needs, goals, and values, and be patient-centred; decision-making should be based on the best evidence available and patient preferences and values; information should be widely accessible to patients; and anticipation of needs should be prioritised over a reactive health service.³⁸ Management should be individualised and target modifiable factors. The number of joints involved, the presence of articular versus periarticular pain, and the degree of movement restriction and functional impairment should also guide the therapeutic plan.

Efforts should be made to prioritise interventions that are safer, more accessible and more cost-effective over treatments that have greater adverse events, are less feasible and more expensive. Active, non-pharmacologic interventions are the mainstay of OA management and should be tried first, followed by or in concert with medications to relieve pain when necessary. Non-pharmacologic therapies include weight management, promotion of physical activity, strengthening exercises, and for patients suitable for these interventions, education and behaviour change support, and use of assistive devices when required.³⁹

Patient's adherence, optimal uptake of recommendations, and behaviour modifications are key elements of OA treatment and can be optimised by education, establishing treatment goals, and periodic monitoring.

Education for patients with OA is important to improve their understanding of their disease and the importance of self-management.⁴⁰ Patients should be informed about the aetiology of OA, the typical fluctuating nature of pain, risk factors (especially the ones that are modifiable and specific to the person), and expected prognosis including most people not progressing to requiring joint

replacement.⁴¹ Clear information about treatment options along with their benefits, harms, and costs should be discussed. Providing this information helps to counter common misconceptions and encourages patients to adopt an active approach in the management of their own disease.⁴²

Goal setting helps the informed patient identify current issues, set priorities, and focus on specific changes. To develop a realistic plan, goals should be agreed upon with patients, considering their preferences and their biopsychosocial context. Also, appropriate goals should be specific, timely, measurable and should be reviewed periodically.

1. 9. Timing of and need for referral to orthopaedic surgeon

Total joint replacement surgery is the most cost effective and clinically effective treatment for end-stage OA^{43, 44} in appropriately selected patients. It should be noted that the lifetime risk of undergoing total joint replacement is estimated to be substantially less than the risk of developing symptomatic hip or knee OA. In the UK, the estimated mortality-adjusted lifetime risk of total hip replacement at age 50 for the year 2005 was 11.6% for women and 7.1% for men. For knee replacement, the risks were 10.8% for women and 8.1% for men.⁴⁵

GPs should consider referring patients with end-stage OA when all appropriate conservative options, delivered for a reasonable period of time, have failed. The indication for referral to an orthopaedic surgeon should be based on a significant decline in quality of life because of established and end-stage joint OA. The hallmarks of end-stage OA include significant joint pain, swelling and deformity which disrupts normal sleep patterns, causes a severe reduction in walking distance such that patients become housebound and avoid ambulation outside, and marked restriction of activities of daily living, such as rising from a chair or toilet seat or difficulty with climbing stairs.⁴⁵ It is important that careful history, examination and investigations (plain joint radiography) are obtained to avoid up to 25% of patients who have been shown to undergo inappropriate joint replacement surgery including minimal symptoms, less radiographic abnormality and unrealistic expectations.⁴⁶

Patients with the best outcomes after total joint replacement have significant pre-operative radiographic joint change (Kellgren-Lawrence grade 3 or 4)^{47, 48}, well-controlled co-morbidities, a BMI no greater than 30 or no lower than 20, and good mental health status.⁴⁹ GPs should consider optimising the medical status of patients to improve post-operative outcomes and to reduce peri-operative complications.⁵⁰ In this regard, patients may benefit from pre-operative expert internal medicine referral. The most common preoperative morbidities include low ferritin, diabetes, hypertension, hyperlipidaemia, back pain, depression, cardiac arrhythmia, coronary artery disease, chronic obstructive pulmonary disease and obesity.⁵¹

Patients planning surgery should maintain the range of motion of their arthritic joint, and should engage in as much strengthening and physical activity as possible (walking, hydrotherapy).^{52, 53} Patients should also ensure that their dental and pedal health is maintained and any dermatologic conditions are treated and stabilised prior to surgery to minimise the devastating complication of prosthetic joint infection.

Not all patients do well even after uncomplicated surgery. Up to 25% of patients presenting for total joint replacement continue to complain of pain and disability after well-performed surgery.^{54, 55} These patients continue to use health resources. Careful preoperative patient selection, shared decision-making about surgery and informing patients about realistic outcomes of surgery are required to minimise the likelihood of dissatisfaction. Objective evidence is available that may identify this cohort of patients,⁴⁹ and for whom alternate non-operative interventions may be more appropriate.

1. 10. Decision aids

Patient decision aids support patients by making their decisions explicit, providing information about options and associated benefits/harms, and helping clarify congruence between decisions and personal values.⁵⁶ According to the International Patient Decision Aids Standards (IPDAS) Collaboration description, decision aids are evidence-based tools designed to prepare patients to participate in making specific and deliberated choices among healthcare options.⁵⁷ Patient decision aids should not replace, but may act as an adjunct to good clinical practice. Patient decision aids are not necessary to deliver good shared decision-making, but well-developed tools will facilitate patient engagement and can be used at a variety of time points throughout the person with OA's pathway, and surround decisions on every aspect of care including exercise and diet, pharmacological management and in the consideration of joint replacement.¹⁸ Decision aids are different from patient information leaflets which aim to only provide information.

In 2014, the guideline Working Group of the UK National Institute for Health and Care Excellence (NICE) reviewed the clinical effectiveness of OA specific decision aids that may be utilised to enable patients to participate in the management of their condition. There was moderate quality evidence that the video booklet decision aid may reduce decisional conflict more than an education leaflet alone,⁵⁸ and low quality evidence that patients' confidence in decision making, self-efficacy and preparation for decision making are increased with decision aids.⁵⁹ Despite a paucity of high quality evidence for any given decision aid, it is important to highlight that decision aids should be used as support tools as part of a discussion with a clinician and not as stand-alone tools.

There is currently no systematic way of determining what types of clinical decision-making support tools are used in Australia, or how commonly they are used by clinicians and their patients. However, practitioners could refer to the principles of shared decision making outlined in the patient experience guideline. The UK National Health Service RightCare has recently developed patient decision aids that are available on the NICE evidence search website

(<https://www.england.nhs.uk/rightcare/shared-decision-making/>), including aids specifically designed for hip (<http://arms.evidence.nhs.uk/resources/hub/1057536/attachment>) and knee OA (<http://arms.evidence.nhs.uk/resources/hub/1057534/attachment>).

2. Method

2.1 Literature review

2.1.1 Literature searches

Our initial systematic literature searches were designed to build upon the literature in the 2009 RACGP *Guideline for the non-surgical management of hip and knee osteoarthritis* and to update the evidence published after the last search date for those guidelines.⁷ To accomplish this, we searched PubMed, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the Cochrane Library (including Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials CENTRAL) for studies published from January 2005 to December 2016. A medical librarian developed and conducted searches using search terms determined from the Working Group's preliminary recommendations, database-specific medical subject headings, free-text terms, and study type filters were applied where appropriate. Studies of adults with hip or knee OA which involved one or more therapeutic interventions of interest were sought. Searches were limited to systematic reviews and randomised controlled trials (RCTs), which are classified as Level 1 and Level 2 evidence according to the National Health and Medical Research Council (NHMRC) hierarchy of evidence (Table 1).⁶⁰

Table 1. NHMRC evidence hierarchy

NHMRC levels of evidence for intervention studies	
Study type	Description
Level I	Evidence obtained from a systematic review of level II studies
Level II	Evidence obtained from at least one properly designed randomised controlled trial.
Level III	Evidence obtained from pseudo-RCT, case-control study, retrospective cohort study, comparative study with concurrent controls or comparative study without concurrent controls
Level IV	Evidence obtained from case series, study of diagnostic yield, cohort study of persons at different stages of disease or cross-sectional study

Adapted from National Health and Medical Research Council additional levels of evidence and grades for recommendations for developers of guidelines. NHMRC, 2009.⁶⁰

No limits were placed on language; studies published in languages other than English were translated whenever possible. Details of the search strategies are available in Appendix 1 of the accompanying Technical document. Electronic searches were supplemented with manual searches of reference lists of recent systematic reviews to ensure all pertinent resources had been obtained. Searches were also performed within published supplements of relevant conference proceedings up to and including August 2017. Working Group members were consulted regarding the evidence procured for each topic and, based on their expert knowledge of prior and emerging research in the field, reference to any additional resources which had not yet been collected were requested. All electronic searches were updated in August 2017.

The initial searches for most interventions were then expanded to identify studies published prior to 2005. This was done to accommodate the transition of the current guidelines to the Grading of

Recommendations Assessment, Development, and Evaluation (GRADE) methodology, and thus to provide a comprehensive assessment of the quality of the entire body of evidence available for a given intervention. Consequently, the Working Group reviewed a GRADE summary table which comprised all available RCT evidence regarding a given intervention to date, in order to make the most informed voting decision.

2.1.2 Study selection and PICO question matching

Systematic reviews and RCTs of adults with hip or knee OA in which the majority of the population ($\geq 80\%$) was aged 45 years or older were included. Only studies reporting on patient health outcomes that were determined to be of interest by the Working Group's recommendations were considered eligible for inclusion. Detailed patient health outcomes of interest, and inclusion and exclusion criteria are presented in Appendix 2 of the accompanying Technical document. The results of literature searches were uploaded onto the CTCIA web-based screening platform (available at <http://rheumatology.tuftsmedicalcenter.org/CTCIA/>), which was used for primary and secondary literature screenings. Primary literature screening involved reviewing each record's title and abstract for eligibility. Primary screening of each record was performed in duplicate by two independent reviewers (any paired combination among the following pool: reviewers - XW, MO, EV, and MM), with conflicts resolved by a third reviewer (RB). Secondary literature screening involved the thorough review of full text articles. This was performed on all publications that were considered potentially eligible during the primary screening. Secondary literature screening followed the same independent duplicate review procedure, with conflict resolution undertaken by the same third reviewer. During the secondary screening, all included articles were tagged with PICO-related terms, such as intervention type(s) and reported outcome(s), to facilitate more efficient matching of the literature with PICO questions. Upon completion of secondary screening, the screening input for the references were exported a database, and references were sorted in sequence by Study Design, then by Intervention, then Comparator, and finally by date. Preliminary PICO designations were assigned to the references within the sorted document based on their Interventions and Comparators; these designations were verified by manual review of the included publications. Prior to the initiation of data extraction, the included articles were summarised by order of their matched PICO questions for the members of the Working Group, who assisted with reconciling possible mismatches or omissions. The study flow diagram in Figure 1, Appendix 2 illustrates in detail the numbers of abstracts identified, full-text manuscripts retrieved, and studies selected for inclusion in the systematic literature review for these guidelines.

2.2 Data extraction and analysis

Data from eligible studies for each PICO question were extracted into RevMan software (<http://tech.cochrane.org/revman>). Risk of bias of the individual studies was assessed using the Cochrane Risk of Bias tool.⁶¹ Data extraction and risk of bias ratings were reviewed for consistency, and any discrepancies were resolved by consensus. Data were extracted on study and population

characteristics; intervention dosage and frequency of administration; concomitant medications; all critical and important efficacy outcomes; and all critical and important safety outcomes. Random effects meta-analyses were conducted in anticipation of some heterogeneity among the studies. Dichotomous outcomes were analysed using the Mantel-Haenszel method and were reported as risk ratios (RRs) with 95% confidence intervals (CIs).⁶² For all continuous outcomes, the mean change from baseline was extracted; when change values were not available, these were calculated using baseline and follow-up means. Continuous outcomes were analysed using the DerSimonian and Laird inverse variance method and reported as standardised mean differences (SMDs) with 95% CI.⁶³ SMDs were calculated to account for variation in the outcome scales. All meta-analyses were conducted using RevMan (<http://tech.cochrane.org/revman>).

2.3 Quality assessment and evidence report formulation

The results of the analyses were exported from RevMan into GRADEpro web-based software to generate a GRADE Evidence Profile for each PICO question.⁶⁴ The quality of evidence available for each outcome was assessed in GRADEpro using GRADE quality assessment criteria (Appendix 3, Table 3.1).⁶⁵ This assessment was performed in duplicate by two independent reviewers (RB, MO) with discrepancies resolved by consensus. The evidence was rated for each outcome judged by the following criteria: risk of bias assessment of all individual studies, inconsistency between trial results, indirectness of evidence, imprecision of the effect estimate, and potential reporting bias.⁶⁶⁻⁶⁹ As per the GRADE methodology, the eventual quality ratings could range between four categories, from “High” to “Moderate” to “Low” to “Very Low”, reflecting the reviewers’ confidence in the effect estimate and its proximity to the true effect of an intervention.⁷⁰ “High” grade evidence is designated a numerical equivalent of 4, with quality downgrades carrying a weight of -1 for “serious” risk or -2 for “very serious” risk. The quality rating “Very Low” carries a numerical equivalent of 1, and once the quality of evidence has been downgraded to this point, it cannot be downgraded further. Once the quality of evidence had been assessed for all reported outcomes, the overall evidence quality was evaluated based on the lowest quality rating given to any of the outcomes which had been designated *a priori* to be “Critical” by the Working Group.⁷¹ When no data were available, the overall quality of evidence was automatically marked as “Very Low” to signify that the recommendations were to be made based on clinical experience alone. The resulting GRADE Evidence Profile contained the pooled effect estimates calculated for each outcome, the quality ratings for each outcome, footnotes containing brief qualitative summaries of the rationales behind quality downgrades, the importance of each outcome, and the overall quality of evidence rating. The final evidence report comprised all the GRADE Evidence Profiles (Technical document Appendix 5).

2.4. Formulation of recommendations

GRADE methodology specifies that guideline Working Groups formulate recommendations based on a consideration of the balance of relative benefits and harms of the treatment options under consideration, the quality of the evidence (i.e. confidence in the effect estimates), patients’ values and

preferences and resource implications.⁷¹ Key to the recommendation is the trade-off between desirable and undesirable patient outcomes; recommendations require estimating the relative value patients place in the outcomes.

A recommendation could be either in favour or against the proposed treatment option and either strong or conditional. The recommendation can also be labelled as conditional neutral, where the Working Group cannot determine the direction of the recommendation.

A GRADE recommendation is categorised as strong if the Working Group is very confident that the benefits of an intervention clearly outweigh the harms (or vice versa); a conditional recommendation denotes uncertainty over the balance of benefits and harms, such as when the evidence quality is low or very low, or when patient preferences or costs are expected to impact the decision.⁷² Thus, conditional recommendations refer to decisions where incorporation of patient preferences is an essential element of decision making.

2.4.1 Consensus building

The Working Group received the evidence report for review before meeting to discuss and decide on the final recommendations. For each PICO question, the Working Group provided initial votes and discussed the direction of the recommendation during monthly teleconferences and two face-to-face meetings until general consensus was reached. Once recommendations were drafted, the Working Group was asked to indicate their extent of support for each recommendation through an online survey voting process.⁷³ An 11-point numerical scale was used to rate the extent of support for each recommendation. A 70% consensus agreement was set as the threshold for accepting a recommendation. If a 70% consensus was not achieved during the initial vote, additional discussions were convened to finalise the recommendations. A second and final voting process (with an agree/disagree response) was then conducted. Final recommendations were accepted with a 70% consensus agreement by Working Group members. Details on the survey and voting data are available in Appendix 4 of the accompanying technical document.

In some instances the Working Group decided to combine certain treatment options based on the review of the evidence and clinical scenario (eg. different types of exercise). In addition, the Working Group identified a number treatments (and the resultant evidence reviews) not required for the guideline as the clinical scenario was uncommon, irrelevant, or redundant (Appendix 3, Table 3.2), or because one of the treatment options for that scenario had been eliminated by another recommendation. Consistent with GRADE guidance, there were some treatment options where the Working Group chose to provide a strong recommendation despite a low quality rating of evidence.⁷¹ In these instances, a written explanation is provided describing the reasons for this decision.

3. Recommendations

3.1 Non-pharmacologic interventions

3.1.1 Self-management education programs

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Self-management education programs – knee and/or hip	<p>We are unable to recommend either for or against formal face-to-face self-management education programs for people with knee and/or hip OA.</p> <p>However, clinicians should provide information to enhance understanding about OA, its prognosis and its optimal management.</p>	conditional (neutral) recommendation	Very low
<p><i>What is it?</i> Formal face-to-face self-management education programs are complex interventions targeting patient education to increase participant’s knowledge about OA and to encourage them to take an active role in management. Programs vary widely in their content, delivery and duration.</p> <p><i>Rationale</i> Very low quality evidence shows they have no significant effects on pain and function (Technical document, Appendix 5, p22, 149). They may also require a considerable time commitment by the person to attend and many Australians may experience access difficulties (e.g. those in rural/remote areas, or those for whom English is not a native language). Nonetheless, the programs have the potential to benefit other relevant health domains such as disease knowledge and self-efficacy and thus may be considered useful for some patients. The Working Group felt that ongoing education and advice provided by the clinician remains integral to person-centred care and shared decision-making.</p> <p><i>Harms</i> No adverse effects reported</p>			

3.1.2 Cognitive behavioural therapy

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Cognitive behavioural therapy – knee and/or hip	<p>We suggest offering cognitive behavioural therapy for people with knee and/or hip OA.</p> <p>Clinicians should consider whether CBT is appropriate taking into account psychological co-morbidities and patient preference. They should be cognizant of issues related to cost and access. It is recommended that CBT is combined with exercise to improve outcomes.</p>	<p>conditional for recommendation</p>	<p>Low (knee)</p> <p>Very low (hip)</p>
<p><i>What is it?</i></p> <p>Cognitive behavioural therapy (CBT) is a psychological intervention that aims to show people how their thinking affects their mood, to help them identify and challenge unhelpful thoughts and to learn practical self-help strategies. It can be used to treat a range of problems that may be relevant for people with OA including pain, depression, anxiety, insomnia and eating problems. The most commonly studied CBT for OA has been pain coping skills training, with or without partner support.</p> <p><i>Rationale</i></p> <p>Low quality evidence in people with knee OA shows that CBT programs can have small benefits for pain and can also improve self-efficacy, pain coping, depression and anxiety ⁷⁴(Technical document, Appendix 5, p24, 152). They are associated with a low risk of adverse events. Very low quality evidence from a limited number of studies indicate that combining CBT with exercise is more effective than either alone (Appendix 5, Technical document, p144, 255) for combination treatments). While there is no evidence of the effects of CBT specifically in people with hip OA, the Working Group felt that benefits seen in people with knee OA and in mixed samples of hip/knee OA are likely to be generalisable to those with hip OA. Clinicians should consider the appropriateness of CBT for patients with knee or hip OA in particular those with psychosocial comorbidities. It may be that certain patients respond better to CBT than others with some evidence showing that responders to pain coping skills training were older and more educated, had moderate to high expectations for treatment outcomes, and greater OA disease severity.⁷⁵ Successful programs have been delivered face-to-face individually or in group settings by a range of health professionals including psychologists, physiotherapists and nurses, as well as via online. The Working Group recommends online programs where available and suited to the patient as they have the potential to improve availability and access and be less costly.^{74, 76}</p> <p><i>Harms</i></p> <p>Low likelihood of adverse effects.</p>			

3.1.3 Exercise

Intervention	Recommendation	Strength of recommendation	Quality of evidence
<p>Land-based exercise – knee</p>	<p>We strongly recommend offering land-based exercise for all people with knee OA to improve pain and function regardless of their age, structural disease severity, functional status or pain levels.</p> <p>Exercise has also been found to be beneficial for other comorbidities and overall health.</p> <p>We strongly recommend muscle strengthening exercise, walking and Tai Chi. We suggest offering stationary cycling and/or hatha yoga.</p> <p>Clinicians should prescribe an individualised exercise program taking into account the person's preference, capability and the availability of resources and local facilities. Dosage should be progressed and realistic goals set.</p> <p>Attention should be paid to strategies to optimise adherence. Referral to an exercise professional to assist with exercise prescription and to provide supervision may be appropriate for some patients.</p>	<p>strong for recommendation (all land based, muscle-strengthening, walking, Tai Chi)</p> <p>conditional for recommendation (stationary cycling, hatha yoga)</p>	<p>Low (land-based, Tai Chi) Very low (hatha yoga, stationary cycling, walking, muscle strengthening)</p>
<p><i>What is it?</i> Exercise performed on land including: muscle strengthening, stretching/range of motion, aerobic conditioning, neuromuscular /balance, cycling, Tai Chi and yoga. Exercise dosage can vary in terms of frequency, intensity and duration. Additionally, the exercise can involve expensive, specialised equipment, or no equipment at all, and can be delivered in a group setting or individually.</p> <p><i>Rationale</i> There is low quality evidence from a large number of RCTs showing that land-based exercise overall has significant and clinically relevant benefits for pain, function and quality of life in the short- to medium term in people with knee OA (Technical document, Appendix 5, p26). The benefits for pain and function are moderate in size and are seen irrespective of patients' age, structural disease severity, pain levels and functional status. In addition to these benefits, other advantages of exercise are that it is beneficial for co-morbidities and overall health and is readily available and cheap. There is evidence that long-term therapeutic exercise is safe and is not associated with an increased risk of structural disease progression.⁷⁷ There are various forms of land-based</p>			

exercise that may be adopted for knee OA. The Working Group strongly recommended muscle strengthening exercise, walking and Tai Chi, based on low quality evidence of significant benefits for pain and function, accessibility of such exercise modes often as community based group programs, and identified impairments in muscle strength and functional ability in many patients. Tai Chi was also recommended as it has additional benefits for balance and falls and thus may be particularly suitable for patients in whom an increased risk of falling has been identified, which is common among people with knee OA. The Working Group conditionally recommended stationary cycling and hatha yoga based on very low quality evidence from a limited number of RCTs (1 cycling and 2 hatha yoga) with small samples sizes showing benefits for pain (stationary cycling and hatha yoga) and function (hatha yoga). However, hatha yoga should be considered only as an adjunctive form of exercise and only for short-term management. Clinicians should educate the patient about the benefits of regular exercise and prescribe an individualised progressive exercise program taking into account patient presentation, functional capacity, comorbidities, preferences and exercise availability. They should emphasise that some discomfort may be experienced with exercise but that this is not likely associated with harm. Some people may benefit from referral to an exercise professional (such as a physiotherapist or exercise physiologist) to assist with exercise prescription and supervision. Attention should be paid to adherence strategies such as written material, log-books, and SMS reminders.

Harms

Very low likelihood of serious adverse effects. Most are minor and include temporary increased pain at affected joint or pain at other sites.

Intervention	Recommendation	Strength of recommendation	Quality of evidence
<p>Land-based exercise - hip</p>	<p>We strongly recommend offering land-based exercise for all people with hip OA to improve pain and function regardless of their age, structural disease severity, functional status or pain levels.</p> <p>Exercise has also been found to be beneficial for other comorbidities and overall health. However, we are unable to specifically recommend either for or against different types of land-based exercise at this stage.</p> <p>Clinicians should prescribe an individualised progressive exercise program taking into account the person's preference, capability and the availability of local facilities.</p> <p>The clinician should monitor the patient's response to the exercise program and could try a different form of land-based exercise if improvements are not evident. Attention should be paid to strategies to optimise adherence. Referral to an exercise professional to assist with exercise prescription and provide supervision may be useful for some patients.</p>	<p>strong for recommendation (when combining all studies of land-based exercise)</p> <p>conditional (neutral) for recommending one type of land based exercise over another (muscle strengthening, walking, stationary cycling, Tai Chi, hatha yoga)</p>	<p>Moderate (land-based)</p> <p>Very low (hatha yoga, Tai Chi, stationary cycling, walking, muscle strengthening)</p>
<p><i>What is it?</i> Exercise performed on land. It can take many forms including: muscle strengthening, stretching/range of motion, aerobic conditioning, neuromuscular /balance, cycling, Tai Chi and yoga. Exercise dosage can vary in terms of frequency, intensity and duration. Additionally, the exercise can involve expensive, specialized equipment, or no equipment at all, and can be delivered in a group setting or individually.</p> <p><i>Rationale</i> Overall, there is moderate quality evidence from a limited number of trials in people specifically with hip OA to support the short-term benefits of land-based exercise, conducted either at home or in groups, on pain and function (Technical document, Appendix 5, p154). Exercise is also beneficial for other comorbidities and overall health. Most studies included multi-modal exercise programs comprising strengthening, range of motion and functional exercise. However, we are unable to recommend either for or against specific types of exercise for hip OA due to either limited or non-existent trials in people with hip OA that isolate the effects of different types of exercise. Clinicians should educate the patient about the benefits of regular exercise and prescribe an individualised progressive exercise program taking into account patient presentation, functional capacity, co-morbidities, preferences and resource availability. They should emphasise that some discomfort may be experienced with exercise but that this is not likely associated with harm. Some people</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
	<p>may benefit from referral to an exercise professional (such as a physiotherapist or exercise physiologist) to assist with exercise prescription and supervision. Attention should be paid to adherence strategies such as written material, log-books, and short message service reminders.</p> <p><i>Harms</i> Very low likelihood of serious adverse effects. Most are minor and include temporary increased pain at affected joint or pain at other sites.</p>		

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Aquatic exercise/hydrotherapy – knee and/or hip	We suggest offering aquatic exercise/hydrotherapy for people with knee and/or hip OA. This will depend upon personal preference and the availability of local facilities.	conditional for recommendation	Low
<p><i>What is it?</i> Aquatic exercise/hydrotherapy is low impact exercise undertaken in water. Water also offers natural resistance which can be used to strengthen muscles. It may be undertaken individually or in group classes in pools located in community settings. In some settings, classes may be specific to those with arthritis and/or musculoskeletal conditions.</p> <p><i>Rationale</i> There is low quality evidence that aquatic exercise leads to small statistically significant improvements in pain, physical function and quality of life in people with knee and/or hip OA (Technical document, Appendix 5, p35, 162). There is a low risk of harms with aquatic exercise. Participation in aquatic exercise requires access to a pool and usually comes at a small financial cost to participants. In addition, some patients with OA may not feel comfortable, or be willing, to exercise in an aquatic environment. Clinicians should thus discuss personal exercise preferences and access to local pool facilities to determine if an individual patient should be advised to undertake aquatic exercise.</p> <p><i>Harms</i> Very low likelihood of serious adverse effects. Most are minor and include temporary increased pain at affected joint or pain at other sites.</p>			

3.1.4 Manual therapy, weight management and heat/cold therapy

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Manual therapy (massage, mobilisation, manipulation) – knee and/or hip	We suggest offering a short course of manual therapy for people with knee and/or hip OA. This should be considered only as an adjunctive treatment to enable engagement with active management strategies and only for short term management, cognisant of issues related to cost and access.	conditional for recommendation	Low (massage) Very low (mobilisation and manipulation)
<p><i>What is it?</i> Manual therapy generally refers to skilled hands-on techniques where accurately determined and specifically directed manual force is applied to the body. The purported aims of manual therapy include reducing pain; increasing range of motion and mobility; reducing soft tissue inflammation; increasing circulation; improving soft tissue repair; inducing relaxation; facilitating movement; and improving function. Manual therapy comprises a number of techniques, the most common being manipulation and mobilisation. Manipulation techniques are defined as forceful small-amplitude, high-velocity movements of a joint often applied at end range. Mobilisation techniques are repetitive passive movement of low velocity and varying amplitudes applied at different points throughout range. Other techniques include soft tissue mobilisation and stretching and myofascial techniques. Massage may also be considered by some to be a form of manual therapy.</p> <p><i>Rationale</i> For some people with knee and/or hip OA, these therapies may have a positive effect on pain and/or function in the short-term (low to very low quality evidence) and there is a very low risk of harm (Technical document, Appendix 5, p36.163). The Working Group felt that for some people with knee and/or hip OA these therapies may be useful as a single, short term (e.g. up to 8-12 weeks) trial and should be used only as an adjunct to active rehabilitation interventions given that they emphasise a passive approach to treatment. When considering manual therapies, clinicians and patients should be aware of possible cost, time and access barriers.</p> <p><i>Harms</i> Very low risk of harm reported.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Weight management – knee and/or hip	We strongly recommend weight management for people with knee and/or hip OA. For those who are overweight or obese, a minimum weight loss target of 7.5% of body weight is recommended. Weight loss should be combined with exercise for greater benefits. For people of healthy body weight, education about the importance of maintaining healthy body weight is essential.	<p>strong for recommendation (weight management)</p> <p>conditional for recommendation (combination weight management plus exercise)</p>	Very low
<p><i>What is it?</i> Weight loss is usually achieved through a combination of dietary modification and exercise, and in extreme cases, bariatric surgery.</p> <p><i>Rationale</i> Overweight/obesity is a major risk factor for onset and progression of symptomatic and radiographic OA, particularly at the knee, and is common among people with knee and/or hip OA. People with OA often present with co-morbidities associated with overweight/obesity such as cardiovascular, gastrointestinal and endocrine conditions and weight management for these conditions is considered best practice. There is limited evidence of very low quality that weight loss alone (achieved via diet and exercise) has no significant effect on either pain or function in people with knee OA (Technical document, Appendix 5, p38, 166), although benefits appear to be more significant with higher amounts of weight loss, starting at a minimum of 7.5% body weight. Dietary weight loss should also be combined with exercise for greater benefits (Technical document, Appendix 5, p140, 251). There are no RCTs of the effects of bariatric surgery in people with hip or knee OA. There are no RCTs investigating weight management specifically in people with hip OA, although the numerous other systemic health benefits of weight loss and maintaining a healthy body weight are most likely transferable to people with hip OA. Despite the limitations of the available RCT evidence in OA, the Working Group felt that the benefits of weight loss in overweight/obese people with knee and/or hip OA outweigh the risks. Clinicians are advised to refer to the NHRMC guidelines for the most effective strategies for managing overweight/obesity in primary care.⁷⁸</p> <p><i>Harms</i> Low risk of harms.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Heat therapy – knee and/or hip	We suggest offering local heat therapy (e.g. hot packs) as a self-management strategy for people with knee and/or hip OA. This should be considered only as an adjunctive treatment.	conditional for recommendation	Very low
<p><i>What is it?</i> Superficial heat can be applied via the use of hot packs or hot water bottles. Heat therapy is purported to relieve muscle tension and soreness and improve blood flow.</p> <p><i>Rationale</i> Heat therapy may be effective in reducing pain for some people with knee and/or hip OA, but the quality of the evidence is very low (Technical document, Appendix 5, p40, 168). Heat therapy is cheap and is generally feasible for patients to undertake independently as a self-management strategy.</p> <p><i>Harms</i> No adverse effects reported. However, patients should be warned about the risks of burns and heat therapy may not be suitable in those with compromised sensation.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Cold therapy – knee and/or hip	We suggest not offering local cold application (e.g. ice packs) for people with knee and/or hip OA.	conditional against recommendation	Very low
<p><i>What is it?</i> Cold therapy is the local application of cold via techniques such as ice packs. It aims to reduce swelling, muscle spasm and pain.</p> <p><i>Rationale</i> Very low quality evidence suggests that the use of cold therapy is not effective in improving pain, function or quality of life in people with knee and/or hip OA (Technical document, Appendix 5, p41,169). While no adverse events have been identified in trials of cold therapy in patients with knee OA, there is emerging clinical evidence that patients with symptomatic knee OA may experience cold hyperalgesia,^{79, 80} suggesting therapeutic use of cold may be unhelpful.</p> <p><i>Harms</i> No adverse effects reported.</p>			

3.1.5 Braces, orthotics, taping, footwear and canes

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Knee braces	<p>We are unable to recommend either for or against the use of varus unloading/re-alignment braces for people with lateral tibiofemoral compartment knee OA.</p> <p>We suggest not offering valgus unloading/re-alignment braces for people with medial compartment tibiofemoral knee OA.</p> <p>We suggest not offering realigning patellofemoral braces for patellofemoral OA.</p>	<p>conditional (neutral) recommendation (varus unloading/re-alignment braces)</p> <p>conditional against recommendation (valgus unloading/re-alignment braces)</p> <p>conditional against recommendation (re-aligning patellofemoral braces)</p>	<p>Low (valgus unloading/re-alignment braces)</p> <p>Very low (varus unloading/re-alignment braces - no RCT data)</p> <p>Very low (realigning patellofemoral braces)</p>
<p><i>What is it?</i></p> <p>Knee braces are widely available for purchase by consumers from pharmacies, clinicians and other healthcare outlets. Varus unloading braces realign the tibiofemoral joint by providing a varus-directed force that aims to reduce valgus malalignment in those with lateral tibiofemoral compartment knee OA, whilst valgus unloading braces provide a valgus-directed force that aims to reduce varus malalignment in those with medial tibiofemoral compartment knee OA. Patellofemoral braces aim to realign patellar position for those with patellofemoral OA.</p> <p><i>Rationale</i></p> <p>There is no RCT evidence about the effects of varus unloading braces on pain or physical function in people with knee OA. There is limited low quality evidence that valgus-unloading braces have no significant effect on pain or physical function (Technical document, Appendix 5, p42). Similarly, there is limited very low quality evidence that patellofemoral realigning braces have no significant effect on pain or function (Technical document, Appendix 5, p45). Knee braces can impose considerable financial cost to the patient, and may be associated with difficulties in applying the brace independently. Patient adherence with wearing knee braces can also be a limiting factor in the appropriateness of such braces.</p> <p><i>Harms</i></p> <p>Low likelihood of adverse effects which can include skin irritation.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Shoe orthotics (medial and lateral wedge insoles – knee, shock absorbing insoles and arch supports - knee and hip)	<p>We are unable to recommend either for or against the use of medial wedged insoles for people with lateral tibiofemoral OA and valgus deformity.</p> <p>We suggest not offering lateral wedge insoles for people with medial tibiofemoral knee OA.</p> <p>We are unable to recommend either for or against the use of shock absorbing insoles or arch supports</p>	<p>conditional (neutral) recommendation (medial wedge insoles for lateral tibiofemoral OA)</p> <p>conditional against recommendation (lateral wedge insoles)</p> <p>conditional (neutral) (shock absorbing insoles, arch supports)</p>	<p>Very low (medial, lateral wedged insoles)</p> <p>Very low (shock absorbing insoles, arch support - no RCT data)</p> <p>Very low (all hip orthotics - no RCT data)</p>
<p><i>What is it?</i></p> <p>Various shoe orthotics designed to alter walking biomechanics are available. Wedge insoles are orthotics placed inside shoes that are angulated on their medial or lateral side thereby shifting the distribution of load across the tibiofemoral compartments. Medial wedge insoles are higher on the medial side shifting weight toward the medial tibiofemoral compartment and are thus applicable for people with lateral compartment tibiofemoral knee OA and valgus knee deformity. Lateral wedge insoles are higher on the lateral side (and may include a subtalar strapping component) shifting weight toward the lateral tibiofemoral compartment and are applicable for those with medial compartment tibiofemoral OA and varus deformity. Shock absorbing insoles are made of material that aims to absorb impact loading during walking. Arch supports are insoles designed to support and re-align the foot.</p> <p><i>Rationale</i></p> <p>Very low quality evidence from a single small RCT investigating medial wedge insoles found significant benefits of a clinically relevant magnitude for pain and function in people with lateral tibiofemoral compartment knee OA and valgus deformity (Technical document, Appendix 5, p46). The Working Group felt that this study provides preliminary evidence that would need to be confirmed in larger trials and as such were unable to recommend either for or against medial wedge insoles. Conversely, for lateral wedge insoles, very low quality evidence from a number of RCTs show no significant benefits for pain, function, quality of life or structural disease progression in people with medial knee OA (Technical document, Appendix 5, p47). As there are no RCT data available in people with either knee or hip OA for either shock absorbing insoles or arch supports, no recommendations about their use can be currently made.</p> <p><i>Harms</i></p> <p>Low likelihood of adverse effects.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Footwear - knee	We suggest not offering unloading shoes, minimalist footwear or rocker-soled shoes for people with symptomatic knee OA. However, clinicians may consider advising patients to wear footwear with shock-absorbing properties and to avoid high heeled shoes.	conditional against recommendation	Very low (unloading shoes, minimalist footwear) Low (rocker soled shoes)
<p><i>What is it?</i> A number of footwear styles have been developed and/or marketed for OA and other musculoskeletal conditions. Unloading shoes are walking shoes that contain variable-density midsoles ± a lateral wedge insole, designed to reduce medial tibiofemoral compartment knee loads. Minimalist shoes are footwear styles that are flexible, flat and non-heeled, advocated to reflect barefoot walking and develop intrinsic foot muscle strength. Rocker-sole shoes are shoes with a thicker than normal sole and a convex curvature in the sagittal plane, designed to create an unstable platform encouraging increased muscle activity while walking.</p> <p><i>Rationale</i> Whilst unloading shoes and minimalist shoes reduce medial tibiofemoral compartment knee joint loading⁸¹⁻⁸³, there is limited evidence of very low quality that these shoe designs offer no additional benefit on pain or clinically relevant effects on function compared to conventional walking shoes (Technical document, Appendix 5, p51). There is limited evidence of low quality that rocker-soled shoes offer no significant benefit on pain or function compared to conventional walking shoes (Technical document, Appendix 5, p54). Clinicians may consider advising patients to consider wearing footwear with shock-absorbing properties, and to advise avoidance of high-heeled shoes given that they increase knee joint loads,⁸⁴ albeit in the absence of RCT data about which individual footwear features are beneficial and/or harmful.</p> <p><i>Harms</i> Low likelihood of adverse effects.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Taping – knee and hip	<p>We are unable to recommend either for or against the use of patellar taping for people with knee OA.</p> <p>We suggest not offering kinesio taping for people with knee and/or hip OA.</p>	<p>conditional (neutral) recommendation (patellar taping)</p> <p>conditional against recommendation (kinesio taping)</p>	Very low
<p><i>What is it?</i> Different forms of taping are available, generally as a self-management strategy. Patellar taping uses rigid tape aiming to create a mechanical re-alignment of the patella in the trochlear groove to reduce pain and improve function. Kinesio taping uses non-rigid tape applied in various configurations and is purported to offer support and stability to muscles and joints and to stimulate somatosensory receptors.</p> <p><i>Rationale</i> There is some evidence that patellar taping can immediately change patellar alignment measured on imaging and can immediately reduce pain.^{85, 86} However, very low quality evidence from a single RCT did not find a significant effect of taping worn continuously for 3 weeks on pain and function compared to sham tape in people with knee OA not specifically selected for patellofemoral pain (Technical document, Appendix 5, p56). It is possible that people with specific patellofemoral pain symptoms may benefit from self-application of patellar taping to minimise pain and enable engagement in physical activity and rehabilitation. A limited number of trials of very low quality and with small sample sizes have evaluated kinesio taping for knee OA. These trials used different configurations of kinesio tape that was re-applied by the clinician after various intervals. There are no trials of kinesio taping for hip OA. The evidence shows no significant benefits of kinesio taping for pain or function (Technical document, Appendix 5, p55,174).</p> <p><i>Harms:</i> Side effects are minor and include skin irritation from the tape.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Assistive walking device – knee and/or hip	We suggest offering an assistive walking device such as a cane for people with knee and/or hip OA, depending on a person's preference and capability.	conditional for recommendation	Low (knee) Very low (hip)
<p><i>What is it?</i> Assistive walking devices include devices such as canes (walking sticks), crutches and walkers. As appropriate to the needs to individual users, these can help walking ambulation by reducing lower limb loading, improving stability, and assisting movement.</p> <p><i>Rationale</i> Patients with knee or hip OA often adopt an abnormal gait pattern due to pain, muscle weakness, joint mobility restrictions or other pain conditions. The use of an assistive walking device may be useful to improve a gait pattern and posture to normalise musculoskeletal loads. There is low quality evidence from one trial that the use of a walking aid (e.g. single point stick) is effective in improving pain and function in people with knee OA (Technical document, Appendix 5, p57). The Working Group felt these data could be reasonably transferred to people with hip OA (very low quality evidence). Clinicians should assess a patient's gait pattern to consider the indication for a walking device. Walking devices also can assist with balance problems and may be indicated for those with an increased risk of falling. It is important that patient is instructed in how to use the device, how to safely and effectively ambulate with the device and how to adjust the device.</p> <p><i>Harms</i> Few adverse events</p>			

3.1.6 Electrotherapies

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Pulsed electromagnetic/shortwave therapy – knee and/or hip OA	We do not recommend either for or against electromagnetic/shortwave therapy for people with knee and/or hip OA.	conditional (neutral) recommendation	Low (knee) Very low (hip)
<p><i>What is it?</i></p> <p>Pulsed electromagnetic therapy, also known as pulsed shortwave therapy, is the application of pulsed electromagnetic fields to the body. As a pulsed mode of delivery, it does not produce a heating effect in the tissues, but is purported to have physiologically beneficial effects at the cellular level based on magnetic field effects. Traditionally, pulsed electromagnetic therapy has been administered by healthcare providers in clinical settings, but advances in technology have led to the increasing availability of small portable devices for self-application.</p> <p><i>Rationale</i></p> <p>There is low quality evidence that pulsed electromagnetic therapy significantly improves pain and function in people with knee OA (Technical document, Appendix 5, p58) by clinically relevant amounts. There is very low quality evidence it has no statistically significant effect on pain or function in people with hip OA (Technical document, Appendix 5, p176). Most studies involved clinician-delivered treatments, at high frequency of servicing, ranging from 3-5 times per week. A minority of studies utilised portable devices that patients applied themselves at home, with treatment dosage ranging from 2 to 12 hours per day.</p> <p>Although the evidence suggests moderate effect sizes and a low risk of harms for pulsed electromagnetic fields in people with knee OA, the Working Group noted that current evidence is restricted to short-term (2-10 weeks) follow-up only, so maintenance of a therapeutic effect remains uncertain. The available evidence suggests 3-5 treatment sessions/week are required for benefits, when this treatment is administered by clinicians. Given the large number of visits required to a health professional for a treatment modality that is passive, the financial cost this may impose on a patient and the evidence suggesting no benefit for hip OA, the Working Group felt that clinician-delivered pulsed electromagnetic therapy should not be offered to people with knee and/or hip OA. The Working Group noted some promising data from a limited number of small trials investigating portable devices but felt further research is required regarding effectiveness, acceptability and adherence.</p> <p><i>Harms</i></p> <p>Low risk of adverse events with no serious adverse events reported.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Other electrotherapy – knee and/or hip (shockwave, interferential, laser)	We suggest not offering electrotherapy modalities of shockwave, interferential or laser for people with knee and/or hip OA.	conditional against recommendation	Low (laser) Very low (shock wave, interferential, laser-hip)
<p><i>What is it?</i> Electrotherapy modalities including shockwave, interferential electrical current and laser therapy are purported to induce physiologically beneficial effects on body tissues at a cellular level, including promotion of cell growth and angiogenesis, minimising inflammatory processes, and modulating pain through actions on the peripheral nervous system. Shockwave therapy is typically delivered by clinicians, while portable units are available for interferential and laser modalities.</p> <p><i>Rationale</i> While very low quality evidence suggests some possible benefits from shockwave and interferential current modalities on pain and function, these findings were limited to one (shockwave) or two (interferential) trials with a limited sample size and serious or very serious risk of bias (Technical document, Appendix 5, p60,63). The Working Group also felt that a cost burden and requirement for frequent clinical visits (for shockwave) were additional factors contributing the recommendation to not offer these interventions. Seven trials using laser therapy among people with knee OA suggest clinically meaningful benefits in short-term pain and function (up to three weeks) – low to very low quality evidence (Technical document, Appendix 5, p65). Despite these positive indications, the Working Group felt it inappropriate to recommend the use of laser for people with knee OA, as the evidence was derived from trials where clinicians were required to deliver the intervention from 2-3 times per week (other than the trial by Stellian (1992) where the intervention was self-administered) and the fact that the current evidence is restricted to short term follow-up of 3 weeks. Further, based on the model of service delivery used in the majority of trials, a considerable cost and time burden is likely to be placed on patients. While there is no direct evidence available for the effects of these modalities in people with hip OA, the Working Group felt the modes of proposed physiologic action of the interventions would be transferable to the hip and the same concerns about cost, time, frequency of clinical visits and very short-term effects would similarly apply.</p> <p><i>Harms</i> Across these modalities, there is no evidence of harm.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Transcutaneous electrical nerve stimulation (TENS) – knee and/or hip	We suggest offering transcutaneous electrical nerve stimulation (TENS) that can be used at home for people with knee and/or hip OA. Clinicians need to provide sufficient instructions on self-use and consider individual accessibility and affordability.	conditional for recommendation	Very low
<p><i>What is it?</i> Transcutaneous electrical nerve stimulation (TENS) uses low voltage electric current delivered through electrodes fixed to the skin to affect peripheral nerve activity (neuromodulation) as a mechanism to modify nociception and the experience of pain. Portable TENS units are now widely available for patients to use at home as a self-management strategy. Unlike other electrotherapy devices, portable TENS may be used as a continuous therapy by patients to modulate pain, allowing them to engage in other activities while the unit is active.</p> <p><i>Rationale</i> Very low quality evidence from four trials in people with knee OA suggests that TENS has a clinically-meaningful effect on pain and function (Technical document, Appendix 5, p61). While no direct evidence is available from trials in people with hip OA, the Working Group felt the mode of action TENS could be transferable to the hip. Trials were limited to 4 weeks follow-up, so it remains uncertain whether treatment effects are maintained beyond this period. Accordingly, the Working Group felt it would be reasonable to offer TENS to patients with knee and/or hip OA as a home-based, pain-modulating adjunct to active rehabilitation interventions.</p> <p><i>Harms</i> No adverse events have been reported in the included trials, however, clinicians should provide information to patients about how to use portable TENS units safely and minimise the risks of possible skin irritation.</p>			

3.1.7 Therapeutic ultrasound

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Therapeutic ultrasound – knee and/or hip OA	We suggest not offering therapeutic ultrasound for people with knee and/or hip OA.	conditional against recommendation	Moderate (knee) Low (hip)
<p><i>What is it?</i> Therapeutic ultrasound is the application of high-frequency sound waves to soft tissues via a treatment head moved over the surface of the skin. It is a passive treatment typically provided by a clinician over a number of treatment sessions.</p> <p><i>Rationale</i> There is moderate quality evidence that therapeutic ultrasound has statistically significant effects on pain and physical function in people with knee OA. There are no RCTs involving participants with hip OA, thus the evidence level for this patient group was downgraded to low quality due to concerns about indirectness (Technical document, Appendix 5, p180). Although the evidence suggests moderate effect sizes, and a low risk of harms, for therapeutic ultrasound in people with knee OA, the Working Group noted that current evidence is restricted to short-term (2-8 weeks) follow-up only and expressed concern about whether benefits are sustainable once treatment was finished. The available evidence suggests that 3-5 treatment sessions/week are required for benefits. Given the large number of visits required to a health professional for a treatment modality that is passive, and the financial cost this may impose on a patient, the Working Group felt that therapeutic ultrasound should not be offered to people with knee and/or hip OA.</p> <p><i>Harms</i> No adverse events reported.</p>			

3.1.8 Acupuncture

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Acupuncture – knee and/or hip	We suggest not offering acupuncture for people with knee and/or hip OA.	conditional against recommendation	Low (knee) Very low (hip)
<p><i>What is it?</i> Acupuncture may be administered by a variety of health professionals and is traditionally applied via insertion of acupuncture needles into acupuncture points, with or without mechanical or electrical stimulation. Laser acupuncture involves the application of low-intensity laser light to acupuncture points, instead of needles. Acupuncture is usually provided as a course of treatment over multiple sessions spread over a number of weeks.</p> <p><i>Rationale</i> There is low quality evidence that traditional acupuncture and electroacupuncture have statistically significant benefits on pain and function compared to sham acupuncture in people with knee OA. However, these benefits are small and not of a clinically relevant magnitude. There is very low quality evidence suggesting no statistically significant effect of laser acupuncture on either pain or function in people with knee OA. There is very low quality evidence that traditional acupuncture has no statistically significant effect on pain or function compared to sham in people with hip OA (Technical document, Appendix 5, p183). Clinicians should not offer acupuncture to people with knee and/or hip OA due to its lack of clinical effectiveness and the necessity of multiple, visits to a clinician for passive treatment that may come at a financial cost to the patient.</p> <p><i>Harms</i> There is a statistically significant increase in risk of adverse events with acupuncture compared to sham in people with knee OA, although most were unrelated to acupuncture treatment (Technical document, Appendix 5 adverse events table).</p>			

3.2 Pharmacologic interventions

3.2.1 Oral analgesics

Intervention	Recommendation	Strength of recommendation	quality of evidence
Paracetamol – knee and/or hip	We are unable to recommend either for or against the use of paracetamol for people with knee and/or hip OA. It might be reasonable to trial paracetamol for a short period and then discontinue use if it is not effective. Clinicians also need to monitor and capture adverse events that may be associated with its use.	conditional (neutral) recommendation	Very low
<p><i>What is it?</i> Paracetamol also known as acetaminophen, is typically used to treat mild to moderate pain and fever. Unlike other common analgesics such as the NSAIDs, aspirin and ibuprofen, paracetamol is generally considered to be a weak inhibitor of the synthesis of prostaglandins (PGs) but does not have a significant anti-inflammatory activity.</p> <p><i>Rationale</i> While paracetamol has long been considered a first-line therapy for OA, this has mainly reflected its relative safety, availability and cost compared with other pharmacological options, including NSAIDs and opioids. Current evidence from a systematic review of RCTs suggests that, on average, the reduction in OA pain achieved with paracetamol is too small to be of clinical relevance.⁸⁷ Moreover, paracetamol is associated with infrequent potential for significant harms, both with short-term excess dosing, and long-term regular use.⁸⁸ Many patients will have tried paracetamol prior to seeking advice from a health care professional. In patients who have experienced a clear benefit that outweighs any potential for harm, it is reasonable to continue paracetamol in the lowest effective dose. Given the variable natural history of OA symptoms, periodic trials of withdrawal of paracetamol are recommended. In patients who have not previously trialled paracetamol in an appropriate dose, a short-term trial may be considered, with cessation of the drug in those who do not respond. Repeated trials of paracetamol in patients for whom it has not been effective are probably not warranted. Practitioners should discuss a cessation strategy with patients who are using regular paracetamol without clear benefit. Importantly, it should be emphasised that replacement of paracetamol with another analgesic drug may not be necessary or appropriate, and that non-pharmacological approaches to management should be optimised.</p> <p><i>Harms</i> There is no significant increase of adverse events (AEs) with the use of paracetamol compared to placebos. However, clinicians should be cautious that paracetamol is more likely to increase the risk of abnormal liver functions and side effects are multiplied when combined with alcoholic drinks.</p>			

Intervention	Recommendation	Strength of recommendation	quality of evidence
Oral Non-steroidal Anti-Inflammatory Drugs (NSAIDs) including COX-2 inhibitors – knee and/or hip	We suggest offering oral NSAIDs for people with knee and/or hip OA. It might be reasonable to trial oral NSAIDs at the lowest effective dose for a short period and then discontinue use if it is not effective. Clinicians also need to inform patients about, monitor and capture adverse events, especially gastrointestinal, renal and cardiovascular, that may be associated with its use.	conditional for recommendation	Moderate
<p><i>What is it?</i> NSAIDs are anti-inflammatory and analgesic agents commonly used for OA. NSAIDs are effective anti-inflammatory and analgesic drugs by virtue of their ability to inhibit biosynthesis of prostaglandins (PGs) at the level of the cyclooxygenase enzyme (COX). It is thought that inhibiting COX-2 leads to the anti-inflammatory, analgesic and antipyretic effects and those NSAIDs also inhibiting COX-1, particularly aspirin, may cause gastrointestinal bleeding and ulcers in large doses.⁸⁹</p> <p><i>Rationale</i> On average, NSAIDs result in small but clinically relevant improvements in pain and function in patients with OA of the knee or hip, and are likely to be more effective than paracetamol for most patients (Technical document, Appendix 5, p74, 188). The direct costs of NSAIDs are relatively low. Evidence for effectiveness is derived from trials of relatively short duration, so the relative benefits versus harms of long-term NSAID therapy are unknown. It is likely that the risk of harms increases with duration of therapy, so the balance of benefits and harms may become less favourable with time. Given the variable natural history of OA symptoms, periodic trials of drug withdrawal are recommended.</p> <p><i>Harms</i> The potential harms of NSAIDs are well recognised, including gastrointestinal (GI), renal and cardiovascular adverse effects. Older persons, who are at higher risk for OA, may also be at higher risk for adverse effects from NSAIDs, so this class of medication should be used with caution. Formal estimation of cardiovascular risk may be worthwhile using a validated tool such as http://www.cvdcheck.org.au/. In patients at low absolute risk of NSAID harms, a judicious trial of NSAIDs may be considered, aiming for the lowest effective dose. Co-prescription of a proton-pump inhibitor or the use of a COX-2 inhibitor should be considered in patients at risk of GI adverse effects. The balance of benefits and risks may vary between NSAIDs and between individuals, however no particular drug is likely to be superior to others, nor is any NSAID free from the potential for harm.</p>			

Intervention	Recommendation	Strength of recommendation	quality of evidence
Oral opioids – knee and/or hip	We do not recommend offering oral opioids for people with knee and/or hip OA.	strong against recommendation	Low (knee) Very low (hip)
<p><i>What is it?</i> Opioids are substances that act on opioid receptors to produce morphine-like effects. Medically they are conceived as powerful pain-relieving substances.</p> <p><i>Rationale</i> Opioid prescription for chronic non-cancer pain (including OA) has increased in recent years despite a lack of high quality evidence demonstrating benefit, particularly with long-term use. Evidence for the efficacy of opioids for the treatment of OA is mostly derived from short-term trials. There is moderate quality evidence from trials that improvement in pain and function with opioids is of marginal clinical significance at best and is offset by the risk of harms (Technical document, Appendix 5, p76,190). Given that opioids result in little to no effect on OA pain and are associated with a risk of serious medical and social harms, we strongly recommend against the use of any opioid preparation for the treatment of OA of the knee or hip. Patients who are already using opioids for OA pain should be monitored closely. The lowest effective dose should be sought, and opportunities for reduction in dose or cessation should be regularly sought, in conjunction with optimisation of non-pharmacological management.</p> <p><i>Harms</i> Common harmful effects may occur in the short-term, such as gastrointestinal disturbance and cognitive dysfunction, leading to discontinuation of the drug in a significant proportion of patients. The risk of additional adverse effects may accumulate with long-term use, including dependence, adverse effects on bone health, endocrine and immune function, and possible potentiation of chronic pain mechanisms. Deliberate misuse of opioids is an uncommon but serious risk associated with opioid prescription. Opioid use is associated with a risk of both non-fatal and fatal overdose. Observational data in patients using opioids for chronic non-cancer pain suggest a risk of death from opioid-related causes as high as 1 in 550 patients.⁹⁰</p>			

3.2.2 Topical analgesics

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Topical NSAIDs – knee and/or hip	We are unable to recommend either for or against the use of topical NSAIDs for people with knee and/or hip OA. It might be reasonable to trial topical NSAIDs for a short period and then discontinue use if not effective. Clinicians also need to monitor and capture the adverse effects along with its use.	conditional (neutral) recommendation	moderate
<p><i>What is it?</i> Topical NSAIDs are applied to unbroken skin where it hurts as gels, creams, sprays, or plasters. Topical NSAIDs penetrate the skin, enter tissues or joints, and reduce processes causing pain in the tissue. Drug levels in the blood with topical NSAIDs are very much lower than with the same drug taken by mouth.</p> <p><i>Rationale</i> The effectiveness of topical NSAID application in OA is variable. Generally, the benefit is small but the risk of harm is also small. Similar to oral NSAIDs, a judicious trial of topical NSAIDs may be considered as adjunctive treatment for short term (several weeks). If unhelpful, they should be ceased. Regarding adjunctive use, it should be noted that current evidence shows that combining a topical NSAID with an oral NSAID confers no additional therapeutic benefit over either agent used alone, but it does increase the number of adverse events.⁹¹</p> <p><i>Harms</i> Usually, adverse events from topical NSAIDs agents are minimal, but there is mild toxicity due to local skin reactions.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Transdermal opioids – knee and/or hip	We do not recommend offering transdermal opioids for people with knee and/or hip OA.	strong against recommendation	Low
<p><i>What is it?</i> Transdermal opioid patch is a long-acting formulation with a delayed onset of effect initially and a prolonged duration of action, as such, they are best reserved for opioid-tolerant patients with stable opioid requirements. Transdermal opioid delivery avoids first-pass metabolism by the liver, increasing bioavailability and limiting variation in plasma concentration.⁹²</p> <p><i>Rationale</i> Evidence is mostly derived from two short-term trials of transdermal opioids, buprenorphine and fentanyl. Similar to oral opioid, the low quality evidence demonstrated the improvements in pain and function are of marginal clinical significance at best and is offset by the risk of harms (Technical document, Appendix 5). Therefore, we are strongly against the use of any opioid preparation for the treatment of OA of the knee or hip.</p> <p><i>Harms</i> Comparing with oral opioid, transdermal patches increased drug bioavailability which enable the use of lower drug doses, thus reducing the incidence of adverse events. However, from the evidence, the risk of adverse effects both significantly increased after administrated with opioid regardless the delivery methods. Other potential risks, such as deliberate misuse, are also not different from oral opioid.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Topical capsaicin – knee and/or hip	We suggest not offering topical capsaicin for people with knee and/or hip OA.	conditional against recommendation	Low
<p><i>What is it?</i></p> <p>Capsaicin is the neurotoxin of hot chilli peppers. It binds selectively to the vanilloid compound receptor (TRPV1) of type C afferent fibres and increases P substance in synaptic cleft.⁹³ While first applications of capsaicin are associated with a burning sensation over the applied surface, after continued use, persistent desensitisation and analgesia occurs both due to P substance neural depletion and reversible and selective destruction of primary afferent fibres.⁹³</p> <p><i>Rationale</i></p> <p>The trial by Kosuwon et al. showed small effects of pain relief in patients with knee OA (Technical document, Appendix 5, p82). Another systematic review of Laslett et al. included five RCTs in patients with mixed OA of the hand (one study), knee (three studies) or several joints (hand, knee, hip or shoulder).⁹⁴ It was found topical capsaicin treatment (a concentrate of 0.025% or 0.075%) four times daily is moderately effective (SMD 0.44; 95% CI 0.25–0.62) in reducing pain intensity over 12 weeks and possibly longer.⁹⁴ These results were consistent across trials, suggesting no differences between different doses of capsaicin and between different application sites. It is uncertain that individuals with multi-joint OA or with relevant co-morbidities benefit from capsaicin. The principle benefit of capsaicin is in neuropathic pain which is not the major pain source in knee or hip OA. Similar to other topical analgesia, the topical application process is very regime orientated and local irritation side effects occur that can be detrimental. These issues often outweigh possible benefits to patients.</p> <p><i>Harms</i></p> <p>Mild application site burning was the most common adverse event associated with topical use of capsaicin, being more common in patients using capsaicin (35 – 100 %), and causally associated with capsaicin use, but rapidly ameliorates with continuing use ⁹⁴. There have been no reports of systemic toxicity with the use of topical capsaicin in OA.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Duloxetine – knee and/or hip	We suggest offering duloxetine for people with knee and/or hip OA.	conditional for recommendation	Moderate (knee) Low (hip)

What is it?

The imbalance of serotonin and norepinephrine systems within central pain pathways have been implicated in the development and maintenance of central sensitisation and associated with chronic pain in OA. Duloxetine is a serotonin and norepinephrine reuptake inhibitor (SNRI) with central nervous system activity. Its analgesic efficacy in central pain is putatively related to its influence on descending inhibitory pain pathways. Research has found it has beneficial impact on pain associated with diabetic neuropathy, fibromyalgia, low back pain and OA.

Rationale

In the three trials reviewed, significant response and moderate effects in both knee pain (SMD 0.43) and function (SMD 0.45) were found over 13 to 16 weeks at doses of 60/120mg (Technical document, Appendix 5, p105,219). However, most study participants were also already using both NSAIDs and paracetamol. The use of duloxetine for knee OA as an adjunctively with NSAIDs, thus reducing the usage of NSAIDs and paracetamol, would be clinically useful to reduce adverse events.⁹⁵ In addition, results differed as to whether significant reduction in depression symptoms was needed for analgesic impact. There is no direct RCT evidence for hip OA, thus using knee OA data to extrapolate to hip or other OA requires additional caution.

Harms

Among the patients in the three included RCTs, treatment with duloxetine was well tolerated, with the majority of adverse events being of mild or moderate intensity, for example, constipation, nausea, hyperhidrosis, cough, myalgia, arthralgia and palpitations.

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Doxycycline – knee and/or hip	We do not recommend offering doxycycline for people with knee and/or hip OA.	strong against recommendation	Low (knee) Very low (hip)
<p><i>What is it?</i> Doxycycline is a tetracycline class antibiotic agent. Besides being an antimicrobial agent, it is a metalloproteinase inhibitor and inhibits the collagenase that cleaves collagen type IX that is present in articular cartilage.⁹⁶</p> <p><i>Rationale</i> While preclinical research and earlier human studies indicated doxycycline might be useful in managing symptomatic knee OA, current evidence found that doxycycline did not reduce the mean severity of joint pain, although pain scores in both treatment groups were low at baseline and remained low throughout the trial, suggesting the presence of a floor effect⁹⁵. Despite there is a small benefit (SMD 0.15 mm) in joint space narrowing, it is outweighed by medication harms (Technical document, Appendix 5, p106,221). There is no RCT of doxycycline for hip OA, thus using knee OA data to extrapolate to hip or other OA requires additional caution.</p> <p><i>Harms</i> Adverse events that occurred significantly more frequently in the doxycycline group than in the placebo group were restricted to recognised side effects of doxycycline (i.e., monilial vaginitis, sun sensitivity, nonspecific gastrointestinal symptoms). However, only a small proportion of subjects reporting doxycycline-related side effects discontinued the study medication prematurely. Subjects in the active treatment group reported fewer urinary tract infections, and there was a trend toward fewer upper respiratory tract infections in the doxycycline group than in the placebo group.</p>			

3.2.3 Anti-osteoporosis drugs

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Bisphosphonates - knee	We suggest not offering bisphosphonates for people with knee and/or hip OA.	conditional against recommendation	Very low
<p><i>What is it?</i> Anti-osteoporotic medications are predominantly used to reduce morbidity and mortality (mainly from fractures) associated with exogenous and endogenous osteoporotic change within bone. Bisphosphonates can inhibit bone resorption and therefore are the mainstream medications for osteoporosis. Osteoporosis may be concomitantly present in patients with OA.</p> <p><i>Rationale</i> Evidence from six trials demonstrated no statistical significant benefits in symptom relief, structural and function improvement. The quality of evidence has varied from moderate to very low with inconsistent results. A meta-analysis of the two largest knee studies using risedronate 15 mg showed outcome ratios (ORs) favouring placebos for WOMAC pain (1.73), function (2.03) and stiffness (1.82). However, eight trials (61.5%) reported bisphosphonates improve pain assessed by VAS scores and two (38.5%) reported significant improvement in WOMAC pain scores compared to control groups.⁹⁷ There were no statistically significant differences or trends were noted for any dose of risedronate. Similarly there was no difference between the five groups with respect to radiographic joint space narrowing, joint space width, or osteophyte formation during the 24 month follow-up.⁹⁷ There is one very low quality trial conducted in 42 patients with hip OA, demonstrating no effects over 24 months (Technical document, Appendix 5, p108).</p> <p><i>Harms</i> Bisphosphonates come with significant side effect profiles and restrictions on some day to day activities such as dental procedures. Treatment with these drugs should be reserved for patients who meet the PBS guidelines for treatment of their osteoporosis but not for the management of OA.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Calcitonin – knee and/or hip	We suggest not offering calcitonin for people with knee and/or hip OA.	conditional against recommendation	Very low
<p><i>What is it?</i> Calcitonin is a natural peptide hormone produced by parafollicular cells (C-cells) in the thyroid gland. The protective activity of calcitonin on bone and cartilage has been demonstrated in many different OA models as well as preliminary clinical settings.⁹⁸ Available as an injection or nasal spray since the 1970s to treat osteoporosis, calcitonin inhibits bone resorption by binding and activating to the calcitonin receptor on osteoclasts.</p> <p><i>Rationale</i> The two phase III studies by Karsdal et al. showed no significant effect of salmon calcitonin on total WOMAC, WOMAC subscores and joint space narrowing (Technical document, Appendix 5, p111,224). There is a potential small effect on markers of bone and cartilage degradation, CTX-I and CTX-II respectively, and no positive balance between bone formation and bone resorption. There are no RCTs of calcitonin for hip OA, thus using knee OA data to extrapolate to hip or other OA requires additional caution.</p> <p><i>Harms</i> There were markedly higher incidences of gastrointestinal disorders and hot flushes in the active treatment arms of included studies. No other adverse events were markedly different between the two groups in either study.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Strontium ranelate – knee and/or hip	We do not recommend offering strontium ranelate for people with knee and/or hip OA.	strong against recommendation	Moderate
<p><i>What is it?</i> Strontium ranelate, a bone-acting agent, has the ability to dissociate the bone-remodelling process and to change the balance between bone resorption and bone formation which has been suggested to be a potential symptom-modifying effect.</p> <p><i>Rationale</i> Data from one moderate quality trial showed no effect of strontium ranelate in altering OA symptoms. However, strontium ranelate treatment had a beneficial effect on joint space widening with an MD of 0.12 mm over three years. Similarly, the risk ratio of radiographic progression (joint space narrowing ≥ 0.5 mm) favours strontium ranelate over three years. As strontium ranelate is not accessible for people in Australia, the Working Group considered this treatment as unfeasible for use.</p> <p><i>Harms</i> Strontium ranelate was well tolerated for the treatment of OA in a study duration over 3 years. Despite its listed side effects such as myocardial infarction, venous thromboembolism events, pulmonary embolism, and hypersensitivity reaction in the approved product information, the European Medicines Agency recommended in 2014 that strontium ranelate remains available for patients with osteoporosis with restrictions relative to patients with existing heart disease.⁹⁹ As strontium ranelate would be used as a daily treatment for OA and its effects could be relatively slow, the potential harm caused by its side effects if a concern.</p>			

3.2.4 Investigational disease modifying OA drugs

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Interleukin-1 (IL-1) inhibitors – knee and/or hip	We do not recommend offering IL-1 inhibitors for people with knee and/or hip OA.	strong against recommendation	Low
<p><i>What is it?</i> This is a group of agents that block the activity of a pro-inflammatory cytokine, interleukin (IL)-1 which is believed to play a role in inducing cartilage matrix degradation through up-regulation of proteolytic enzymes.¹⁰⁰ The most common IL-1 inhibitors are the IL-1 receptor antagonist, anakinra, the soluble decoy receptor rilonacept and the neutralising monoclonal anti-IL-1β antibody, canakinumab. In addition, a monoclonal antibody directed against the IL-1 receptor, AMG 108 and a neutralising anti-IL-1α or IL-1β antibody, ABT-981 are currently in clinical trials.</p> <p><i>Rationale</i> Results are from one 3-arm trial of a single intra-articular injection of anakinra at a dose of 50 mg (n=34) and 150 mg (n=67). The mean improvement from baseline to week 12 in the WOMAC score was not statistically different between the anakinra and placebo groups (Technical document, Appendix 5, p115,228). A placebo-controlled RCT of AMG-108 which is not included in the evidence table has showed non-statistically significant improvement on WOMAC pain after subcutaneous administration of AMG-108.¹⁰¹ As IL-1 inhibitors require an authority prescription which cannot be prescribed by a GP, GPs need to work with specialists to get access to these agents. The Working Group discussed the limitations in current efficacy and safety, access and costs and considered it was not a feasible nor cost-effective treatment. There are currently no trials that have investigated the benefits and safety of IL-1 inhibitors in people with hip OA. Using knee OA data to extrapolate to hip or other OA requires additional caution.</p> <p><i>Harms</i> The percentage of patients reporting adverse events (AEs) was similar between the placebo group and the anakinra groups (Technical document, Appendix 5, p115,228). The most common AE was arthralgia (10%), with similar rates between the anakinra 150 mg group and the placebo group but a lower rate for the anakinra 50 mg group (3%). Headache (10% versus 1%), upper respiratory tract infection (8% versus 1%), back pain (8% versus 3%), and extremity pain (6% versus 0%) occurred more often in the anakinra 150 mg group than in the placebo group. Infections were reported in 10% of patients, more frequently for the anakinra 150 mg group compared with the anakinra 50 mg or the placebo group.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Anti-nerve growth factor (NGF) – knee and/or hip	We suggest not offering anti-nerve growth factor for people with knee and OA	conditional against recommendation	Moderate
<p><i>What is it?</i></p> <p>Nerve growth factor (NGF) is a secretory soluble protein that binds to two different cell surface receptors, the 75 kDa neurotrophin receptor (p75NTR) and the high-affinity NGF-specific tyrosine kinase receptor (TrkA). It is critical for normal development of sympathetic neurons and sensory neurons responsible for nociception and temperature sensation.¹⁰²</p> <p>A humanised monoclonal antibody, tanezumab, was developed specifically to inhibit NGF from binding to its receptors on pain-signalling neurons. Fulranumab is a fully humanized recombinant immunoglobulin G2 (IgG2) monoclonal antibody that specifically neutralises the biological actions of human NGF.</p> <p><i>Rationale</i></p> <p>Results from 5 trials of tanezumab and 1 trial of fasinumab showed a statistically significant lower WOMAC pain and function score compared to placebos with a pooled SMD of 0.6 and 0.64 respectively (Technical document, Appendix 5, p118,231). The dosage of tanezumab differed between phase II and phase III studies included in the systematic review. There were two phase II studies of tanezumab by Lane et al. and Nagashima et al., which demonstrated SMD ranging from -0.31 to 0.94 with five different dose groups (10 µg/kg, 25 µg/kg, 50 µg/kg, 100 µg/kg, and 200 µg/kg).¹⁰¹ The other phase III studies evaluated a narrower dose range (2.5 mg, 5 mg and 10 mg) and reported a correspondingly narrower range of SMD, from 0.26 to 0.61, all being statistically significantly different from placebo. In the study of fasinumab, all 3 doses of fasinumab were associated with significant improvements compared with placebo in walking knee pain and WOMAC total and subscale scores.</p> <p>In the included hip studies, statistically significant but less clinically relevant effects were found on WOMAC pain and function scores with pooled SMDs of 0.33 and 0.4 respectively (Technical document, Appendix 5, p118,231). The study conducted by Sanga et al. evaluated fulranumab with two different dosing frequencies (1 and 3 mg every 4 weeks and 3, 6 and 10 mg every 8 weeks), showing a numerical difference from the active control (oxycodone), although no differentiation was seen between either fulranumab dose and placebo in the same study.</p> <p>The Working Group discussed that anti-NGF requires off-label prescribing and is expensive which limited its accessibility and affordability.</p> <p><i>Harms</i></p> <p>Based on current evidence, the numbers of adverse events were not significantly different between treatment and placebo groups. Reported adverse events included arthralgia, headache, upper respiratory tract infection and abnormal peripheral sensation (e.g. paraesthesia, dysesthesia, hyperaesthesia and hypoesthesia). A meta-analysis of tanezumab safety suggested tanezumab plus NSAID treatment had a higher occurrence of serious adverse events than use of NSAID alone.¹⁰³ A recent adjudication of joint-related adverse events in the tanezumab clinical program reported tanezumab was not associated with an increased risk of osteonecrosis, but was associated with an increased risk of rapidly progressive OA, especially in patients on higher doses of tanezumab, tanezumab combined with NSAIDs, or pre-existing subchondral insufficiency fractures.¹⁰⁴</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Fibroblast growth factor (FGF) – knee and/or hip	We do not recommend offering fibroblast growth factor for people with knee and/or hip OA.	strong against recommendation	Very low
<p><i>What is it?</i> Sprifermin is a recombinant and truncated version of human fibroblast growth factor (FGF)-18 that binds to and specifically activates FGF receptor-3 in cartilage to promote chondrocyte proliferation and cartilage matrix production.</p> <p><i>Rationale</i> There is one trial of 190 patients with knee OA evaluating the effects of intra-articular injection of sprifermin as a single treatment and as a multiple-dose regimen (3 doses of either 10 µg, 30 µg, or 100 µg). Results showed all groups had improved WOMAC pain scores, with statistically significantly less improvement at 12 months in patients receiving the 100 µg dose of sprifermin compared with patients receiving placebo. No statistically significant relationship between treatment group and reduction in central medial femorotibial compartment cartilage thickness was observed. However, sprifermin was associated with statistically significant, dose-dependent reductions in loss of total and lateral femorotibial cartilage thickness and volume and in joint space widening in the lateral femorotibial compartment (Technical document, Appendix 5, p120,233). The reasons for the seemingly preferential effect on the lateral knee compartment in the present and previous studies are not clear. In OA, the status of cartilage differs between the medial and lateral femorotibial compartments, with the medial compartment more commonly severely affected. An anabolic agent acting on cartilage may be less effective in tissue that is severely damaged. Currently, sprifermin is expensive and mainly available in phase II trials. No trials have investigated the benefits and safety of sprifermin in people with hip OA. Using knee OA data to extrapolate to hip or other OA requires additional caution.</p> <p><i>Harms</i> According to the findings from two recent trials, the overall proportion of patients experiencing at least one treatment emergent adverse event (TEAE) was not increased in the sprifermin group versus placebo (Technical document, Appendix 5, p120,233). Incidence, severity, and nature of reported TEAEs raised no local or systemic safety concerns for doses up to 300 µg.¹⁰⁵</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Colchicine – knee and/or hip	We suggest not offering colchicine for people with knee and/or hip OA.	conditional against recommendation	Very low
<p><i>What is it?</i></p> <p>Colchicine is a medication most commonly used to treat gout. It is a toxic natural product and secondary metabolite, originally extracted from plants of the genus colchicum. The hypothesis of action of colchicine is that it can block inflammasome-mediated inflammatory and biochemical joint degradation. The therapeutic use of colchicine has extended beyond gouty arthritis and familial Mediterranean fever, to OA, pericarditis, and atherosclerosis.¹⁰⁶</p> <p><i>Rationale</i></p> <p>There is currently a lack of high quality evidence supporting use of colchicine for symptomatic relief for people with knee OA. While two small trials (one comparing colchicine to placebo and one comparing the combination of colchicine and an anti-inflammatory medication to the anti-inflammatory medication alone) indicate colchicine may provide symptomatic relief (Technical document, Appendix 5), its efficacy and safety remains unproven. In both trials participants who received colchicine reported more gastrointestinal adverse effects and the benefit to risk profile needs to be investigated in larger studies. One randomised placebo-controlled trial for people with knee OA that commenced enrolment of 120 participants in June 2014 in Singapore is reported to have been completed (ClinicalTrials.gov Identifier: NCT02176460), but so far the results have not been published. One additional trial was identified in a search of the WHO International Clinical Trials Registry Platform (ICTRP). This trial is reported to have recruited 81 participants between March and September 2012 in Iran and was retrospectively registered in September 2015 (IRCT2015071623240N1). These results have also not been published. There are currently no trials investigating the benefits and safety of colchicine in people with OA of the hip.</p> <p><i>Harms</i></p> <p>There are no significant adverse events in the included trials of colchicine. The most commonly reported adverse events encountered with colchicine were gastrointestinal adverse events such as loose bowel movements and pain in the abdomen, which were usually mild.</p>			

Intervention	Recommendation	Strength of recommendation	quality of evidence
Methotrexate – knee and/or hip	We suggest not offering methotrexate for people with knee and/or hip OA.	conditional against recommendation	Low
<p><i>What is it?</i> Methotrexate is a chemotherapy agent and immune system suppressant, which is commonly used to treat cancer and autoimmune diseases such as rheumatoid arthritis and psoriasis. For treating inflammatory arthritis, multiple mechanisms appear to be involved, including the inhibition of enzymes involved in purine metabolism, leading to accumulation of adenosine; inhibition of T cell activation and suppression of intercellular adhesion molecule expression by T cells; and inhibition of methyltransferase activity, leading to deactivation of enzyme activity relevant to immune system function.</p> <p><i>Rationale</i> Very low quality evidence from one small trial of 56 patients used 7.5 mg methotrexate weekly versus placebo for painful knee OA and did not find a reduction in pain at 4 months (Technical document, Appendix 5, p124). Another open-label study by Wenham et al has evaluated effects of methotrexate for pain relief in patients with knee OA. At 24 weeks, 13/30 participants (43%) had achieved $\geq 30\%$ reduction in VAS pain, of whom 7 (23%) had achieved $\geq 50\%$ reduction. Four participants (13%) had experienced a flare. Thirteen of 30 (43%) participants achieved OARSI responder criteria.¹⁰⁷ An ongoing pragmatic phase III trial (ISRCTN77854383) has been designed to confirm these inconsistent findings. In terms of cost and access, methotrexate is a relatively cheap and widely available. Currently, there is no direct evidence for hip OA.</p> <p><i>Harms</i> Side-effects of methotrexate can include gastrointestinal side-effects, haematological abnormalities and elevated liver transaminases. Side-effects resulting in discontinuation of the drug vary in frequency from 15 to 17%, but have been shown to reduce to 4% in the second year of treatment.^{108, 109}</p>			

3.2.5 Intra-articular injections

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Corticosteroid injection – knee or hip	We suggest offering an intra-articular corticosteroid injection for people with knee OA for short term use. Clinicians need to be cautious of the potential harms of repeated use.	conditional for recommendation	Very low
<p><i>What is it?</i> Corticosteroids are medications that mimic the effects of the hormone cortisol, which is produced naturally by the adrenal glands. Cortisol helps lower levels of prostaglandins and downplays the interaction between certain white blood cells involved in the immune response. Corticosteroid injection is frequently used for short term symptom relief in the setting of a flare of joint symptoms or when a rapid reduction in symptoms is required.</p> <p><i>Rationale</i> The studies upon which the recommendation is based were at serious risk of bias and were generally small in size. The overall quality of the evidence was judged to be low to very low (Technical document, Appendix 5, p126,239). Beneficial effects on knee pain and knee function were demonstrated at up to 6 weeks. These findings were not present when follow-up was extended to 3 months. For hip pain, the clinical benefits were demonstrated for up to 12 weeks, however, there is lack of long-term data. In addition, considering the complexity of the hip joint, image guidance would be required which further adds to the costs. The Working Group considered intra-articular corticosteroid injections can be used as an adjunct to core treatment for short term reduction of moderate to severe pain in people with knee or hip OA.</p> <p><i>Harms</i> Serious and total adverse events were not significantly increased versus placebo. There are however concerns of more rapid cartilage loss with repeated injections with no benefit in long term symptom outcomes at 2 years so these injections should be used judiciously.¹¹⁰</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Viscosupplementation injection – knee and/or hip	<p>We suggest not offering viscosupplementation injection for people with knee OA.</p> <p>We do not recommend offering viscosupplementation injection for people with hip OA</p>	<p>conditional against recommendation</p> <p>strong against recommendation</p>	Low
<p><i>What is it?</i></p> <p>Hyaluronate is a naturally occurring component of the cartilage and the synovial fluid. It is responsible for the rheologic properties of synovial fluid, enabling it to act as a lubricant or shock absorber. In OA, synovial hyaluronate is depolymerised and cleared at higher rates than normal. The therapeutic goal of administration of intraarticular hyaluronate is to provide and maintain intra-articular lubrication, which increases the viscoelastic properties of synovial fluid; this form of therapy is therefore sometimes termed “viscosupplementation.” It is also claimed that hyaluronate exerts anti-inflammatory, analgesic, and possibly chondroprotective effects on the articular cartilage and joint synovium.¹¹¹</p> <p><i>Rationale</i></p> <p>The major analyses upon which the recommendation is based were considered to be at serious risk of bias, but the large number of studies analysed involved, in total, a large number of patients. For both knee pain, function and adverse events, the overall quality of the evidence was judged to be moderate. Despite some inconsistency about the conclusions among the analyses a positive effect, albeit small and not clinically relevant, was demonstrated for pain and function.</p> <p>The recommendation for hip OA is based on three small RCTs which were judged to be not at serious risk of bias (Technical document, Appendix 5, p241). The overall quality of evidence was judged to low. No effect on pain nor function was demonstrated and the risk of total and serious adverse events and local reactions was greater in the supplementation group. In addition, for a hip injection, image guidance would be required further adding to complexity and cost. However, the increased risk of total and serious adverse events concerned the Working Group and when cost and complexity of the intervention were taken into account a conditional against recommendation was agreed upon.</p> <p><i>Harms</i></p> <p>Minor side effects include pain at the injection site (which occurs in 1 to 33% of patients), local joint pain and swelling (in <1 to 30%), and local skin reactions (in 3 to 21%).¹¹¹ Pseudoseptic reactions (occurring in 1 to 3% of patients), which are characterised by inflammation and swelling of the joint that are not caused by infection, can be severe and may require further medical treatment. These reactions usually occur after sensitisation with the second or third injection of a series or with a repeat treatment course. True joint infections have also been reported, but these appear to be rare.¹¹²</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Platelet-rich plasma (PRP) injection – knee and/or hip	We are unable to recommend either for or against the use of platelet-rich plasma injection for people with knee and/or OA	conditional (neutral) recommendation	Very low
<p><i>What is it?</i> Platelet-rich plasma (PRP) is an autologous concentration of a high number of platelets in a small volume of plasma, and it is prepared by centrifugation of blood. Platelets contain significant amounts of cytokines and growth factors which are capable of stimulating cellular growth, vascularisation, proliferation, tissue regeneration and collagen synthesis.</p> <p><i>Rationale</i> The studies upon which the recommendation is based were at serious risk of bias and inconsistency and were generally small in size (Technical document, Appendix 5, p130,243). The overall quality of the evidence was judged to be very low. Beneficial effects on both knee pain and WOMAC function were demonstrated at 6 months. With the concern of potential reporting bias and low quality data, the beneficial effects are likely to be over inflated. In addition, there is no consensus on eligible patient selection, the number and frequency of injections, the preparation technique, or the appropriate platelet concentration,¹¹³ leading to large variations in the design of PRP trials. No RCT was conducted in hip. However, during Working Group discussions, it was suggested that the mechanism of action should be no different in OA of the hip. Therefore, the findings might be transferrable to hip OA but with a particular caution in terms of the complexity of a hip joint. The cost of PRP treatment is high and additional equipment might be required for the preparation and administration.</p> <p><i>Harms</i> Most common treatment related adverse events were local swelling and transient regional pain. PRP did not increase the risk of adverse events compared with hyaluronic acid and saline according to other systematic reviews.¹¹⁴</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Stem cell therapy – knee and/or hip	We do not recommend offering stem cell therapy for people with knee OA	strong against recommendation	Very low
<p><i>What is it?</i> Stem cells are cells that have the ability to divide and develop into many different cell types in the body and can be categorised as pluripotent and multipotent. Mesenchymal stem cells (MSCs) are a common form of multipotent cells that may offer an alternative to cartilage repair techniques not hampered by availability and donor site morbidity. MSCs can be isolated from adipose tissue, bone marrow, synovial tissue, and other sources.</p> <p><i>Rationale</i> The two studies upon which the recommendation is based were at very serious risk of bias and were small in size. The overall quality of the evidence was judged to be low to very low. Beneficial effects on both pain and function were demonstrated at up to 6 months. The differences reported for both pain and function appeared to be remarkably good (Technical document, Appendix 5, p131,245). As they deviate significantly from those of other successful interventions replication is required in high quality, large RCTs before a more favourable recommendation could be considered.</p> <p><i>Harms</i> No serious adverse events were reported in those trials. There are two groups reporting minor adverse events including mild pain and effusion after the injections, which persisted for no more than 7 days.^{115, 116}</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Dextrose prolotherapy – knee and/or hip	We suggest not offering dextrose prolotherapy for people with knee OA	conditional against recommendation	Low
<p><i>What is it?</i> Hypertonic dextrose injection, also termed as prolotherapy, is an injection-based treatment used for a variety of painful chronic musculoskeletal pain conditions. The core practice principle of prolotherapy is injection of relatively small volumes (0.5–6 ml) of an irritant solution, usually hypertonic dextrose, at painful ligament and tendon attachments, as well as in adjacent joint spaces. The hypothesised mechanisms for pain relief include stimulation of local healing, reduction of joint instability through the strengthening of stretched or torn ligaments and stimulation of cellular proliferation.</p> <p><i>Rationale</i> The recommendation is based on the evidence of only one small RCT of low quality. The risk of bias in this study was judged as not serious. No clinically significant effects were found for pain at 24 and 52 weeks follow-up. In terms of function no clinically significant effects were found, for pain at 24 but at 52 weeks a marginally significant effect was recorded (Technical document, Appendix 5, p132, 246). Further high quality RCTs with low risk of bias and specifically for hip OA are required. The Working Group has considered that since prolotherapy is relatively cheap and accessible a conditional against recommendation was agreed upon.</p> <p><i>Harms</i> The study reported self-limited bruises after both dextrose (n = 3) and saline injections (n = 5). This was an expected side effect and deemed to be of minimal clinical relevance due to its transient nature. No serious adverse events were reported; however, this may be because the study sample size is not large enough to detect uncommon adverse events.¹¹⁷</p>			

3.3 Herbal therapies, supplements and nutraceuticals

Supplement use in the context of osteoarthritis management is widespread throughout the community. In general, they are readily available and relatively inexpensive (approximately \$30+ per month per supplement). Usually they are taken in the form of an oral capsule on a daily basis. As can be seen in the evidence summary there is frequently marked heterogeneity (Technical document, Appendix 5, p83,197).

Frequently outlandish claims are made about the curative potential and marked treatment effects that can be seen with the use of these agents. It is important to be cautious in advocating for these but where someone feels marked therapeutic benefit, to not underestimate the potential for placebo effects and if safe and inexpensive, not undermine these placebo effects. For patients that are very enthusiastic about taking complementary and alternative therapies such as supplements it's generally advised they do so cognisant of potential side-effects, potential for interactions with regular medication use and to use them for a period of time (for example 4 to 6 weeks) and cease if there is no benefit gained.

3.3.1 Herbal therapies

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Avocado-soybean unsaponifiables – knee and/or hip	We are unable to recommend for or against the use of avocado-soybean unsaponifiables for people with knee and/or hip OA.	conditional (neutral) recommendation	Very low
<p><i>What is it?</i> An extract of avocado and soybean oils, known as avocado/soybean unsaponifiables (ASU). Available in Australia. The usual dose is around 300mg daily.</p> <p><i>Rationale</i> The 2014 Cochrane review reports ASU 300 mg produced a small and clinically questionable improvement in symptoms, and probably no increased adverse events compared to placebo after three to 12 months treatment.¹¹⁸ In the new evidence review for this guideline short term pain and function up to 6 months was improved by about 0.5 standard deviations and there were no significant longer term benefits in pain or function. The studies examining the use of supplements are often of low quality-constrained by small sample sizes, industry publication bias and potential for positive publication bias. The Working Group discussed in the context of low to very low quality studies, despite some suggesting beneficial effects it is prudent to use caution and advocate further research is needed before a firm recommendation to use or not use ASU.</p> <p><i>Harms</i> In pooled data from 5 RCTs spanning 3 months to 3 years follow up, with a total of nearly 600 patients there was no significant increase in adverse events over placebo.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Boswellia serrata extract – knee and/or hip	We are unable to recommend for or against the use of boswellia serrata for people with knee and/or hip OA.	conditional (neutral) recommendation	Very low
<p><i>What is it?</i> Boswellia serrata, also known as Indian frankincense is a tree that is native to India and Arabia. The resin of Indian frankincense contains substances that may decrease inflammation. The usual dose is 100mg of enriched Boswellia serrata daily.</p> <p><i>Rationale</i> The three small RCTs show significant short term benefits in pain and function, however they are all sponsored by the same company raising concern about possible bias. The Working Group discussed in the context of low to very low quality studies, despite suggesting beneficial effects, it is prudent to use caution and advocate further research is needed before a firm recommendation to use or not use Boswellia serrata.</p> <p><i>Harms</i> Limited data on safety available. In 2 RCTs with follow up of 30-90 days pooled (n=117) there was no significant increase in adverse events over placebo. (Technical document, Appendix 5, p85,199).</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Curcuma/curcuminoid – knee and/or hip	We are unable to recommend for or against the use of curcuma/curcuminoid for people with knee and/or hip OA.	conditional (neutral) recommendation	Low
<p><i>What is it?</i> Curcuma, also known as turmeric, is a commonly used yellow spice. There is insufficient research to recommend a particular dose, and there is concern about variation in the concentration and bio-availability of curcuma in a range of products marketed for arthritis. It is readily available in Australia.</p> <p><i>Rationale</i> The three small RCTs show significant short term (6-8 weeks) benefits in pain and function, however they are all industry sponsored raising concern about possible bias and there was inconsistency in the results. All of the studies were conducted in knee OA, so extrapolation to hip or other OA requires additional caution. The Working Group discussed in the context of low to very low quality studies, despite suggesting beneficial effects, it is prudent to use caution and advocate further research is needed before a firm recommendation to use or not use Curcuma.</p> <p><i>Harms</i> Limited data on safety available. In 2 RCTs with follow up of 6-8 weeks pooled (n=113) there was no significant increase in serious adverse events over placebo though there was a non-statistically significant increase in gastrointestinal adverse events 15.8% vs 7.1% in placebo. (Technical document, Appendix 5, p86,200)</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Pycnogenol – knee and/or hip	We are unable to recommend either for or against the use of pycnogenol for people with knee and/or hip OA.	conditional (neutral) recommendation	Low (knee) Very low (hip)
<p><i>What is it?</i> A pine bark Pinus pinaster (synonym Pinus maritima) extract Pycnogenol®. The doses used in the reviewed RCTs were 100-150mg of pine bark extract daily.</p> <p><i>Rationale</i> Three small RCTs showed short term benefits in pain and function however they could not be pooled due to heterogeneity and reporting weaknesses. All were industry sponsored trials with the larger trial at very high risk of bias. Evidence is based on studies of knee OA so be cautious with extrapolation to other OA sites. The Working Group discussed in the context of low to very low quality studies, despite suggesting beneficial effects, it is prudent to use caution and advocate further research is needed before a firm recommendation on the use of pine bark extract.</p> <p><i>Harms</i> Limited data on safety available. In 2 RCTs with follow up to 3 months (n=137) there was no significant increase in serious adverse events over placebo. (Technical document, Appendix 5, p88,202)</p>			

3.3.2 Nutraceuticals

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Glucosamine – knee and/or hip	We suggest not offering glucosamine for people with knee and/or hip OA.	conditional against recommendation	Very low (knee) Low (hip)
<p><i>What is it?</i> Glucosamine is a sugar naturally produced by the body. It is one of the building blocks of cartilage. Glucosamine comes in two forms – glucosamine sulfate and glucosamine hydrochloride. The usual dose is 1500mg daily. Glucosamine supplements are usually made from crab, lobster or shrimp shells, although some supplements are made from a plant form of glucosamine. They are available as tablets or liquid and often in combination with chondroitin.</p> <p><i>Rationale</i> Overall there is very low quality evidence from a large number of RCTs showing that glucosamine provides some benefits to pain in the short-term but no apparent benefits to function, quality of life or joint space narrowing. When the studies are restricted to higher quality trials there is no benefit demonstrated. There is only one RCT of the effect on hip OA which failed to demonstrate a benefit. The Working Group discussed the concerns in the literature of publication bias, effects being driven by small industry sponsored trials and the overall poor quality of the positive trials. Larger publicly funded trials generally demonstrate no effect over placebo. In the context of high-quality trial data that suggests no effect the Working Group recommended a conditional against to discourage the widespread use of glucosamine and chondroitin. This discussion occurred in the context of the cost associated with ongoing supplement use, competing treatment priorities where this might be prioritised over more effective interventions and the effect of direct-to-consumer marketing of supplements. If someone presents, and is taking glucosamine or chondroitin and is feeling marked symptomatic benefit as a consequence of its consumption, it is appropriate not to discourage whatever placebo effects may come from use of the supplements.</p> <p><i>Harms</i> Overall there was a low risk of adverse effects reported in the trials. Shellfish allergy and interactions with warfarin and diabetes are of concern and trials are likely to have excluded patients with those conditions more carefully than usual practice (Technical document, Appendix 5, p90,204).</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Chondroitin – knee and/or hip	We suggest not offering chondroitin for people with knee and/or hip OA.	conditional against recommendation	Very low
<p><i>What is it?</i> Chondroitin is component of connective tissues and bone. It is believed to help draw water and nutrients into the cartilage, keeping it spongy and healthy. Chondroitin is available as chondroitin sulfate supplements, which are made from bovine (cow) or shark cartilage. The usual dose is 800-1200 mg daily as a tablet, capsule or powder.</p> <p><i>Rationale</i> There are a large number of trials (Technical document, Appendix 5, p92, 206) with at least 7 of them industry sponsored. When all 16 studies are pooled there is a clinically and statistically significant effect on pain and function in the short term (up to 3 months), which lessens to clinically not significant by 6 to 12 months, and no effect is demonstrated at 24 months. However, if the analysis is restricted to either studies of higher quality or studies free of industry sponsorship, no benefit is demonstrated. There are some moderate to long term (12 to 24 months) benefits on joint space narrowing, but these are not clinically meaningful (Technical document, Appendix 5, p92, 206). The studies are all in patients with knee OA so extrapolation to hip or other joints requires further caution. The Working Group discussed the concerns in the literature of publication bias, effects being driven by small industry sponsored trials and the overall poor quality of the positive trials. In the context of high-quality trial data that suggests no effect the Working Group recommended a conditional against to discourage the widespread use of glucosamine and chondroitin. This discussion occurred in the context of the cost associated with ongoing supplement use, competing treatment priorities where this might be prioritised over more effective interventions and with lots of people currently using this as a consequence of outlandish marketing claims that are not consistent with the scientific evidence. If someone presents, and is taking glucosamine or chondroitin and is feeling marked symptomatic benefit as a consequence of its consumption, it is appropriate not to discourage whatever placebo effects may come from use of the supplements.</p> <p><i>Harms</i> Pooled data from 6 trials and more than 1000 patients shows the risk of adverse events is comparable to placebo.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Glucosamine and chondroitin in compound form – knee and/or hip	We suggest not offering glucosamine and chondroitin in compound form for people with knee and/or hip OA.	conditional against recommendation	Very low
<p><i>What is it?</i> Glucosamine and chondroitin are often marketed in a combination, at the same doses use as individual components. There does not appear to be any beneficial drug-drug synergistic interaction.</p> <p><i>Rationale</i> With pooling (where possible) of results from the 9 available RCTs no benefit for pain or function or joint space narrowing was demonstrated. All patients in all trials had OA knee as the joint of study so extrapolation to hip needs additional caution. The Working Group discussed the concerns in the literature of publication bias, effects being driven by small industry sponsored trials and the overall poor quality of the positive trials. In the context of high-quality trial data that suggests no effect the Working Group recommended a conditional against to discourage the widespread use of glucosamine and chondroitin. This discussion occurred in the context of the cost associated with ongoing supplement use, competing treatment priorities where this might be prioritised over more effective interventions and with lots of people currently using this as a consequence of outlandish marketing claims that are not consistent with the scientific evidence. If someone presents, and is taking glucosamine or chondroitin and is feeling marked symptomatic benefit as a consequence of its consumption it is appropriate not to discourage whatever placebo effects may come from use of the supplements.</p> <p><i>Harms</i> As with the individual components, the reported rates of adverse events were similar to placebo.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Vitamin D – knee and/or hip	We suggest not offering vitamin D for people with knee and/or hip OA.	conditional against recommendation	Low (knee) Very low (hip)
<p><i>What is it?</i> Vitamin D is a hormone that controls calcium levels in the blood which is crucial for bone, cartilage and muscle development. Oral supplementation with vitamin D is readily available. In these studies, a daily dose of 800-2000 IU, or a monthly dose of 50,000-60,000 IU were used.</p> <p><i>Rationale</i> There were four RCTs (1-3 years duration), all without serious risk of bias. There was however very serious inconsistency in the results, leading to low quality evidence. When combined there is a suggestion of a favourable effect, statistically significant but not reaching what was regarded as clinical significance (SMD >0.4) The results for function were similar to the effect estimates. There was no evidence of favourable structural effects on cartilage volume or joint space narrowing. Notably one study in vitamin D deficient patients also failed to show clinically meaningful beneficial effects (Technical document, Appendix 5, p96, 211). All patients in all studies had knee OA as the joint of study so extrapolation to hip or other joints requires additional caution.</p> <p><i>Harms</i> Relatively safe, a non-statistically significant increase in hypercalciuria. No clinical effects or safety concerns.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Omega-3 fatty acids - knee and/or hip	We suggest not offering omega-3 fatty acids for people with knee and/or hip OA.	conditional against recommendation	Very low
<p><i>What is it?</i> Omega 3 polyunsaturated fatty acids are mainly produced by marine organisms (i.e. oils of marine origin such as oil from whole fish, seal or mussels). Widely available. Usage varied by region and diseases, the usual dose is 1-2 g/day.</p> <p><i>Rationale</i> Pooled data from five RCTs (durations from 15 to 26 weeks) demonstrate no benefits on pain and function in populations of hip and knee OA. Three studies received at least one high risk of bias. Most trials used marine oil from whole fish, but some used cod liver oil, mussel extracts. High heterogeneity was expected from pooling different types of omega-3 fatty acids, and measures within each outcome (Technical document, Appendix 5, p98, 213). The optimal type of omega-3 fatty acids could not be established in OA because only few trials included marine oil from sources other than whole fish. There are high variations in doses of eicosapentaenoic acid (EPA) from 0.01 to 1.7 g/day, and doses of docosahexaenoic acid (DHA) from 0.01 to 1.10 g/day. There is a controlled trial which is not included showing no additional benefit of a high-dose fish oil (4.5 g/day) compared to low-dose fish oil (0.45 g/day).</p> <p><i>Harms</i> Side-effects are usually minor and uncommon.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Collagen – knee and/or hip	We are unable to recommend either for or against the use of collagen for people with knee and/or hip OA.	conditional (neutral) recommendation	Low (knee) Very low (hip)
<p><i>What is it?</i> There are many types of collagen and related derivatives which can be extracted from chicken cartilage, pork skin and bovine bone. These are sometimes available in hydrolysed form to help absorbing and distributing to joint tissues. There is insufficient research to recommend a particular dose.</p> <p><i>Rationale</i> Pooled results from six studies showed short term (13 to 26 weeks) clinical benefits in pain, however, results have very serious inconsistency across included studies. Available data from four studies showed no effect in function. All of the studies were conducted in knee OA, so extrapolation to hip or other OA requires additional caution. The Working Group discussed the concerns in the literature of publication bias, effects being mostly driven by industry sponsored trials and the overall poor quality of the positive trials.</p> <p><i>Harms</i> Relatively safe, a non-statistically significant increase in gastrointestinal adverse events.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Methylsulfonylmethane – knee and/or hip	We are unable to recommend either for or against the use of methylsulfonylmethane for people with knee and/or hip OA.	conditional (neutral) recommendation	Very low
<p><i>What is it?</i> Methylsulfonylmethane (MSM) is an organosulfur molecule that can be synthesised commercially from dimethylsulfoxide (DMSO). DMSO is a pungent solvent that has been used as an application for pain relief over arthritic joints. MSM has the advantage of being odourless and can be easily taken orally in the form of a pill or a powder. The optimal dosing of MSM is not known, but 1-2 g twice a day is often offered in clinical practice.</p> <p><i>Rationale</i> There are three trials with short study durations from 12 to 13 weeks. Pooled data showed statistically and clinically significant benefits in pain. Even larger effects were found in function but with very serious inconsistency and high heterogeneity across studies. Two trials received at least one high risk of bias rating due to inappropriate randomisation technique and potential reporting bias, respectively (Technical document, Appendix 5, p102, 216). The doses in the trials ranged from 1.5g/day to 6 g/day for 12 weeks. All of the studies were conducted in knee OA, so extrapolation to hip or other OA sites requires additional caution. The Working Group discussed the concerns in the literature of publication bias, effects being mostly driven by industry sponsored trials and the overall poor quality of the positive trials.</p> <p><i>Harms</i> Relatively safe. Minor side effects were recorded including gastrointestinal adverse events, fatigue and headaches but not statistically significant compared to placebo.</p>			

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Diacerein – knee and/or hip	We suggest not offering diacerein for people with knee and/or hip OA.	conditional against recommendation	Very low
<p><i>What is it?</i> Diacerein is purified compound with an anthraquinone structure that interferes with pro-inflammatory interleukin (IL) -1 and the secretion of metalloproteinases without affecting the synthesis of prostaglandins. It is widely available on prescription in Europe, but not available in Australia. The dose used in the trials was 50mg twice a day.</p> <p><i>Rationale</i> Five trials were included with time durations ranging from 8 weeks to 12 months, all receiving high risk of bias due to weak allocation concealment and random sequence generation. Very low quality evidence from four trials indicated a small clinical benefit on pain reduction. Data from five trials indicated statistically significant effects on function, but did not reach the clinically meaningful threshold. Analysis of one study demonstrated no benefit in reducing joint space narrowing (Technical document, Appendix 5, p103, 217). The Working Group discussed the concerns in the literature of publication bias, effects being mostly driven by industry sponsored trials and the overall poor quality of the positive trials. A search of regulatory websites found a recommendation from the European Medicines Agency (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) that the marketing authorisation of diacerein should be suspended across Europe because of harms (particularly the risk of severe diarrhoea and potentially harmful effects on the liver) outweighing benefits. However, this guidance is not final as the PRAC recommendation will be re-examined. All of the studies were conducted in knee OA, so extrapolation to hip or other OA sites requires additional caution.</p> <p><i>Harms</i> Adverse events were significantly increased after using diacerein, mainly diarrhoea (RR 3.50, 95%CI 1.95 to 6.27). There is an increase in rash, but the between-group difference was not significant.</p>			

3.4 Surgical interventions

Intervention	Recommendation	Strength of recommendation	Quality of evidence
Arthroscopic lavage and debridement, meniscectomy and cartilage repair – knee OA	We do not recommend offering arthroscopic, lavage and debridement, meniscectomy and cartilage repair for people with knee OA unless the person also has mechanical symptoms of a clinically locked knee as per Australian Knee Society Arthroscopy Position Statement.	Strong against recommendation	Very low (lavage and debridement) Low (meniscectomy) Very low (cartilage repair)
<p><i>What is it?</i> Arthroscopic surgery in persons with knee OA is widely available and commonly occurs. It allows a surgeon to visualise the interior joint space. Arthroscopic joint lavage uses saline irrigation to remove particulate material, such as cartilage fragments and calcium crystals. In arthroscopic debridement, whereby surgical instruments are used to smooth any rough articular surfaces. The goals of arthroscopic lavage and debridement are to decrease synovitis and improve joint motion. Arthroscopic meniscectomy is an outpatient minimally invasive surgical procedure used to treat a torn meniscus cartilage in the knee.</p> <p><i>Rationale</i> There is evidence (very low quality) that there is no apparent benefit in terms of pain, function or quality of life (Technical document, Appendix 5, p133, 247) when performed for joint lavage, debridement and meniscectomy in the setting of knee OA. Arthroscopy occurs more commonly in the private hospital setting than public hospitals. It is important to note that arthroscopy rates in knee OA have been declining in the last few years. In the context of an intervention where there is debatable benefit, measurable costs and potentially serious harms the Working Group strongly recommends against the use of arthroscopy for lavage and debridement in the setting of knee osteoarthritis. The Australian Orthopaedic Association and the Knee Society position statement (https://www.kneesociety.org.au/resources/aks-arthroscopy-position-statement.pdf) strongly states that arthroscopy is not indicated for the treatment of knee OA.</p> <p><i>Harms</i> Side effects from arthroscopic surgeries can include local pain and swelling, infection, prolonged drainage from the surgical site, bleeding into the joint, and thrombophlebitis. It is also associated with a number of potential harms including deep venous thrombosis, premature joint replacement, and rarely, pulmonary embolism and death.</p>			

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