



RACGP

Royal Australian College of General Practitioners

Guideline for the management of knee and hip osteoarthritis

Second edition



Guideline for the management of knee and hip osteoarthritis. Second edition

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We acknowledge the Traditional Custodians of the lands and seas on which we work and live, and pay our respects to Elders, past, present and future.

Publication Approval



Australian Government
National Health and Medical Research Council

The guideline recommendations on pages 5–12 of this document were approved by the Chief Executive Officer of the National Health and Medical Research Council (NHMRC) on 9 July 2018 under section 14A of the *National Health and Medical Research Council Act 1992*. In approving the guideline recommendations, NHMRC considers that they meet the NHMRC standard for clinical practice guidelines. This approval is valid for a period of five years.

NHMRC is satisfied that the guideline recommendations are systematically derived, based on the identification and synthesis of the best available scientific evidence, and developed for health professionals practising in an Australian healthcare setting.

This publication reflects the views of the authors and not necessarily the views of the Australian Government.



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management of knee
and hip osteoarthritis*

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About this guideline

The Royal Australian College of General Practitioners (RACGP) first developed *Guidelines for the non-surgical management of hip and knee osteoarthritis* in 2009. Since then, there has been substantial progress in evaluating the effectiveness and safety of commonly used and new therapies for osteoarthritis (OA). The objective of this new guideline is to present the best available, current scientific evidence for OA interventions, covering all interventions other than joint replacement for the hip and knee.

Target population and audience

This guideline applies to all adults 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 people with OA. This is reflected in the multidisciplinary composition of the guideline development working group, including consumer representatives.

Acronyms

| | | | |
|----------------|--|------------------|---|
| ACR | American College of Rheumatology | MSM | methylsulfonylmethane |
| AIHW | Australian Institute of Health and Welfare | NATSIHS | National Aboriginal and Torres Strait Islander Health Survey |
| ASU | avocado/soybean unsaponifiables | NGF | nerve growth factor |
| BMI | body mass index | NHMRC | National Health and Medical Research Council |
| CALD | culturally and linguistically diverse | NICE | National Institute for Health and Care Excellence |
| CBT | cognitive behavioural therapy | NPRS | Numeric Pain Rating Scale |
| CENTRAL | Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials | NSAID | nonsteroidal anti-inflammatory drug |
| CI | confidence interval | OA | osteoarthritis |
| CINAHL | Cumulative Index to Nursing and Allied Health Literature | OARSI | Osteoarthritis Research Society International |
| COI | conflict of interest | OR | odds ratio |
| COX | cyclooxygenase | p75NTR | 75 kDa neurotrophin receptor |
| COX-2 | cyclooxygenase-2 | PBS | Pharmaceutical Benefits Scheme |
| CRP | C-reactive protein | PG | prostaglandin |
| CT | computed tomography | PHN | Primary Health Network |
| DALYs | disability-adjusted life-years | PICO | patient/population/problem, intervention, comparison/control, outcome |
| DHA | docosahexaenoic acid | PPI | proton-pump inhibitor |
| DMOADs | disease-modifying osteoarthritis drugs | PRAC | Pharmacovigilance Risk Assessment Committee |
| DMSO | dimethylsulfoxide | PRP | platelet-rich plasma |
| EMA | European Medicines Agency | RACGP | The Royal Australian College of General Practitioners |
| EPA | eicosapentaenoic acid | RCT | randomised controlled trial |
| ESR | erythrocyte sedimentation rate | RR | relative risk |
| FGF | fibroblast growth factor | SES | socioeconomic status |
| GP | general practitioner | SMD | standardised mean difference |
| GRADE | Grading of Recommendations Assessment, Development and Evaluation | SNRI | serotonin and norepinephrine reuptake inhibitor |
| HANDI | <i>Handbook of non-drug interventions</i> | TEAE | treatment-emergent adverse event |
| HOOS | Hip Disability and Osteoarthritis Outcome Score | TENS | transcutaneous electrical nerve stimulation |
| ICTRP | International Clinical Trials Registry Platform | TGA | Therapeutic Goods Administration |
| IgG2 | immunoglobulin G2 | TNF-alpha | tumour necrosis factor alpha |
| IL-1 | interleukin-1 | TrkA | tyrosine kinase receptor |
| IPDAS | International Patient Decision Aids Standards | TRPV1 | Transient Receptor Potential Vanilloid 1 |
| KOOS | Knee Injury and Osteoarthritis Outcome Score | VAS | Visual Analog Scale |
| MBS | Medicare Benefits Schedule | WHO | World Health Organization |
| MD | mean difference | WOMAC | Western Ontario and McMaster Universities Osteoarthritis Index |
| MRI | magnetic resonance imaging | | |
| MSC | mesenchymal stem cell | | |

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Conflicts of interest

This guideline was produced in accordance with the rules and processes outlined in the RACGP Conflict of Interest Policy. The RACGP Conflict of Interest Policy is available at www.racgp.org.au/support/policies/organisational

Conflict of interest (COI) disclosures are available in the *Guideline for the management of knee and hip osteoarthritis: Administrative report*.

All guideline development working group members completed a COI register before the commencement of guideline development. Any additional COIs were declared at the start of all meetings, and appropriately recorded. If a member declared a COI relating to a specific intervention (except researching), they did not participate in the discussion or decision-making for the intervention.

The development of the *Guideline for the management of knee and hip osteoarthritis* is funded in part by Medibank Better Health Foundation. It provided support for the development of systematic literature reviews, data extraction and compilation of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) summary report.

Future review of this guideline

This guideline will be reviewed no less than once every five years.

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Summary: Plain language

Osteoarthritis (OA) is a chronic disease and the most common form of chronic arthritis. It is characterised by joint pain, stiffness and swelling, and mainly affects the hands, knees and hips. OA most frequently occurs in people aged >55 years, although younger people can also be affected. Risk factors for OA include joint injury, being overweight or obese, and older age. As the population ages, and increased rates of obesity, the number of Australians with OA is expected to rise from 2.2 million in 2015 to almost 3.1 million by 2030. There is currently no cure for OA, but there are many treatments and approaches to managing the long-term symptoms of this disease. General practitioners (GPs) are often the first point of contact in the healthcare system for a person with OA. This guideline provides Australian GPs with advice and recommendations for the management of people with knee and/or hip OA. The guideline has a strong focus on self-management and non-surgical treatments to improve the health of people with knee and/or hip OA. A summary of the key recommendations are:

Lifestyle:

- Regular exercise is important for relieving pain and improving function in people with knee and/or hip OA. For knee OA, land-based exercise such as muscle strengthening exercises, walking and Tai Chi are strongly recommended. Other land-based exercise that could be considered for some people with knee OA include stationary cycling and Hatha yoga. The best land-based exercise for people with hip OA could not be determined because of limited research. Aquatic exercise may be considered for some people with knee and/or hip OA.
- Weight management is strongly recommended for people with knee and/or hip OA who are overweight or obese.

Non-drug treatments:

- Cognitive behavioural therapy (CBT) could be considered for some people, particularly in conjunction with exercise, and taking into account existing mental health conditions, personal preference, cost and access.
- Heat packs or hot water bottles may be applied as a self-management strategy.
- Using a cane or other devices (eg walker, crutches) may be appropriate for some people with knee and/or hip OA to help improve pain, mobility and balance.
- A short course of manual therapy or massage could be considered for some people with knee and/or hip OA as an adjunct to lifestyle management.
- Transcutaneous electrical nerve stimulation (TENS) that can be used at home may be appropriate for some people with knee and/or hip OA.
- There is a conditional recommendation against the following treatments (refer to [Section 3. Recommendations](#) for an explanation on conditional recommendation)
 - therapeutic ultrasound
 - shockwave therapy
 - laser therapy
 - interferential therapy
 - footwear marketed for knee OA
 - cold therapy
 - valgus braces and lateral wedge insoles for medial knee OA
 - patellofemoral braces
 - kinesio taping.

- Due to a lack of high-quality evidence, no recommendation can be made for the following
 - formal self-management programs
 - varus unloading braces and medial wedge insoles for lateral knee OA
 - shock-absorbing insoles
 - arch supports
 - patellar taping
 - pulsed electromagnetic/shortwave therapy.

Medication:

- Nonsteroidal anti-inflammatory drugs (NSAIDs; eg ibuprofen), taken orally at low doses for short periods are recommended for some people with knee and/or hip OA. Monitoring for possible adverse effects of the drugs is necessary.
- Although there is no recommendation either for or against NSAIDs applied locally to the skin, it may be reasonable to trial topical NSAIDs for a short period, with monitoring of possible adverse effects, then discontinue use if not effective.
- Although there is no recommendation either for or against paracetamol, it may be reasonable to trial paracetamol for a short period in some people with knee and/or hip OA, with monitoring of possible adverse effects, then discontinue use if not effective.
- Corticosteroid injections could be offered for short-term symptom relief for some people with knee and/or hip OA, but care should be taken with repeated injections because of potential harm.
- Duloxetine could be considered for some people with knee and/or hip OA when other forms of pain relief are inadequate.
- There is a strong recommendation against the use of the following
 - oral and transdermal opioids
 - viscosupplementation injection for hip OA
 - doxycycline
 - strontium ranelate
 - interleukin-1 (IL-1) inhibitors
 - stem cell therapy.
- There is a conditional recommendation against the use of the following
 - capsaicin for knee and/or hip OA
 - bisphosphonates
 - calcitonin
 - anti-nerve growth factor (NGF)
 - colchicine
 - methotrexate
 - viscosupplementation injection for knee OA
 - dextrose prolotherapy
 - omega 3 fatty acids
 - diacerein.

- Due to a lack of high-quality evidence, no recommendation can be made for the following
 - injections of platelet-rich plasma (PRP)
 - nonsteroidal anti-inflammatory creams applied locally
 - capsaicin for hip OA
 - collagen
 - methylsulfonylmethane.

Complementary and alternative therapies, and nutraceuticals:

- The following complementary and alternative therapies should not be offered
 - glucosamine and chondroitin nutraceuticals
 - vitamin D
 - acupuncture.
- Due to a lack of high-quality evidence, no recommendations can be made about the following herbal supplements
 - avocado/soybean unsaponifiables (ASU)
 - Indian frankincense (*Boswellia serrata* extract)
 - turmeric
 - pine bark extract.

Surgical interventions:

- There is a strong recommendation against surgery such as arthroscopic lavage and debridement, meniscectomy and cartilage repair for people with knee OA, unless the person also has signs and symptoms of a 'locked knee'.

Recommendations

The Royal Australian College of General Practitioners (RACGP) has used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to rate the quality of evidence and determine the strength of recommendations. The recommendations have been formulated using the GRADE evidence-to-decision framework by considering:

- the quality of evidence
- the balance between benefits and harms
- values and preferences
- resource use
- other relevant considerations.

Strength of recommendations

| Recommendation | Description |
|---|--|
| Strong recommendation for the intervention | The working group is very confident that the benefits of an intervention clearly outweigh the harms (or vice versa) |
| Strong recommendation against the intervention | The working group is very confident that the harms of an intervention clearly outweigh the benefits |
| Conditional recommendation for the intervention | Denotes uncertainty over the balance of benefits, such as when the evidence quality is low or very low, or when personal preferences or costs are expected to impact the decision, and as such refer to decisions where consideration of personal preferences is essential for decision making |
| Conditional recommendation against the intervention | Denotes uncertainty over the balance of harms, such as when the evidence quality is low or very low, or when personal preferences or costs are expected to impact the decision, and as such refer to decisions where consideration of personal preferences is essential for decision making |
| 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
- 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 for their patient. More information about the GRADE approach can be found within [Section 2.4 Formulation of recommendations](#).

Algorithm

The accompanying algorithm ([Appendix 1. Algorithm – Holistic assessment, diagnosis and management of knee and/or hip osteoarthritis](#)) has been developed from information in the guideline to guide the holistic assessment and diagnosis, non-surgical management and surgical management of symptomatic OA in adults.

Summary of recommendations

Strong recommendations for the intervention

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|-------------------------------------|--|--|--|
| 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</p> <p>We strongly recommend walking, muscle-strengthening exercise, and specifically, Tai Chi</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. Realistic goals should be set. Dosage should be progressed with full consideration given to the frequency, duration and intensity of exercise sessions, number of sessions, and the period over which sessions should occur</p> <p>Attention should be paid to strategies to optimise adherence. Referral to an exercise professional to assist with exercise prescription and provide supervision either in person or remotely may be appropriate for some people</p> | Strong for recommendation (all land-based exercise, walking, muscle-strengthening exercise, Tai Chi) | Low (all land-based, Tai Chi) Very low (walking, muscle-strengthening exercise) |
| 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</p> <p>The type of exercise that is most beneficial is not yet known. Clinicians should prescribe an individualised progressive exercise program, taking into account the person's preference, capability and the availability of local facilities. Realistic goals should be set. Dosage should be progressed with full consideration given to the frequency, duration and intensity of exercise sessions, number of sessions, and the period over which sessions should occur</p> <p>The clinician should monitor the person'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 either in person or remotely may be useful for some people</p> | Strong for recommendation (when combining all studies of land-based exercise) | Moderate (land-based) |
| Weight management – Knee and/or hip | <p>We strongly recommend weight management for people with knee and/or hip OA. For those who are overweight (BMI ≥ 25 kg/m²) or obese (BMI ≥ 30 kg/m²), a minimum weight loss target of 5–7.5% of body weight is recommended. It is beneficial to achieve a greater amount of weight loss given that a relationship exists between weight loss and symptomatic benefits. 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 | Very low |

BMI, body mass index; OA, osteoarthritis

Strong recommendations against the intervention

| 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) |
| 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 |
| 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) |
| 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 |
| 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 |
| FGF – Knee and/or hip | We do not recommend offering FGF for people with knee and/or hip OA | Strong against recommendation | Very low |
| Viscosupplementation injection – Hip | We do not recommend offering viscosupplementation injection for people with hip OA | Strong against recommendation | Low |
| Stem cell therapy – Knee and/or hip | We do not recommend offering stem cell therapy for people with knee and/or hip OA | Strong against recommendation | Very low |
| Arthroscopic, lavage and debridement, meniscectomy and cartilage repair – Knee | 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's 'Arthroscopy position statement' | Strong against recommendation | Very low (lavage and debridement) Low (meniscectomy) Very low (cartilage repair) |

FGF, fibroblast growth factor; IL-1, interleukin-1; OA, osteoarthritis

Conditional recommendations for the intervention

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|--|--|------------------------------|
| Cognitive behavioural therapy (CBT) – Knee and/or hip | <p>It may be appropriate to offer CBT for some people with knee and/or hip OA.</p> <p>Clinicians should consider whether CBT is appropriate, taking into account psychological comorbidities and personal preference. They should be cognisant of issues related to cost and access. It is recommended that CBT is combined with exercise to improve outcomes. CBT may be offered face-to-face or via online programs</p> | Conditional for recommendation | Low (knee) Very low (hip) |
| Stationary cycling and Hatha yoga – Knee | <p>It may be appropriate to offer stationary cycling and/or Hatha yoga for some people with knee OA</p> <p>Exercise has also been found to be beneficial for other comorbidities and overall health</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. Realistic goals should be set. Dosage should be progressed with full consideration given to the frequency, duration and intensity of exercise sessions, number of sessions, and the period over which sessions should occur</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 either in person or remotely may be appropriate for some people</p> | Conditional for recommendation | Very low |
| Aquatic exercise/hydrotherapy – Knee and/or hip | <p>It may be appropriate to offer aquatic exercise/hydrotherapy for some people with knee and/or hip OA. This will depend upon personal preference and the availability of local facilities</p> | Conditional for recommendation | Low |
| Massage therapy – Knee and/or hip | <p>It may be appropriate to offer a short course of massage therapy for some 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, cognisant of issues related to cost and access</p> | Conditional for recommendation | Low |
| Manual therapy (stretching, soft tissue and/or joint mobilisation and/or manipulation) – Knee and/or hip | <p>It may be appropriate to offer a short course of manual therapy (stretching, soft tissue and/or joint mobilisation and/or manipulation) for some 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, cognisant of issues related to cost and access</p> | Conditional for recommendation | Very low |
| Weight management plus exercise – Knee and/or hip | <p>It may be appropriate to offer a combination of weight management plus exercise for some people with knee and/or hip OA. For those who are overweight (BMI ≥ 25 kg/m²) or obese (BMI ≥ 30 kg/m²), a minimum weight loss target of 5–7.5% of body weight is recommended. It is beneficial to achieve a greater amount of weight loss given that a relationship exists between the amount of weight loss and symptomatic benefits. 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> | Conditional for recommendation (combination weight management plus exercise) | Low (knee) Very low (hip) |

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|---|--|--------------------------------|------------------------------|
| Heat therapy – Knee and/or hip | It may be appropriate to offer local heat therapy (eg hot packs) as a self-management home strategy for some people with knee and/or hip OA. This should be considered only as an adjunctive treatment | Conditional for recommendation | Very low |
| Assistive walking device – Knee and/or hip | It may be appropriate to offer an assistive walking device (eg cane) for some people with knee and/or hip OA, depending on a person's preference and capability | Conditional for recommendation | Low (knee) Very low (hip) |
| TENS – Knee and/or hip | It may be appropriate to offer TENS that can be used at home for some 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 |
| Oral NSAIDs including COX-2 inhibitors – Knee and/or hip | It may be appropriate to offer oral NSAIDs for some people with knee and/or hip OA It might be reasonable to trial oral NSAIDs at the lowest effective dose for a short period, then discontinue use if not effective. Clinicians also need to inform people, monitor and capture adverse events, especially gastrointestinal, renal and cardiovascular, which may be associated with use of NSAIDs | Conditional for recommendation | Moderate |
| Duloxetine – Knee and/or hip | It may be appropriate to offer duloxetine for some people with knee and/or hip OA Duloxetine currently does not have an indication via the TGA for OA, and should be considered as an investigational medication only. It could be considered for some people with knee and/or hip OA when other forms of pain relief are inadequate | Conditional for recommendation | Moderate (knee) Low (hip) |
| Corticosteroid injection – Knee and/or hip | It may be appropriate to offer an intra-articular corticosteroid injection for some people with knee and/or hip OA for short-term pain relief Clinicians need to be cautious of the potential harms of repeated use | Conditional for recommendation | Very low |

BMI, body mass index; CBT, cognitive behavioural therapy; COX-2, cyclooxygenase-2; NSAIDs, nonsteroidal anti-inflammatory drugs; OA, osteoarthritis; TENS, transcutaneous electrical nerve stimulation; TGA, Therapeutic Goods Administration

Conditional (neutral) recommendations for the intervention

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|---|---|--|--|
| Self-management education programs – Knee and/or hip | 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 However, clinicians should provide information to enhance understanding about OA, its prognosis and its optimal management | Conditional (neutral) recommendation | Very low |
| Specific forms of land-based exercise – Hip | Exercise has been found to be beneficial for other comorbidities and overall health. However, we are unable to specifically recommend either for or against one type of land-based exercise for hip OA over another 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. Realistic goals should be set. Dosage should be progressed, with full consideration given to the frequency, duration and intensity of exercise sessions, number of sessions, and the period over which sessions should occur The clinician should monitor the person'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 either in person or remotely may be useful for some people | Conditional (neutral) recommendation for recommending one type of land-based exercise over another (eg walking, muscle strengthening, stationary cycling, Tai Chi, Hatha yoga) | Very low (walking, muscle strengthening, stationary cycling, Tai Chi, Hatha yoga) |
| Varus unloading knee braces for lateral tibiofemoral compartment knee OA | We are unable to recommend either for or against the use of varus unloading/realignment braces for people with lateral tibiofemoral compartment knee OA | Conditional (neutral) recommendation (varus unloading/realignment braces) | Very low (varus unloading/realignment – no RCT data) |
| Shoe orthotics (medial wedge insoles – Knee; shock-absorbing insoles and arch supports – knee and/or 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 | Conditional (neutral) recommendation (medial wedged insoles) | Very low (medial wedged insoles) Very low (shock-absorbing insoles, arch support – no RCT data) |
| | We are unable to recommend either for or against the use of shock-absorbing insoles or arch supports for knee and/or hip OA | Conditional (neutral) recommendation (shock-absorbing insoles, arch support) | Very low (all hip orthotics – no RCT data) |
| Patellar taping – Knee | We are unable to recommend either for or against the use of patellar taping for people with knee OA | Conditional (neutral) recommendation | Very low |
| Pulsed electromagnetic/shortwave therapy – Knee and/or hip | We are unable to recommend either for or against electromagnetic/shortwave therapy for people with knee and/or hip OA | Conditional (neutral) recommendation | Low (knee) Very low (hip) |
| 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 However, 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 |

| 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 |
| Topical capsaicin – Hip | We are unable to recommend either for or against the use of topical capsaicin for people with hip OA | Conditional (neutral) recommendation | Very low |
| PRP injection – Knee and/or hip | We are unable to recommend either for or against the use of PRP injection for people with knee and/or OA | Conditional (neutral) recommendation | Very low |
| ASU – Knee and/or hip | We are unable to recommend for or against the use of ASU for people with knee and/or hip OA | Conditional (neutral) recommendation | Very low |
| <i>Boswellia serrata</i> extract – Knee and/or hip | We are unable to recommend for or against the use of <i>Boswellia serrata</i> 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 |
| Pine bark extract – Knee and/or hip | We are unable to recommend either for or against the use of pine bark extract for people with knee and/or hip OA | Conditional (neutral) recommendation | Low (knee) Very low (hip) |
| 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) |
| MSM – Knee and/or hip | We are unable to recommend either for or against the use of MSM for people with knee and/or hip OA | Conditional (neutral) recommendation | Very low |

ASU, avocado/soybean unsaponifiables; MSM, methylsulfonylmethane; NSAIDs, nonsteroidal anti-inflammatory drugs; OA, osteoarthritis; PRP, platelet-rich plasma; RCT, randomised controlled trial

Conditional recommendations against the intervention

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|---|--|------------------------------------|--|
| Cold therapy – Knee and/or hip | We suggest not offering local cold application (eg ice packs) for people with knee and/or hip OA | Conditional against recommendation | Very low |
| Valgus unloading/realignment knee braces for medial tibiofemoral compartment and realigning patellofemoral braces for patellofemoral OA | We suggest not offering valgus unloading/realignment braces for people with medial tibiofemoral compartment knee OA | Conditional against recommendation | Low |
| | We suggest not offering realigning patellofemoral braces for patellofemoral OA | Conditional against recommendation | Very low |
| Shoe orthotics (lateral wedge insoles) – Knee | We suggest not offering lateral wedge insoles for people with medial tibiofemoral knee OA | Conditional against recommendation | Very low |
| 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 people with OA to wear footwear with shock-absorbing properties and avoid high-heeled shoes | Conditional against recommendation | Very low (unloading shoes, minimalist footwear) Low (rocker-sole shoes) |
| Kinesio taping – Knee and hip | We suggest not offering kinesio taping for people with knee and/or hip OA | Conditional against recommendation | Very low |
| Other electrotherapy – Knee and/or hip (eg 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 (shockwave, interferential, laser-hip) |
| Therapeutic ultrasound – Knee and/or hip | 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 (ie traditional, laser, electrical) for people with knee and/or hip OA | Conditional against recommendation | Low (knee) Very low (hip) |
| Topical capsaicin – Knee | We suggest not offering topical capsaicin for people with knee OA | Conditional against recommendation | Low |
| Bisphosphonates – Knee and/or hip | 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 |
| Anti-NGF – Knee and/or hip | We suggest not offering NGF for people with knee and/or hip OA | Conditional against recommendation | Moderate |
| Colchicine – Knee and/or hip | We suggest not offering colchicine for people with knee and/or hip OA | Conditional against recommendation | Very low |
| Methotrexate – Knee and/or hip | We suggest not offering methotrexate for people with knee and/or hip OA | Conditional against recommendation | Low |
| Viscosupplementation – Knee | We suggest not offering viscosupplementation injection for people with knee OA | Conditional against recommendation | Low |
| Dextrose prolotherapy – Knee and/or hip | We suggest not offering dextrose prolotherapy for people with knee and/or hip OA | Conditional against recommendation | Low |

| 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 |
| Diacerein – Knee and/or hip | We suggest not offering diacerein for people with knee and/or hip OA | Conditional against recommendation | Very low |

NGF, nerve growth factor; OA, osteoarthritis

1. Background

1.1 Introduction

Osteoarthritis (OA) is a chronic disease that mostly affects the hands, knees and hips. The *2014–15 National health survey* shows that an estimated 2.1 million Australians (9% of the population) of all ages have this condition.¹ A more rapid increase in OA prevalence occurs after the age of 45 years; for those aged >55 years, the prevalence of OA increases to more than 60%.¹

With the ageing Australian population, and increasing rates of obesity, the numbers of Australians with OA is expected to increase from an estimated 2.1 million in 2015 to an estimated 3.1 million (12% of the population) by 2030.¹ Globally, hip and knee OA was ranked as the 11th highest contributor to global disability,² and is 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 more than \$2.1 billion in 2015, and by 2030, these are forecast to exceed \$2.9 billion.⁵ Broader economic costs are estimated to be around \$22 billion annually.⁶

Strategies for relieving pain, minimising disability and slowing disease progression around OA 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 delaying knee replacements alone would be more than \$233 million in 2030.⁵

General practitioners (GPs) are often the first point of contact within the healthcare system for someone with OA. In 2015–16, OA was managed in 26 per 1000 general practice encounters at all ages.⁷ While OA is a chronic condition that imposes a significant burden in terms of years lived with disability, it has a much lesser impact on mortality; therefore, it is often not prioritised by treating health practitioners.

1.2 Objective

The Royal Australian College of General Practitioners (RACGP) published *Guidelines for the non-surgical management of hip and knee osteoarthritis* in 2009.⁸ Since then, substantial progress has 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 up-to-date evidence for OA interventions, other than joint replacement for the hip and knee. Additionally, it is 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:

- What is the efficacy and safety of non-pharmacological (including complementary) interventions for adults with symptomatic knee and/or hip OA?
- What is the efficacy and safety of pharmacological interventions for adults with symptomatic knee and/or hip OA?
- What is the efficacy and safety of arthroscopic surgical procedures for adults with symptomatic knee and/or hip OA?

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

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

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

- increase awareness of the new release and improve uptake of the guideline
- build awareness of project initiation and progress
- seek support and buy-in from stakeholders
- increase awareness and alignment with other national initiatives, including the Australian Commission on Safety and Quality in Health Care's *Osteoarthritis of the knee clinical care standard*, RACGP's *Handbook of non-drug interventions* (HANDI), RACGP *gplearning's* osteoarthritis education module, and Arthritis Australia's MyJointPain website.

1.3 Scope and target population

This update of the 2009 guideline:

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

This guideline will apply to all adults diagnosed with symptomatic OA of the knee and/or hip across the disease trajectory, and is 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 people with knee and/or hip OA in the community. Although foot osteoarthritis is an important source of symptoms in the general community and a prevalent problem, it was not practical within the scope of work to include it in this guideline.

1.4 Target audience

The primary target audience for this guideline is Australian GPs in primary care settings in metropolitan, regional, rural and remote areas. 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 sport and exercise medicine physicians, rheumatologists, orthopaedic surgeons, physiotherapists, occupational therapists, pharmacists, podiatrists, pain physicians, psychologists, exercise physiologists, dietitians, nurses, chiropractors and osteopaths. 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.⁹ Social and economic circumstances, including income, education, employment and social support affect the health of individuals in these areas, placing them at greater risk of poor health.⁹ Furthermore, evidence suggests that poor health, including high rates of arthritis, may worsen poverty in low-income to middle-income countries because of the inability of individuals to work and fulfil community roles.¹⁰

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 2009–10, people in lower socioeconomic households spent proportionately less on medical and healthcare than those in households with higher SES (3% in low compared with 5.1% in high of weekly equivalised expenditure).¹¹ The Australian Institute of Health and Welfare (AIHW) reports that Aboriginal and Torres Strait Islander peoples and CALD communities often lack access to nutritious and affordable food,^{12,13} are less likely to engage in physical activity and have higher rates of overweight and obesity.^{9,14}

After adjusting for age, the prevalence of OA in Aboriginal and Torres Strait Islander peoples is similar to prevalence in the total Australian population.¹⁵ However, areas of lower socioeconomic status generally have higher prevalence of OA in comparison with areas with high socioeconomic status (9.5% compared to 7.2%).¹⁵

In Australia, Aboriginal and Torres Strait Islander peoples with arthritis have fewer visits to GPs and other health professionals.¹⁶ Ensuring access to appropriate and specialised services are particularly important to reduce any 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.¹⁷ In Aboriginal and Torres Strait Islander and CALD communities, connecting individuals to community-based health programs has also been demonstrated to be effective.^{18,19}

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 people with hip and/or knee OA

1.6.1 Holistic assessment

An initial assessment of people with OA should be based on 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.²⁰ 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 the patient–professional partnership, and collaborative care in which patients and healthcare professionals make shared decisions related to treatment to improve outcomes.²¹ Personal preferences for certain types of therapies should also be considered, as adherence to treatment recommendations and outcomes can be compromised if the management plan does not meet the person's preferences and beliefs. Furthermore, people with OA are predominantly older adults and often have different personal priorities and aspirations, which may affect treatment choice. The use of patient-reported measures, inclusive of outcomes and experience, is an important beginning of, and component of, holistic assessment of individuals with hip and/or knee OA. These measures capture a patients' perspective about how their OA impacts on their life, health and wellbeing, and their experience in receiving care. Patient-reported measures are important tools used during the clinical consultation and in multidisciplinary team discussions to contribute to shared clinical decision making and patient-centred care.

People with knee and/or hip 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 some misconceptions (eg exercise will worsen OA, 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** – effect of the condition 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** – nature of pain, other sites of pain, self-help strategies; analgesics use, doses, frequency and side effects; current understanding about persistent pain
- **Functional capacity** – including walking ability, stair climbing, sit-to-stand, balance
- **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; injury/buckling

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

1.6.2 Evaluation of treatment response

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

Diagnosis and evaluation of treatment response in OA is primarily based on clinical assessment. 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 (refer to [Section 1.7.1 Clinical diagnosis](#) and [Section 1.7.2 Limited role for imaging](#)).

There is a variety of clinical tools aimed at evaluating the clinical status and patient-reported outcomes that are mainly used in clinical research. A few commonly used instruments for assessing self-reported pain and function include:

- Numeric Pain Rating Scale (NPRS)²²
- Visual Analog Scale (VAS) for Pain²³
- Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire²⁴
- Knee Injury and Osteoarthritis Outcome Score (KOOS)²⁵
- Hip Disability and Osteoarthritis Outcome Score (HOOS).²⁶

In addition, the 30-second chair-stand test, 40-metre fast-paced walk test, stair-climb test, timed up-and-go test, and six-minute walk test were recommended as complementary tests to patient report measures. The 30-second chair-stand test, 40-metre fast-paced walk test and stair-climb test 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.²⁷

1.7 Diagnosis of hip and/or knee OA

1.7.1 Clinical diagnosis

The diagnosis of knee and/or hip OA can be made based on:

- **Background risk** – population prevalence of knee or hip OA
- **Person's risk factors for OA** – for example, age, gender, body mass index (BMI), occupation
- **Person's symptoms** – persistent knee/hip pain, brief morning stiffness and functional limitation
- **Adequate physical examination** – crepitus, restricted movement and bony enlargement.

Plain radiograph is not needed, but could be considered for atypical presentations.²⁸

A typical knee OA diagnosis can be made without requiring further investigations if a person:^{29,30}

- is aged 45 years or older
- has activity-related joint pain
- has morning stiffness that lasts <30 minutes²⁰
- has crepitus on active motion
- has bony enlargement
- has no detectable warmth.

Additional features that may be present include:³¹

- deformity – fixed flexion and/or varus (less commonly valgus for the knee)
- instability
- peri-articular or joint-line tenderness
- pain on patellofemoral compression.

Similar to knee OA, hip OA can be diagnosed by clinical features alone, according to American College of Rheumatology (ACR) criteria.³² Early physical signs of hip OA include restriction of internal rotation and abduction of the affected hip, with pain occurring at the end of the range of motion.³²

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) that are suggestive of tumour, septic arthritis, crystal arthritis, other inflammatory arthritides (eg rheumatoid arthritis), osteonecrosis, fracture or serious bony pathology, is required during the clinical examination. If any of these are detected, the individual should be referred to an appropriate health practitioner. Involvement of other joints may suggest a wide range of alternative diagnoses.

In clinical practice, laboratory tests (eg rheumatoid factor, erythrocyte sedimentation rate [ESR], synovial fluid aspirate for crystal confirmation, C-reactive protein [CRP]) would be requested to confirm or exclude co-existent inflammatory disease (eg calcium pyrophosphate crystal deposition, gout, rheumatoid arthritis) in people 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.³¹

1.7.2 Limited role for imaging

OA is typically diagnosed clinically, and the role of imaging is limited. 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. It may be beneficial for people with atypical symptoms to be referred to a specialist for magnetic resonance imaging (MRI) investigation as referral by a GP is not reimbursed by the Medicare Benefits Schedule (MBS).

Imaging for OA follow-up is recommended only if there are unexpected rapid progression of symptoms or change in clinical characteristics that need to be confirmed (eg increasing severity of OA).^{20, 28} However, it has been noted that many structural abnormalities seen on imaging are very common in older populations,³³ and these abnormalities should be considered in the appropriate clinical context.

There is a lack of co-occurrence of the radiographic changes and symptoms of OA.³⁴ In people with frequent hip pain, only 15.6% showed evidence of radiographic OA (Kellgren–Lawrence grade 3 or 4).³⁵ Studies have shown that 15–81% of people with radiographic OA have knee pain.³⁴ In addition, the accuracy of the association between symptoms and radiographic OA could be affected by:^{36–38}

- extent of radiographic views
- definitions of pain measurements
- different groups (eg ethnicity, gender) included in the study
- other potential confounders.

If imaging is required, conventional (plain) radiography should be used before other modalities. Soft tissues are best imaged by ultrasound or MRI, and bone by computed tomography (CT) or MRI.

Consideration of radiographic views is important for optimising detection of OA features; in particular, for the knee, weight-bearing and patellofemoral views²⁸ 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. However, MRI

has a definite role in excluding or confirming infrequent differential diagnoses (eg osteonecrosis, avascular necrosis, insufficiency fracture). The systematic use of imaging in the diagnostic process is not recommended in cases with a typical clinical presentation because of the absence of strong evidence supporting the additional impact on the certainty of diagnosis using imaging.²⁸

Key messages regarding imaging in OA:

- OA can be diagnosed clinically, and 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.^{39, 40}
- Serious underlying pathologies are unlikely to be missed, even if people with a clinical diagnosis of OA have no routine imaging.²⁰
- Imaging can lead to increased use of harmful interventions.

1.8 Formulating a management plan

OA management should include a holistic assessment considering the global needs of the individual.²⁰ Personal preferences for certain types of therapies should be assessed, as adherence and outcomes may be compromised if the management plan does not match the person's preferences and beliefs.

Broadly speaking, OA management goals are to minimise pain, optimise function and participation, and to empower the person to self-manage. Given the modest effects of individual treatment approaches, a combination of therapeutic approaches is commonly used. Clinicians should also aim to target modifiable risk factors (eg obesity, strength, depression).

The principles of chronic disease management apply to the care of people with OA, and are based on the following:⁴¹

- care should be continuous; tailored to the person according to individual needs, goals, and values; and be person-centred
- decision-making should be based on the best evidence available, and personal preferences and values
- information should be widely accessible to individuals
- anticipation of needs should be prioritised over a reactive health service.

The number of joints involved, degree of pain, movement restriction and functional impairment, and presence of comorbidities should also guide the management plan. Involvement of partners, family and friends is important to provide the individual with support to self-manage their condition, and is one of the pillars of patient-centred care.

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-pharmacological 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-pharmacological therapies include weight management, promotion of physical activity, strengthening exercises, education and behaviour change support.⁴²

Patient 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.

1.8.1 Education

Education for people with OA is important to improve their understanding of their disease and the importance of self-management.⁴³ Individuals should be informed about the aetiology of OA, the typical fluctuating nature of pain, risk factors (especially those that are modifiable and specific to the person), and expected prognosis, including most people not progressing to requiring joint replacement.⁴⁴

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 individuals to adopt an active approach in the management of their own disease.⁴⁵ Language is important, and terms such as 'wear and tear'

and 'bone-on-bone' should be avoided, as this can lead to pessimism about treatment outcomes (ie nothing can be done) and misbeliefs (eg exercise is detrimental and unsafe) that can affect individual engagement. It is also important to instil a sense of optimism and hope, and facilitate positive expectations about treatment outcome.

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

1.8.2 Multidisciplinary care

As OA is a chronic condition that is often associated with a number of comorbidities and psychosocial issues, many people receive substantial benefits when care is provided using a multidisciplinary team approach. While it is recognised that not all people will require such an approach to management, a key role of GPs is to determine whether a multidisciplinary team approach is necessary, and if so, to refer to appropriately skilled health professionals (actual or virtual) in the community or hospital settings. Many people with chronic pain are best managed in primary care or the community level with multidisciplinary support, including self-care, while specialist services in hospitals typically focus on treating people who are more complex. GPs are ideally placed to play the role of care coordinator to ensure management continuity, whereby there is a consistent, coherent and collaborative approach to management from all team members who are responsive to the person's changing needs. The GP can also delegate certain care coordination activities to another suitable health professional, such as practice nurse or team physiotherapist.

Practice nurses can be invaluable in partnership with GPs in care planning and goal setting. Support of allied health professionals will greatly enhance capacity to include all the concepts of chronic care. It will also add value to the person's experience and outcomes with allied health professionals' expertise in the care of people with OA and the common comorbidities. Some people may need to be referred to practitioners with requisite knowledge and skills in exercise therapy and behaviour change (eg physiotherapists, sports and exercise physicians, exercise physiologists) to prescribe an individualised exercise/physical activity program and facilitate long-term adherence. Physiotherapists and other practitioners with expertise in manual therapy/massage can provide this as a short-term adjunct to facilitate engagement in lifestyle interventions. Referral to dietitians/nutritionists may benefit people who are overweight or obese and require an individualised dietary assessment and management plan. Occupational therapists can provide specific approaches to self-management (eg occupational and home adaptations). Podiatrists/orthotists may be consulted for prescription of shoe orthoses and braces.

While pain management is a high priority in the clinical care of people, there are broader psychological effects arising from a physical health condition that may necessitate psychological intervention to improve a person's ability to live with and manage OA. For some individuals, referral to a multidisciplinary pain clinic or a pain specialist may be warranted, particularly if the person is having difficulties managing pain despite current best practice. Based on a systematic assessment of falls risk, referral to a falls clinic may be beneficial. Referral to other medical practitioners (eg rheumatologists, sports and exercise physicians) may be appropriate for complicated cases, or if symptoms persist or worsen. For people with advanced knee and/or hip OA who continue to have substantial pain and functional difficulty despite high-quality conservative management, referral to an orthopaedic surgeon could be considered in discussion with the person (refer to [Section 1.9 Timing of and need for referral to an orthopaedic surgeon](#)).

1.8.3 Implementation and referral pathways

As part of the development of this guideline, a specific implementation plan was developed to ensure and optimise appropriate dissemination and use of the guideline. It is important to recognise that there are already a number of good resources in existence that should be used to facilitate evidence-based care. These include:

- Victoria and New South Wales both have programs that promote, instil and optimise coordinated multidisciplinary care
 - Victoria's [Model of care for osteoarthritis of the hip and knee](#)
 - New South Wales' [Osteoarthritis chronic care program – Model of care](#)

- Australian Commission on Safety and Quality in Health Care's *Osteoarthritis of the knee – Clinical care standard*
- RACGP's *HANDI* has a number of resources relevant to OA management
 - [Exercise: Knee osteoarthritis](#)
 - [Walking cane: Knee osteoarthritis](#)
 - [Mediterranean diet: Reducing cardiovascular disease risk](#)
 - [Taping: Knee osteoarthritis](#)
- RACGP's *gplearning* has educational modules on OA
- Health Pathways through local Primary Health Networks (PHNs) and [Painaustralia](#)
- NPS MedicineWise' [Knee and hip osteoarthritis](#)

Consumer information resources and services for patient education and support for self-management are provided by support organisations:

- Arthritis Australia's [MyJointPain](#)
- [Arthritis Australia](#)
- [MOVE muscle, bone & joint health](#)
- [painHEALTH](#)

These organisations provide printed and online information, which help reinforce education and self-management advice provided to individuals by clinicians. They may also offer support groups, exercise sessions and other services valuable for social support.

Where possible, GPs should use existing services and referral pathways to optimise targeting appropriate evidence-based care and recommendations within this guideline. These could include allied health referrals (using the Chronic Disease Management MBS items) and access to relevant multidisciplinary state/territory government initiatives.

1.9 Timing of and need for referral to an orthopaedic surgeon

Total joint replacement surgery is the most cost-effective and clinically effective treatment for end-stage OA^{46,47} in appropriately selected individuals. 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 and/or knee OA. In the UK, the estimated mortality-adjusted lifetime risk of total hip replacement at age 50 in 2005 was 11.6% for women and 7.1% for men. For total knee replacement, the risks were 10.8% for women and 8.1% for men.⁴⁸

GPs should consider referring individuals 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 people become housebound and avoid ambulation outside, and marked restriction of activities of daily living (eg rising from a chair or toilet seat, difficulty with climbing stairs).⁴⁸ It is important that careful history, examination and investigations (plain joint radiography) are obtained to avoid up to 25% of people who have been shown to undergo inappropriate joint replacement surgery, including minimal symptoms, less radiographic abnormality and unrealistic expectations.⁴⁹

People who receive the best outcomes following total joint replacement have:

- significant pre-operative radiographic joint change (Kellgren–Lawrence grade 3 or 4)^{50,51}
- well-controlled comorbidities
- a BMI no greater than 30 or no lower than 20
- good mental health status.⁵²

GPs should consider optimising the medical status of people to improve post-operative outcomes and reduce peri-operative complications.⁵³ In this regard, individuals may benefit from pre-operative expert internal medicine referral. The most common pre-operative morbidities include low ferritin, diabetes, hypertension, hyperlipidaemia, back pain, depression, cardiac arrhythmia, coronary artery disease, chronic obstructive pulmonary disease and obesity.⁵⁴

People who are planning surgery should maintain the range of motion of their arthritic joint, and should engage in as much strengthening and physical activity as possible (eg walking, hydrotherapy).^{55,56} Individuals 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 people do well even after uncomplicated surgery. Up to 25% of individuals who had a total joint replacement continue to complain of pain and disability after well-performed surgery.^{57,58} These individuals continue to use health resources. Careful pre-operative patient selection – including considering the poor outcomes that are more common in people who are depressed, have minimal radiographic disease, minimal pain and who are morbidly obese – shared decision-making about surgery and informing individuals about realistic outcomes of surgery are required to minimise the likelihood of dissatisfaction. Objective evidence is available that may identify this cohort of individuals,⁵² and for whom alternate non-operative interventions may be more appropriate.

1.10 Decision aids

Patient decision aids support individuals by making their decisions explicit, providing information about options and associated benefits/harms, and helping clarify congruence between decisions and personal values.⁵⁹ According to the International Patient Decision Aids Standards (IPDAS) collaboration description, decision aids are evidence-based tools designed to prepare individuals to participate in making specific and deliberated choices among healthcare options.⁶⁰ 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; however, well-developed tools will facilitate patient engagement and can be used at various points throughout the person's journey, and surround decisions on every aspect of care including exercise and diet, pharmacological management and in consideration of joint replacement.²⁰ Decision aids are different from patient information leaflets, which aim to only provide information.

In 2014, the UK National Institute for Health and Care Excellence (NICE) reviewed the clinical effectiveness of OA-specific decision aids that may be used to enable individuals 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,⁶¹ and low-quality evidence that patients' confidence in decision making, self-efficacy and preparation for decision making are increased with decision aids.⁶² 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 shared decision programs that are available on the NICE evidence search website, including aids specifically designed for hip and knee OA.

2. Method

The key questions to be answered in the guideline were determined using the patient/population/problem, intervention, comparison/control, outcome (PICO) format. PICO questions are provided in Appendix 2. PICO.

2.1 Literature review

2.1.1 Literature searches

The initial systematic literature search was designed to build upon the literature in the first edition, and to update the evidence published after the last search date for those guidelines.⁸ 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. (For detailed information on search strategies, refer to Appendix 1 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*.) A medical librarian developed and conducted searches using search terms determined by 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 and/or knee OA that 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).⁶³

Table 1. NHMRC evidence hierarchy⁶³

| 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 (RCT) |
| 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 with permission from National Health and Medical Research Council. Additional levels of evidence and grades for recommendations for developers of guidelines. Canberra: NHMRC, 2009.

No limits were placed on language, and studies published in languages other than English were translated whenever possible. Details of the search strategies are available in Appendix 1 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*. Electronic searches were supplemented with manual searches of reference lists of recent systematic reviews to ensure all pertinent resources were 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 that were not 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 guideline to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology, 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 and/or knee OA in which the majority of the enrolled study population ($\geq 80\%$) was aged 45 years or older were included. Only studies reporting participant 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 *Guideline for the management of knee and hip osteoarthritis: Technical document*.

The results of the literature searches were uploaded onto the [Centre for Treatment Comparison and Integrative Analysis \(CTCIA\) web-based screening platform](#), 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 pool of investigators from the working group or named in the *Guideline for the management of knee and hip osteoarthritis: Technical document* – Xia Wang, Mikala Osani, Elizaveta Vaysbrot and Mia-Cara Musetti), with conflicts resolved by a third reviewer (Raveendhara Bannuru). Secondary literature screening involved the thorough review of full-text articles. This was performed on all publications 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 secondary screening, all included articles were tagged with PICO-related terms (eg intervention type(s), 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 on a database, and references were sorted in sequence by 'Study design', then by 'Intervention', 'Comparator', and finally 'Date'.

Preliminary PICO designations were assigned to the references within the sorted document based on their 'Interventions' and 'Comparators'; these designations were verified by a 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 of the *Guideline for the management of knee and hip osteoarthritis: Technical document* 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 the [RevMan](#) software. Risk of bias of the individual studies was assessed using the Cochrane Risk of Bias tool.⁶⁴ Data extraction and risk of bias ratings were reviewed for consistency, and any discrepancies were resolved by consensus within the working group. Data were extracted on:

- study and population characteristics
- intervention dosage and frequency of administration
- concomitant medications
- all critical and important efficacy outcomes
- 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 (relative risk; RR) with 95% confidence intervals (CIs).⁶⁵ 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.⁶⁶ SMDs were calculated to account for variation in the outcome scales. All meta-analyses were also conducted using RevMan.

2.3 Quality assessment and evidence report formulation

The results of the analyses were exported from RevMan into GRADEpro, a web-based software, to generate a GRADE Evidence Profile for each PICO question.⁶⁷ The quality of evidence available for each outcome was assessed in GRADEpro using GRADE quality assessment criteria (Table 3.1, Appendix 3 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).⁶⁸ This assessment was performed in duplicate by two independent reviewers (Investigators Raveendhara Bannuru and Mikala Osani as named in the *Guideline for the management of knee and hip osteoarthritis: Technical document*), with discrepancies resolved by consensus. The evidence was rated for each outcome judged by the following criteria:^{69–72}

- risk of bias assessment of all individual studies
- inconsistency between trial results
- indirectness of evidence
- imprecision of the effect estimate
- potential reporting bias.

As per GRADE methodology, the eventual quality ratings are sorted into four categories: 'High', 'Moderate', 'Low' and 'Very low'. These categories reflect the reviewers' confidence in the effect estimate and its proximity to the true effect of an intervention.⁷³ '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 'Very low' rating carries a numerical equivalent of 1; once the quality of evidence has been downgraded to this point, it cannot be downgraded further.

Once the quality of evidence has been assessed for all reported outcomes, the overall evidence quality was evaluated based on the lowest quality rating given to any of the outcomes that were designated *a priori* to be 'Critical' by the working group.⁷⁴ When no data was available for a recommendation, the overall quality of evidence was automatically marked as 'Very low' to signify that this recommendation was made based on clinical experience alone. The resulting GRADE Evidence Profile contained:

- pooled effect estimates calculated for each outcome
- quality ratings for each outcome
- footnotes containing brief qualitative summaries of the rationales behind quality downgrades
- importance of each outcome
- overall quality of evidence rating.

The final evidence report comprised all the GRADE Evidence Profiles (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

2.4 Formulation of recommendations

GRADE methodology specifies that guideline working groups formulate recommendations based on:⁷⁴

- consideration of the balance of relative benefits and harms of the treatment options under consideration
- quality of the evidence (ie confidence in the effect estimates)
- a person's values and preferences
- resource implications.

Key to the recommendation is the trade-off between desirable and undesirable patient outcomes; recommendations require estimating the relative value individuals place in the outcomes.

A recommendation could either be in favour or against the proposed treatment option, and 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 (eg evidence quality is low or very low), or when personal preferences or costs are expected to affect the decision.⁷⁵ Thus, conditional recommendations refer to decisions where incorporation of personal 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 the recommendations were drafted, the working group was asked to indicate their extent of support for each recommendation through an online survey voting process.⁷⁶ 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 recommendation. 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 *Guideline for the management of knee and hip osteoarthritis: 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 (Table 3.2, Appendix 3 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*), 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.⁷⁴ In these instances, a written explanation is provided describing the reasons for this decision.

3. Recommendations

3.1 Non-pharmacological interventions

3.1.1 Self-management education programs

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|---|---|--------------------------------------|---------------------|
| Self-management education programs – Knee and/or hip | We are unable to recommend either for or against formal face-to-face self-management education programs for people with knee and/or hip osteoarthritis (OA). However, clinicians should provide information to enhance understanding about OA, its prognosis and its optimal management. | Conditional (neutral) recommendation | Very low |

What is it?

Formal face-to-face self-management education programs are complex interventions targeting patient education in order 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.

Rationale

Very low-quality evidence shows this intervention has no significant effect on pain and function (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Self-management education programs may also require a considerable time commitment by the person to attend, and many Australians may experience access difficulties (eg those in rural or remote areas, those for whom English is not a native language). Nonetheless, the programs have the potential to benefit other relevant health domains (eg disease knowledge, self-efficacy), thus may be considered useful for some people. The working group felt that ongoing education and advice provided by the clinician remains integral to person-centred care and shared decision-making.

Harms

No adverse effects reported.

3.1.2 Cognitive behavioural therapy

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|---|--|--------------------------------|------------------------------|
| Cognitive behavioural therapy (CBT) – Knee and/or hip | It may be appropriate to offer CBT for some people with knee and/or hip osteoarthritis (OA). Clinicians should consider whether CBT is appropriate, taking into account psychological comorbidities and personal preference. They should be cognisant of issues related to cost and access. It is recommended that CBT is combined with exercise to improve outcomes. CBT may be offered face-to-face or via online programs. | Conditional for recommendation | Low (knee) Very low (hip) |

What is it?

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.

Rationale

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 anxiety⁷⁷ (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). CBT for knee OA is associated with a low risk of adverse events. Very low-quality evidence from a limited number of studies indicates that combining CBT with exercise is more effective than either alone (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

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 mixed samples of hip/knee OA are likely to be generalisable to those with hip OA. Clinicians should consider the appropriateness of CBT for people with knee and/or hip OA; in particular, those with psychosocial comorbidities. It may be that certain people 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.⁷⁸ 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. Evidence-based online CBT programs are an alternative option for people with limited accessibility to face-to-face treatment.^{77,79}

Harms

Low likelihood of adverse effects.

3.1.3 Exercise

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|----------------------------|--|--|--|
| Land-based exercise – Knee | <p>We strongly recommend offering land-based exercise for all people with knee osteoarthritis (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 walking, muscle-strengthening exercise and Tai Chi. It may be appropriate to offer stationary cycling and/or Hatha yoga for some people with knee OA.</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. Realistic goals should be set. Dosage should be progressed with full consideration given to the frequency, duration and intensity of exercise sessions, number of sessions, and the period over which sessions should occur.</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 either in person or remotely may be appropriate for some people.</p> | <p>Strong for recommendation (all land-based exercise, walking, muscle-strengthening exercise, Tai Chi)</p> <p>Conditional for recommendation (stationary cycling, Hatha yoga)</p> | <p>Low (land-based, Tai Chi)</p> <p>Very low (walking, muscle strengthening, stationary cycling, Hatha yoga)</p> |

What is it?

This recommendation is specific to exercise performed on land for people with knee OA, including muscle strengthening, stretching/range of motion, aerobic conditioning, neuromuscular/balance, cycling, Tai Chi and yoga. Exercise dosage can vary in frequency, intensity and duration. Additionally, the exercise can involve expensive, specialised equipment, or no equipment at all; it can be delivered in a group setting or individually, either in-person or remotely via telephone or videoconference.

Rationale

There is low-quality evidence from a large number of randomised controlled trials (RCTs) that found 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 (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). The benefits for pain and function are moderate in size, and are seen irrespective of the patients' age, structural disease severity, pain levels and functional status. In addition to these benefits, other advantages of exercise include its benefits for comorbidities and overall health, and is readily available and cheap. There is evidence that long-term therapeutic exercise is safe and not associated with an increased risk of structural disease progression.⁶⁰ There are various forms of land-based exercise that may be adopted for knee OA. The working group strongly recommended walking, muscle-strengthening exercise 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 people. Tai Chi was also recommended as it has additional benefits for balance and falls, thus may be particularly suitable for people in whom an increased risk of falling has been identified – something 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 for cycling and 2 for Hatha yoga), with small samples sizes showing benefits for pain (stationary cycling and Hatha yoga) and function (Hatha yoga). However, Hatha yoga should only be considered as an adjunctive form of exercise, and only for short-term management. Clinicians should educate the individual about the benefits of regular exercise, and prescribe an individualised progressive exercise program by taking into account individual presentation, functional capacity, comorbidities, preferences and exercise availability. Clinicians should emphasise that some discomfort may be experienced with exercise, but that this is not likely to be associated with harm. Some people may benefit from referral to an exercise professional (eg physiotherapist, exercise physiologist) to assist with exercise prescription and supervision. Attention should be paid to adherence strategies (eg written material, logbooks, text message reminders).

Harms

There is a very low likelihood of serious adverse effects; most are minor and include temporary increased pain at the affected joint or pain at other sites.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|---------------------------|--|---|---|
| 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.</p> <p>Clinicians should prescribe an individualised progressive exercise program, taking into account the person's preference, capability and the availability of local facilities. Realistic goals should be set. Dosage should be progressed with full consideration given to the frequency, duration and intensity of exercise sessions, number of sessions, and the period over which sessions should occur.</p> <p>The clinician should monitor the person'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 either in person or remotely may be useful for some individuals.</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 (eg walking, muscle strengthening, stationary cycling, Tai Chi, Hatha yoga)</p> | <p>Moderate (land-based)</p> <p>Very low (walking, muscle strengthening, stationary cycling, Tai Chi, Hatha yoga)</p> |

What is it?

This recommendation is specific to exercise performed on land for people with hip OA, 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; it can be delivered in a group setting or individually, either in-person or remotely via telephone or videoconference.

Rationale

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 (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). 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 any specific type of exercise for hip OA because of limited or non-existent trials in people with hip OA that isolate the effects of different types of exercise. Clinicians should educate the individual about the benefits of regular exercise, and prescribe an individualised progressive exercise program, taking into account patient presentation, functional capacity, comorbidities, preferences and resource availability. Clinicians should emphasise that some discomfort may be experienced with exercise, but that this is not likely to be associated with harm. Some people may benefit from referral to an exercise professional (eg physiotherapist, exercise physiologist) to assist with exercise prescription and supervision. Attention should be paid to adherence strategies (eg written material, logbooks, SMS reminders).

Harms

There is a very low likelihood of serious adverse effects; most are minor and include temporary increased pain at the affected joint or pain at other sites.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|---|--------------------------------|---------------------|
| Aquatic exercise/ hydrotherapy – Knee and/or hip | It may be appropriate to offer aquatic exercise/hydrotherapy for some people with knee and/or hip OA. This will depend upon personal preference and the availability of local facilities. | Conditional for recommendation | Low |

What is it?

Aquatic exercise/hydrotherapy are 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 located in community settings. In some settings, classes may be specific to those with arthritis and/or musculoskeletal conditions.

Rationale

There is low-quality evidence that aquatic exercise lead to small statistically significant improvements in pain, physical function and quality of life in people with knee and/or hip OA (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). There is a low risk of harm 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 people 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 a person should be advised to undertake aquatic exercise. Although the benefits in pain reduction and function from aquatic exercise therapy in the treatment of hip and/or knee OA are smaller than the effects from land-based exercise therapy, people who experience too much pain to exercise in a full weight-bearing environment can benefit from aquatic exercise therapy.

Harms

There is a very low likelihood of serious adverse effects; most are minor and include temporary increased pain at the affected joint or pain at other sites.

3.1.4 Manual therapy, weight management and heat/cold therapy

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|--|--------------------------------|---------------------|
| Massage therapy – Knee and/or hip | It may be appropriate to offer a short course of massage therapy for some people with knee and/or hip osteoarthritis (OA). This should be considered only as an adjunctive treatment to enable engagement with active management strategies, and only for short term, cognisant of issues related to cost and access. | Conditional for recommendation | Low |
| Manual therapy (stretching, soft tissue and/or joint mobilisation and/or manipulation) – Knee and/or hip | It may be appropriate to offer a short course of manual therapy (stretching, soft tissue and/or joint mobilisation and/or manipulation) for some 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, cognisant of issues related to cost and access. | Conditional for recommendation | Very low |

What is it?

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
- 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 movements 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.

Rationale

The evidence is from very low-quality or low-quality data. For some people with knee and/or hip OA, these therapies may have a positive effect on pain and/or function over a short term (low-quality to very low-quality evidence), and there is a very low risk of harm (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). The working group felt that for some people with knee and/or hip OA, these therapies may be useful as a single, short-term (eg up to 8–12 weeks) trial, and should be used only as an adjunct to active rehabilitation interventions, given they emphasise a passive approach to treatment. When considering manual therapies, clinicians and individuals should be aware of possible cost, time and access barriers.

Harms

There is a very low risk of harm reported.

| 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 (body mass index [BMI] ≥ 25 kg/m ²) or obese (BMI ≥ 30 kg/m ²), a minimum weight loss target of 5–7.5% of body weight is recommended. It is beneficial to achieve a greater amount of weight loss given that a relationship exists between the amount of weight loss and symptomatic benefits. 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 |

What is it?

Weight loss is usually achieved through a combination of dietary modification and exercise, and in extreme cases, bariatric surgery.

Rationale

Overweight/obesity is a major risk factor for the 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 comorbidities associated with overweight/obesity (eg cardiovascular, gastrointestinal, 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 through diet and exercise) has no significant effect on either pain or function in people with knee OA (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*), although benefits appear to be more significant with higher amounts of weight loss – starting at a minimum of 5–7.5% body weight loss. Ideally, it is beneficial to achieve a greater amount of weight loss.^{81,82} Dietary weight loss should also be combined with exercise for greater benefits (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). There is no randomised controlled trial (RCT) on the effects of bariatric surgery in people with hip and/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 people who are overweight/obese with knee and/or hip OA outweigh the risks. Clinicians are advised to refer to the National Health and Medical Research Council's (NHMRC's) guidelines for the most effective strategies for managing overweight/obesity in primary care.⁸³

Harms

There are low risk of harms associated with this recommendation. However, there are currently no clearly defined BMI thresholds for older adults (aged >65 years). There is evidence to suggest that the cut-offs should be higher for older adults.⁸⁴ The need for weight loss in older adults should be considered on an individual basis. If weight loss is appropriate, care should be taken to ensure maintenance of lean body mass and bone density, especially when it is accompanied with high intensity resistance and/or impact loading training.⁸⁵ People should be monitored for bone health if needed and strengthening exercise included as part of the treatment program.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--------------------------------|---|--------------------------------|---------------------|
| Heat therapy – Knee and/or hip | It may be appropriate to offer local heat therapy (eg hot packs) as a self-management home strategy for some people with knee and/or hip OA. This should be considered only as an adjunctive treatment. | Conditional for recommendation | Very low |

What is it?

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.

Rationale

Heat therapy may be effective in reducing pain for some people with knee and/or hip OA, but the quality of evidence is very low (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Heat therapy is cheap and generally feasible for people to undertake independently as a self-management strategy.

Harms

There are no adverse effects reported. However, individuals should be warned about the risks of burns and heat therapy may not be suitable in those with compromised sensation.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--------------------------------|---|------------------------------------|---------------------|
| Cold therapy – Knee and/or hip | We suggest not offering local cold application (eg ice packs) for people with knee and/or hip OA. | Conditional against recommendation | Very low |

What is it?

Cold therapy is the local application of cold via techniques (eg ice packs). It aims to reduce swelling, muscle spasm and pain.

Rationale

There is very low-quality evidence suggesting 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 (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

Harms

While no adverse events have been identified in trials of cold therapy in people with knee OA, there is emerging clinical evidence that individuals with symptomatic knee OA may experience cold hyperalgesia,^{86,87} suggesting therapeutic use of cold may be unhelpful.

3.1.5 Braces, orthotics, taping, footwear and canes

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--------------|---|---|--|
| Knee braces | We are unable to recommend either for or against the use of varus unloading/realignment braces for people with lateral tibiofemoral compartment knee osteoarthritis (OA). | Conditional (neutral) recommendation (varus unloading/realignment braces) | Very low (varus unloading/realignment – no randomised controlled trial [RCT] data) |
| | We suggest not offering valgus unloading/realignment braces for people with medial tibiofemoral compartment knee OA. | Conditional against recommendation (valgus unloading/realignment braces) | Low (valgus unloading/realignment braces) |
| | We suggest not offering realigning patellofemoral braces for patellofemoral OA. | Conditional against recommendation (realigning patellofemoral braces) | Very low (realigning patellofemoral braces) |

What is it?

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.

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.

Rationale

There is no RCT evidence on 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 (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Similarly, there is limited, very low-quality evidence that patellofemoral realigning braces have no significant effect on pain or function (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Knee braces can impose a considerable financial cost to an individual, and may be associated with difficulties in applying the brace independently. Adherence with wearing knee braces can also be a limiting factor in the appropriateness of such braces.

Harms

There is a low likelihood of adverse effects, which can include skin irritation.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|---|---|---|--|
| Shoe orthotics (medial and lateral wedge insoles – knee, shock-absorbing insoles and arch supports – knee and/or 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. | Conditional (neutral) recommendation (medial wedge insoles for lateral tibiofemoral OA) | Very low (medial, lateral wedged insoles) |
| | We suggest not offering lateral wedge insoles for people with medial tibiofemoral knee OA. | Conditional against recommendation (lateral wedge insoles) | Very low (medial, lateral wedged insoles) |
| | We are unable to recommend either for or against the use of shock-absorbing insoles or arch supports for knee and/or hip OA. | Conditional (neutral) recommendation (shock-absorbing insoles, arch supports) | Very low (shock-absorbing insoles, arch support – no RCT data) |
| | | | Very low (all hip orthotics – no RCT data) |

What is it?

Various shoe orthotics that are 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 towards 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 a material that aims to absorb impact loading during walking. Arch supports are insoles designed to support and realign the foot.

Rationale

Very low-quality evidence from a single, small RCT investigating medial wedge insoles found significant benefits of clinically relevant magnitude for pain and function in people with lateral tibiofemoral compartment knee OA and valgus deformity (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). The working group felt that this study provides preliminary evidence that would need to be confirmed in larger trials and, as such, was unable to recommend either for or against medial wedge insoles. Conversely, for lateral wedge insoles, very low-quality evidence from a number of RCTs found no significant benefits for pain, function, quality of life or structural disease progression in people with medial knee OA (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). As there is 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.

Harms

There is a low likelihood of adverse effects.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|-----------------|---|------------------------------------|--|
| 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 people to wear footwear with shock-absorbing properties and avoid high-heeled shoes. | Conditional against recommendation | Very low (unloading shoes, minimalist footwear) Low (rocker-sole shoes) |

What is it?

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 and a lateral wedge insole, designed to reduce medial tibiofemoral compartment knee loads. Minimalist shoes are footwear styles that are flexible, flat and non-heeled, advertised 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, thereby encouraging increased muscle activity while walking.

Rationale

While unloading and minimalist shoes reduce medial tibiofemoral compartment knee joint loading,⁸⁸⁻⁹⁰ there is limited evidence of very low quality that these shoes offer no additional benefit on pain or clinically relevant effects on function, compared with conventional walking shoes (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). There is limited evidence of low quality that rocker-sole shoes offer no significant benefit on pain or function, compared with conventional walking shoes (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Clinicians may consider advising people to consider wearing footwear with shock-absorbing properties, and to advise avoidance of high-heeled shoes, given they increase knee joint loads,⁹¹ albeit in the absence of RCT data about which individual footwear features are beneficial and/or harmful.

Harms

There is a low likelihood of adverse effects.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--------------------------|--|--|---------------------|
| Taping – knee and/or hip | We are unable to recommend either for or against the use of patellar taping for people with knee OA. | Conditional (neutral) recommendation (patellar taping) | Very low |
| | We suggest not offering kinesio taping for people with knee and/or hip OA. | Conditional against recommendation (kinesio taping) | |

What is it?

Different forms of taping are available, generally as a self-management strategy. Patellar taping uses rigid tape that aims to create a mechanical realignment of the patella in the trochlear groove in order to reduce pain and improve function. Kinesio taping uses non-rigid tape that is applied in various configurations; it is purported to offer support and stability to muscles and joints, and to stimulate somatosensory receptors.

Rationale

There is some evidence that patellar taping can immediately change patellar alignment measured on imaging and reduce pain.^{92,93} However, very low-quality evidence from a single RCT did not find any significant effect of taping when worn continuously for three weeks on pain and function, compared with sham tape in people with knee OA not specifically selected for patellofemoral pain (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). 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 reapplied by the clinician after various intervals. There is no trial of kinesio taping for hip OA. The evidence shows no significant benefits of kinesio taping for pain or function (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

Harms

The side effects are minor, and include skin irritation from the tape.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|--|--------------------------------|------------------------------|
| Assistive walking device – Knee and/or hip | It may be appropriate to offer an assistive walking device (eg cane) for some people with knee and/or hip OA, depending on a person's preference and capability. | Conditional for recommendation | Low (knee) Very low (hip) |

What is it?

Assistive walking devices include devices such as canes (eg 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. They may also help reduce falls risk.

Rationale

People with knee and/or hip OA often adopt an abnormal gait pattern because of pain, muscle weakness, joint mobility restrictions or other pain conditions. The use of an assistive walking device may be useful to improve gait pattern and posture to normalise musculoskeletal loads. There is low-quality evidence from one trial that the use of a walking aid (eg single point stick) is effective in improving pain and function in people with knee OA (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). The working group felt these data could be reasonably transferred to people with hip OA (very low-quality evidence). Clinicians should assess an individual'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 the individual is instructed on how to use the device, how to safely and effectively ambulate with the device, and how to adjust the device.

Harms

There are a few adverse events associated with this recommendation.

3.1.6 Electrotherapies

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|---|--------------------------------------|------------------------------|
| Pulsed electromagnetic/shortwave therapy – Knee and/or hip | We are unable to recommend either for or against electromagnetic/shortwave therapy for people with knee and/or hip osteoarthritis (OA). | Conditional (neutral) recommendation | Low (knee) Very low (hip) |

What is it?

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, healthcare providers in clinical settings have administered pulsed electromagnetic therapy, but advances in technology have led to the increasing availability of small portable devices for self-application.

Rationale

There is low-quality evidence that pulsed electromagnetic therapy significantly improves pain and function in people with knee OA (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*) by clinically relevant amounts. There is very low-quality evidence that pulsed electromagnetic therapy has no statistically significant effect on pain or function in people with hip OA (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Most studies involved clinician-delivered treatments, at high frequency of servicing, ranging from three to five times per week. A minority of studies used portable devices that individuals applied themselves at home, with treatment dosage ranging from two to 12 hours per day.

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 (two to 10 weeks) follow-up only, so maintenance of a therapeutic effect remains uncertain. The available evidence suggests that three to five treatment sessions per week are required for benefits when this treatment is administered by clinicians. Given the large number of visits to a healthcare professional required for a treatment modality that is passive, the financial cost this may impose on an individual, 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.

Harms

There is a low risk of adverse events, with no serious adverse events reported.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|---|------------------------------------|--|
| Other electrotherapy – Knee and/or hip (eg 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 (shockwave, interferential, laser-hip) |

What is it?

Electrotherapy modalities (eg shockwave, interferential electrical current, 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
- 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.

Rationale

While very low-quality evidence suggests some possible benefits from shockwave and interferential current modalities on pain and function, these findings were limited trials (one for shockwave and two for interferential), with a limited sample size and serious or very serious risk of bias (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). The working group also felt that the 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); however, the quality of evidence is low to very low (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Despite these positive indications, the working group felt that it was inappropriate to recommend the use of laser for people with knee OA. This is because the evidence was derived from trials where clinicians were required to deliver the intervention two to three times per week (other than the trial by Stellian,⁹⁴ where the intervention was self-administered), and the fact that the current evidence is restricted to short-term follow-up of three weeks. Furthermore, 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 individuals. 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.

Harms

There is no evidence of harm across these modalities.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|--|--------------------------------|---------------------|
| Transcutaneous electrical nerve stimulation (TENS) – Knee and/or hip | It may be appropriate to offer TENS that can be used at home for some 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 |

What is it?

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 people to use at home as a self-management strategy. Unlike other electrotherapy devices, portable TENS may be used as a continuous therapy by individuals to modulate pain, allowing them to engage in other activities while the unit is active.

Rationale

Very low-quality evidence from four trials in people with knee OA suggests that TENS has a clinically meaningful effect on pain and function (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). While no direct evidence is available from trials in people with hip OA, the working group felt that the mode of action with TENS could be transferable to the hip. Trials were limited to four 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 individuals with knee and/or hip OA as a home-based, pain-modulating adjunct to active rehabilitation interventions.

Harms

No adverse events have been reported in the included trials. However, clinicians should provide information to people about how to use portable TENS units safely and minimise the risks of possible skin irritation.

3.1.7 Therapeutic ultrasound

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|---|------------------------------------|------------------------------|
| Therapeutic ultrasound – Knee and/or hip | We suggest not offering therapeutic ultrasound for people with knee and/or hip osteoarthritis (OA). | Conditional against recommendation | Moderate (knee) Low (hip) |

What is it?

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.

Rationale

There is moderate-quality evidence that therapeutic ultrasound has statistically significant effects on pain and physical function in people with knee OA. There is no randomised controlled trial (RCT) involving participants with hip OA, thus the evidence level for this population group was downgraded to low quality because of concerns about indirectness (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). 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 (two to eight weeks) follow-up only. The working group also expressed concern about whether benefits are sustained once treatment finished. The available evidence suggests that three to five treatment sessions per 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 an individual, the working group felt that therapeutic ultrasound should not be offered to people with knee and/or hip OA.

Harms

Generally, there is no evidence to suggest that ultrasound therapy is unsafe. In view of its mechanisms of action, ultrasound therapy is rather unlikely to cause serious adverse events, but active surveillance of harms with formal monitoring of potential adverse events is clearly desirable.

3.1.8 Acupuncture

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|---|---|------------------------------------|------------------------------|
| The evidence for different forms of acupuncture (ie traditional, laser, electro) was considered separately (Appendix 5 of the <i>Guideline for the management of knee and hip osteoarthritis: Technical document</i>). | | | |
| Acupuncture – Knee and/or hip | We suggest not offering acupuncture (ie traditional, laser, electro) for people with knee and/or hip osteoarthritis (OA). | Conditional against recommendation | Low (knee) Very low (hip) |

What is it?

Acupuncture may be administered by a variety of health professionals. It is traditionally applied via the 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.

Rationale

There is low-quality evidence that traditional, laser and electro acupuncture have statistically significant benefits on pain and function, compared with sham acupuncture in people with knee OA (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). 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 with sham in people with hip OA (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Clinicians should not offer acupuncture to people with knee and/or hip OA because of 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 individual.

Harms

There is a statistically significant increase in the risk of adverse events with acupuncture, compared with sham in people with knee OA, although most were unrelated to acupuncture treatment (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

3.2 Pharmacological 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 osteoarthritis (OA). However, 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 |

What is it?

Paracetamol, also known as acetaminophen, is typically used to treat mild-to-moderate pain and fever. Unlike other common analgesics (eg nonsteroidal anti-inflammatory drugs [NSAIDs], aspirin, 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.

Rationale

While paracetamol has long been considered first-line therapy for OA, this has mainly reflected its relative safety, availability and cost, compared with other pharmacological options (eg NSAIDs, opioids). Current evidence from a systematic review of randomised controlled trials (RCTs) suggests that, on average, the reduction in OA pain achieved with paracetamol is too small to be of clinical relevance.⁹⁵ Moreover, paracetamol is associated with infrequent potential for significant harms, both short-term excess dosing and long-term regular use.⁹⁶

Many people will have tried paracetamol prior to seeking advice from a health professional. In those 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 are recommended. In people who have not previously trialed 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 those for whom it has not been effective are probably not warranted.

Practitioners should discuss a cessation strategy with people who regularly use paracetamol without clear benefit. Importantly, it should be emphasised that the replacement of paracetamol with another analgesic drug may not be necessary or appropriate, and that non-pharmacological approaches to management should be optimised.

Harms

There is no significant increase of adverse events with the use of paracetamol, compared with 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.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|---|--|--------------------------------|---------------------|
| Oral NSAIDs including cyclooxygenase-2 (COX-2) inhibitors – Knee and/or hip | <p>It may be appropriate to offer oral NSAIDs for some people with knee and/or hip OA.</p> <p>It might be reasonable to trial oral NSAIDs at the lowest effective dose for a short period, then discontinue use if not effective. Clinicians also need to inform individuals about, monitor and capture adverse events, especially gastrointestinal, renal and cardiovascular, which may be associated with use of NSAIDs.</p> | Conditional for recommendation | Moderate |

What is it?

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 PGs at the level of the COX. It is thought that inhibiting COX-2 leads to the anti-inflammatory, analgesic and antipyretic effects, and those NSAIDs also inhibiting COX-1 may cause gastrointestinal bleeding and ulcers in large doses.⁹⁷

Rationale

On average, the use of NSAIDs result in small but clinically relevant improvements in pain and function in individuals with knee and/or hip OA, and are likely to be more effective than paracetamol for most people (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). 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; therefore, 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.

Harms

The potential harms of NSAIDs are well recognised, and include gastrointestinal, renal and cardiovascular adverse effects. Older persons, who are at higher risk for OA, may also be at higher risk of 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 (eg www.cvdcheck.org.au).

In individuals at low absolute risk of harms, a judicious trial of NSAIDs may be considered, aiming for the lowest effective dose. Co-prescription of a proton-pump inhibitor (PPI) or the use of a COX-2 inhibitor should be considered in people at risk of gastrointestinal 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.

| 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) |

What is it?

Opioids, including morphine, are substances derived from opium. Opioids act on binding opioid receptors, which are principally found in the central and peripheral nervous system, and gastrointestinal tract. Medically, opioids are conceived as powerful pain-relieving substances, and have been shown to be effective for acute pain.

Rationale

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 in 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 (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Given opioids results in little to no effect on OA pain, and is associated with a risk of serious medical and social harms, we strongly recommend against the use of any opioid preparation for the treatment of knee and/or hip OA. People 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.

Harms

Common harmful effects may occur in the short-term (eg gastrointestinal disturbance, cognitive dysfunction), leading to a discontinuation of the drug in a significant proportion of individuals. 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 those using opioids for chronic non-cancer pain suggest a risk of death from opioid-related causes as high as one in 550 individuals.⁹⁸

| 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 |

What is it?

Transdermal opioid patch is a long-acting formulation with a delayed onset of effect initially and a prolonged duration of action and, as such, these are best reserved for opioid-tolerant individuals with stable opioid requirements. Transdermal opioid delivery avoids first-pass metabolism by the liver, increasing bio-availability and limiting variation in plasma concentration.⁹⁹

Rationale

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 (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Therefore, we are strongly against the use of any opioid preparation for the treatment of OA of the knee or hip.

Harms

Compared with oral opioid, transdermal patches increase drug bio-availability, which enables the use of lower drug doses, thus reducing the incidence of adverse events. However, from the evidence, the risk of adverse effects significantly increased after administration of opioids, regardless of the delivery methods. Other potential risks, such as deliberate misuse, are also not different from oral opioids.

3.2.2 Topical analgesics

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|---|--|--------------------------------------|---------------------|
| Topical nonsteroidal anti-inflammatory drugs (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 osteoarthritis (OA). It might be reasonable to trial topical NSAIDs for a short period then discontinue use if not effective. Clinicians also need to monitor and capture the adverse effects along with its use. | Conditional (neutral) recommendation | Moderate |

What is it?

Topical NSAIDs are applied to unbroken skin where there is pain as gels, creams, sprays or plasters. Topical NSAIDs penetrate the skin, enter tissues or joints, and reduce processes that are causing pain in the tissue. Drug levels in the blood with topical NSAIDs are much lower than with the same drug taken by mouth.

Rationale

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 an adjunctive treatment for the short term (several weeks). If unhelpful, topical NSAIDs should be ceased. Regarding adjunctive use, it should be noted that current evidence found 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.¹⁰⁰

Harms

Usually, adverse events from topical NSAIDs agents are minimal, but there is mild toxicity because of local skin reactions.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|-------------------------------------|---|--------------------------------------|---------------------|
| Topical capsaicin – knee and/or hip | We suggest not offering topical capsaicin for people with knee OA. | Conditional against recommendation | Low |
| | We are unable to recommend either for or against the use of topical capsaicin for people with hip OA. | Conditional (neutral) recommendation | Very low |

What is it?

Capsaicin is the neurotoxin of hot chilli peppers. It binds selectively to the vanilloid compound receptor (Transient Receptor Potential Vanilloid 1 [TRPV1]) of type C afferent fibres, and increases P substance in synaptic cleft.¹⁰¹ While first applications of capsaicin are associated with a burning sensation over the applied surface, with continued use, persistent desensitisation and analgesia occurs because of P substance neural depletion, and reversible and selective destruction of primary afferent fibres.¹⁰¹

Rationale

Evidence from one trial demonstrated that 0.025% of topical capsaicin had small effects of pain relief in people with knee OA (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). It is uncertain whether individuals with multi-joint OA or with relevant comorbidities will 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 can be detrimental. These issues often outweigh possible benefits to individuals.

Harms

Mild application site burning was the most common adverse event associated with the topical use of capsaicin (35–100%), but rapidly ameliorates with continuing use.¹⁰² There have been no reports of systemic toxicity with the use of topical capsaicin in OA.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|---------------------------------|--|--------------------------------|------------------------------|
| Duloxetine – Knee and/or hip | It may be appropriate to offer duloxetine for some 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 the 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 a beneficial effect on pain associated with diabetic neuropathy, fibromyalgia, low back pain and OA.

Rationale

In the three trials reviewed, significant response and moderate effects in knee pain (standardised mean difference [SMD] 0.43) and function (SMD 0.45) were found over 13–16 weeks at doses of 60/120 mg (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). However, most study participants were also already using NSAIDs and paracetamol. The use of duloxetine for knee OA adjunctively with NSAIDs, thus reducing the usage of NSAIDs and paracetamol, would be clinically useful to reduce adverse events.¹⁰³ In addition, results differed as to whether significant reduction in depression symptoms was needed for analgesic impact.

There is no direct randomised controlled trial (RCT) evidence for hip OA; thus, using knee OA data to extrapolate to hip or other OA requires additional caution.

Duloxetine currently does not have an indication via the Therapeutic Goods Administration (TGA) for OA, and should be considered as an investigational medication only.

Harms

Among the participants in the three included RCTs, treatment with duloxetine was well tolerated, with the majority of adverse events being of mild or moderate intensity (eg constipation, nausea, hyperhidrosis, cough, myalgia, arthralgia, palpitations).

Note: subsequent to preparing the grade tables and developing the recommendations, we became aware that one of the studies cited, that by Abou-Raya et al, has been retracted. The recent meta-analysis on duloxetine, which does not include the Abou-Raya study, shows little heterogeneity and remarkable consistency with the effect estimates that we have found.
<https://academic.oup.com/painmedicine/article/16/7/1373/1918203>

| 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) |

What is it?

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.¹⁰⁴

Rationale

Preclinical research and earlier human studies indicated doxycycline might be useful in managing symptomatic knee OA. However, 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, which may suggest the presence of a floor effect.¹⁰³ Despite the small benefit (SMD 0.15 mm) in joint space narrowing, it is outweighed by medication harms (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

There is no RCT of doxycycline for hip OA, thus using knee OA data to extrapolate to hip or other OA requires additional caution.

Doxycycline currently does not have an indication via the TGA for OA, and should be considered as an investigational medication only.

Harms

Adverse events that occurred significantly more frequently in the doxycycline group than the placebo group were restricted to recognised side effects of doxycycline (ie 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 the placebo group.

3.2.3 Anti-osteoporosis drugs

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|-----------------------------------|--|------------------------------------|---------------------|
| Bisphosphonates – Knee and/or hip | We suggest not offering bisphosphonates for people with knee and/or hip osteoarthritis (OA). | Conditional against recommendation | Very low |

What is it?

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 those with OA.

Rationale

Evidence from six trials found no statistically significant benefits in symptom relief, and structural and functional 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 found the odds ratios (ORs) favouring placebos for Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain (1.73), function (2.03) and stiffness (1.82). However, eight trials (61.5%) reported that bisphosphonates improved pain assessed by Visual Analogue Scale (VAS) scores, and two (38.5%) reported significant improvement in WOMAC pain scores, compared with control groups.¹⁰⁵ There were no statistically significant differences or trends 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 at 24-month follow-up.¹⁰⁵

There is one very low-quality trial conducted in 42 participants with hip OA, demonstrating no effect over 24 months (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

Bisphosphonates currently do not have an indication via the Therapeutic Goods Administration (TGA) for OA, and should be considered as investigational medications only.

Harms

Bisphosphonates come with significant side effect profiles and restrictions on some day-to-day activities (eg dental procedures). Treatment with these drugs should be reserved for individuals who meet the Pharmaceutical Benefits Scheme (PBS) guidelines for treatment of their osteoporosis, but not for the management of OA.

| 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 |

What is it?

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 and preliminary clinical settings.¹⁰⁶ 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.

Rationale

The two phase III studies found no significant effect of salmon calcitonin on total WOMAC, WOMAC subscores and joint space narrowing (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). There is a potentially 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 is no randomised controlled trial (RCT) of calcitonin for hip OA; thus, using knee OA data to extrapolate to hip or other OA requires additional caution.

Harms

There were markedly higher incidences of gastrointestinal disorders and hot flushes in the active treatment arms of the included studies. No other adverse events were markedly different between the two groups in either study.

| 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 |

What is it?

Strontium ranelate, a bone-acting agent, has the ability to dissociate the bone-remodelling process, and change the balance between bone resorption and formation, which has been suggested to be a potential symptom-modifying effect.

Rationale

Data from one moderate-quality trial found no effect of strontium ranelate in altering OA symptoms. However, strontium ranelate treatment had a beneficial effect on joint space widening, with a mean difference (MD) of 0.12 mm over three years. Similarly, the risk ratio of radiographic progression (joint space narrowing ≥ 0.5 mm) favoured 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.

Harms

Strontium ranelate was well tolerated for the treatment of OA in a study duration over three years. Despite its listed side effects in the approved product information (eg myocardial infarction, venous thromboembolism events, pulmonary embolism, hypersensitivity reaction), the European Medicines Agency recommended in 2014 that strontium ranelate should remain available for individuals with osteoporosis, with restrictions relative to those with existing heart disease.¹⁰⁷ 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 is a concern.

3.2.4 Investigational disease-modifying OA drugs (DMOADs)

| 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 osteoarthritis (OA). | Strong against recommendation | Low |

What is it?

This is a group of agents that block the activity of a pro-inflammatory cytokine, IL-1, which is believed to play a role in inducing cartilage matrix degradation through the up-regulation of proteolytic enzymes.¹⁰⁸ The most common IL-1 inhibitors are:

- IL-1 receptor antagonist – anakinra
- soluble decoy receptor – rilonacept
- neutralising monoclonal anti-IL-1 β antibody – canakinumab.

In addition, a monoclonal antibody directed against the IL-1 receptor, AMG-108 and a neutralising anti-IL-1 α or IL-1 β antibody, ABT-981 are currently in clinical trials.

Rationale

Results from a three-arm trial of a single intra-articular injection of anakinra at a dose of 50 mg (n = 34) and 150 mg (n = 67) were available. The mean improvement from baseline at week 12 on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score was not statistically different between the anakinra and placebo groups (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

A placebo-controlled randomised controlled trial (RCT) of AMG-108, (which is not included in Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*) found non-statistically significant improvement on WOMAC pain after subcutaneous administration of AMG-108.¹⁰⁹

As IL-1 inhibitors require an authority prescription, which cannot be prescribed by general practitioners (GPs), GPs need to work with specialists to get access to these agents. The working group discussed the limitations in current efficacy, safety, access and costs, and considered that IL-1 inhibitors are 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.

Harms

The percentage of participants reporting adverse events was similar between the placebo and anakinra groups (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). The most common adverse event was arthralgia (10%), with similar rates between anakinra 150 mg and placebo groups, 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 participants, more frequently for the anakinra 150 mg group, compared with the anakinra 50 mg or the placebo group.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|---|------------------------------------|---------------------|
| Anti-nerve growth factor (NGF) – Knee and/or hip | We suggest not offering NGF for people with knee and/or hip OA. | Conditional against recommendation | Moderate |

What is it?

NGF is a secretory soluble protein that binds to two different cell surface receptors – 75 kDa neurotrophin receptor (p75NTR) and high-affinity NGF-specific tyrosine kinase receptor (TrkA). It is critical for normal development of sympathetic and sensory neurons that are responsible for nociception and temperature sensation.¹¹⁰

A humanised monoclonal antibody, tanezumab, was developed specifically to inhibit NGF from binding to its receptors on pain-signalling neurons. Fulranumab is a fully humanised recombinant immunoglobulin G2 (IgG2) monoclonal antibody that specifically neutralises the biological actions of human NGF.

Rationale

Results from five trials of tanezumab and one of fasinumab found a statistically significant lower WOMAC pain and function score, compared with placebos with a pooled standardised mean differences (SMDs) of 0.6 and 0.64 respectively (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). 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 (References 3 and 5 in PICO, 2.8.3 – Knee in Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*) 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, 200 µg/kg).¹⁰⁹ The other phase III studies evaluated a narrower dose range (2.5 mg, 5 mg, 10 mg), and reported a correspondingly narrower range of SMD from 0.26 to 0.61, all of which are statistically significantly from placebo. In the study of fasinumab, all three doses of fasinumab were associated with significant improvements, compared with placebo in walking knee pain and WOMAC total and subscale scores.

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 (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). The study (Reference 3 in PICO, 2.8.3 – Hip in Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*) evaluated fulranumab with two different dosing frequencies (1 and 3 mg every four weeks; 3, 6 and 10 mg every eight 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.

The working group discussed that anti-NGF requires off-label prescribing and is expensive, which limited its accessibility and affordability.

Harms

Based on current evidence, the number of adverse events was not significantly different between treatment and placebo groups. Reported adverse events included arthralgia, headache, upper respiratory tract infection and abnormal peripheral sensation (eg paraesthesia, dysesthesia, hyperaesthesia, hypoesthesia). A meta-analysis of tanezumab safety suggested the use of tanezumab plus nonsteroidal anti-inflammatory drug (NSAID) treatment had a higher occurrence of serious adverse events than NSAID alone.¹¹¹ A recent adjudication of joint-related adverse events in the tanezumab clinical program reported that the drug was not associated with an increased risk of osteonecrosis, but was associated with an increased risk of rapidly progressive OA, especially in people on higher doses of tanezumab, tanezumab plus NSAIDs, or pre-existing subchondral insufficiency fractures.¹¹²

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|--|-------------------------------|---------------------|
| 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 |

What is it?

Sprifermin is a recombinant and truncated version of human FGF-18 that binds to, and specifically activates, FGF receptor-3 in cartilage in order to promote chondrocyte proliferation and cartilage matrix production.

Rationale

There is one trial of 190 participants with knee OA evaluating the effects of intra-articular injection of sprifermin as a single treatment and multiple-dose regimen (three doses of either 10, 30 or 100 µg). Results found that all groups had improved WOMAC pain scores, with statistically significantly less improvement at 12 months in participants receiving the 100 µg dose of sprifermin, compared with participants 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 the loss of total and lateral femorotibial cartilage thickness and volume, and in joint space widening in the lateral femorotibial compartment (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). 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 trial has 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.

Harms

According to the findings in two recent trials, the overall proportion of participants experiencing at least one treatment-emergent adverse event (TEAE) was not increased in the sprifermin group, compared with the placebo group (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Incidence, severity and nature of reported TEAEs raised no local or systemic safety concerns for doses up to 300 µg.¹¹³

| 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 |

What is it?

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.¹¹⁴

Rationale

There is currently a lack of high-quality evidence supporting the use of colchicine for symptomatic relief for people with knee OA. While two small trials (one comparing colchicine to placebo; one comparing the combination of colchicine and an anti-inflammatory medication to the anti-inflammatory medication alone) indicate colchicine may provide symptomatic relief (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*), its efficacy and safety remains unproven. In the 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 (Identifier: NCT02176460; ClinicalTrials.gov), but the results have not been published. One additional trial was identified in a search of the World Health Organization's (WHO's) 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.

Colchicine currently does not have an indication via the Therapeutic Goods Administration (TGA) for OA, and should be considered as an investigational medication only.

Harms

There was no significant adverse event in the included trials of colchicine. The most commonly reported adverse events encountered with colchicine were gastrointestinal adverse events (eg loose bowel movements, pain in the abdomen), which were usually mild.

| 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 |

What is it?

Methotrexate is a chemotherapy agent and immune system suppressant, which is commonly used to treat cancer and autoimmune diseases (eg rheumatoid arthritis, 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
- T-cell activation and suppression of intercellular adhesion molecule expression by T-cells
- methyltransferase activity, leading to deactivation of enzyme activity relevant to immune system function.

Rationale

There is very low-quality evidence from one small trial of 56 participants who used 7.5 mg of methotrexate weekly versus placebo for painful knee OA, which did not find a reduction in pain at four months (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Another open-label study evaluated the effects of methotrexate for pain relief in participants with knee OA. At 24 weeks, 13/30 participants (43%) achieved $\geq 30\%$ reduction in Visual Analogue Scale (VAS) pain, of whom, seven (23%) had achieved $\geq 50\%$ reduction. Conversely, four participants (13%) experienced a flare. Thirteen of 30 (43%) participants achieved Osteoarthritis Research Society International's responder criteria.¹¹⁵ 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.

Methotrexate does not currently have an indication via the TGA for OA, and should be considered as an investigational medication only.

Harms

The 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.^{116,117}

3.2.5 Intra-articular injections

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|--|--------------------------------|---------------------|
| Corticosteroid injection – Knee and/or hip | It may be appropriate to offer an intra-articular corticosteroid injection for some people with knee and/or hip osteoarthritis (OA) for short-term pain relief. Clinicians need to be cautious of the potential harms of repeated use. | Conditional for recommendation | Very low |

What is it?

Corticosteroids are medications that mimic the effects of the hormone cortisol, which is produced naturally by the adrenal glands. Cortisol helps to lower the levels of prostaglandins and downplays the interaction between certain white blood cells involved in the immune response. Corticosteroid injections are frequently used for the short-term symptom relief of a flare of joint symptoms or when a rapid reduction in symptoms is required.

Rationale

The studies upon which the recommendation is based were at serious risk of bias and generally small in size. The overall quality of the evidence was judged to be low to very low (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Beneficial effects on knee pain and function were demonstrated at up to six weeks. These findings were not present when follow-up was extended to three 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 would further add 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.

Harms

Serious and total adverse events were not significantly increased, compared with placebo. However, there are concerns of more rapid cartilage loss with repeated injections with no benefit in long-term symptom outcomes at two years, so these injections should be used judiciously.¹¹⁸

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|---|------------------------------------|---------------------|
| Viscosupplementation injection – Knee and/or hip | We suggest not offering viscosupplementation injection for people with knee hip OA. | Conditional against recommendation | Low |
| | We do not recommend offering viscosupplementation injection for people with hip OA. | Strong against recommendation | |

What is it?

Hyaluronate is a naturally occurring component of cartilage and synovial fluid, and 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 intraarticular hyaluronate administration is to provide and maintain intraarticular lubrication. This in turn increases the viscoelastic properties of synovial fluid, and is sometimes termed ‘viscosupplementation’. It has also been reported that hyaluronate exerts anti-inflammatory, analgesic and possibly chondroprotective effects on the articular cartilage and joint synovium.¹¹⁹

Rationale

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 participants. For knee pain, function and adverse events, the overall quality of the evidence was judged to be moderate. Despite some inconsistency on the conclusions among the analyses, a positive effect, albeit small and not clinically relevant, was demonstrated for pain and function.

The recommendation for hip OA is based on three small randomised controlled trials (RCTs), which were judged to not be at serious risk of bias (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). 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 viscosupplementation 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 the complexity of the intervention were taken into account, a conditional against recommendation was agreed upon.

Harms

Minor side effects include pain at the injection site (1–33%), local joint pain and swelling (<1–30%), and local skin reactions (3–21%).¹¹⁹ Pseudo-septic reactions (1–3%), 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.¹²⁰

| 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 PRP injection for people with knee and/or hip OA. | Conditional (neutral) recommendation | Very low |

What is it?

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.

Rationale

The studies upon which the recommendation is based were at serious risk of bias and inconsistency, and were generally small in size (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). The overall quality of the evidence was judged to be very low. Beneficial effects on both knee pain and Western Ontario and McMaster Universities (WOMAC) function were demonstrated at six months. With the concern of potential reporting bias and low-quality data, the beneficial effects are likely to be overinflated. In addition, there is no consensus on eligible participant selection, number and frequency of injections, preparation technique, or appropriate platelet concentration,¹²¹ leading to large variations in the design of PRP trials.

No RCT was conducted in hip OA. However, during working group discussions, it was suggested that the mechanism of action should be no different in hip OA. Therefore, the findings might be transferrable to hip OA, but with a particular caution in terms of the complexity of the hip joint.

The cost of PRP treatment is high, and additional equipment might be required for the preparation and administration.

Harms

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.¹²²

| 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 and/or hip OA. | Strong against recommendation | Very low |

What is it?

Stem cells are cells that have the ability to divide and develop into many different types of cell 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 that is not hampered by availability and donor site morbidity. MSCs can be isolated from adipose tissue, bone marrow, synovial tissue and other sources.

Rationale

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 pain and function were demonstrated at up to six months. The between-group differences reported for pain and function appeared to be remarkably good (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). As they deviate significantly from those of other successful interventions, replication is required in high quality, large RCTs before a more favourable recommendation can be considered.

Consistent with a recent position statement from the [Australian College of Sports and Exercise Physicians](#), stem cell administration should be part of a rigorously designed study and the priority for individual health and welfare.¹²³

Harms

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 seven days.^{124,125}

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|---|------------------------------------|---------------------|
| Dextrose prolotherapy – Knee and/or hip | We suggest not offering dextrose prolotherapy for people with knee and/or hip OA. | Conditional against recommendation | Low |

What is it?

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, and 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.

Rationale

The recommendation is based on the evidence of only one small RCT of low quality. The risk of bias in this study was not determined to be 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 weeks, but a marginally significant effect was recorded at 52 weeks (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Furthermore, high-quality RCTs with low risk of bias and specifically for hip OA are required.

As prolotherapy is relatively cheap and accessible, it is likely to be injudiciously used. The working group agreed on a 'Conditional against recommendation'.

Harms

The study reported self-limited bruises after dextrose (n = 3) and saline (n = 5) injections. This was an expected side effect and deemed to be of minimal clinical relevance because of 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.¹²⁶

3.3 Herbal therapies, supplements and nutraceuticals

Supplement use in the context of osteoarthritis (OA) management is widespread throughout the community. In general, these are readily available and relatively inexpensive (\geq \$30 per month per supplement). These supplements are usually 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 in the evidence (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

Individuals should be assisted in making informed decisions by considering the potential and known risks and benefits of the therapies they seek to use to relieve pain. Careful consideration should be given to the available information, and claims of curative potential and marked treatment effects that can be achieved with the use of these agents. It is important to be cautious when advocating for these supplements; however, when someone feels marked therapeutic benefit, do not underestimate the potential for placebo effects, particularly if these are safe and inexpensive. For people who are very enthusiastic about taking complementary and alternative therapies (eg supplements), it is generally advised they do so cognisant of potential side effects and interactions with regular medication use, and to use these for a period of time (eg four to six 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 (ASU) – Knee and/or hip | We are unable to recommend for or against the use of ASU for people with knee and/or hip OA. | Conditional (neutral) recommendation | Very low |

What is it?

An extract of avocado and soybean oils, known as ASU, is available in Australia. The usual dose is around 300 mg daily.

Rationale

The 2014 Cochrane review reports ASU 300 mg produced a small and clinically questionable improvement in symptoms, and probably no increased adverse events, compared with placebo after three to 12 months treatment.¹²⁷ In the new evidence review for this guideline, short-term pain and function up to six months was improved by about 0.5 standard deviations, and there were no significant longer-term benefits in pain or function. 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 that in the context of low-quality to very low-quality studies, despite some suggestion of beneficial effects, it is prudent to use caution. The working group advocates that further research is needed before a firm recommendation on ASU can be made.

Harms

In pooled data from five randomised controlled trials (RCTs) spanning three months to three years follow-up, with a total of nearly 600 participants, there was no significant increase in adverse events over placebo.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|---|--------------------------------------|---------------------|
| <i>Boswellia serrata</i> extract – Knee and/or hip | We are unable to recommend for or against the use of <i>Boswellia serrata</i> for people with knee and/or hip OA. | Conditional (neutral) recommendation | Very low |

What is it?

Boswellia serrata, also known as Indian frankincense, is a tree that is native to India and Arabian Peninsula. The resin of Indian frankincense contains substances that may decrease inflammation. The usual dose is 100 mg of enriched *Boswellia serrata* daily.

Rationale

Three small RCTs found significant short-term benefits in pain and function; however, these are all sponsored by the same company, raising concern about possible bias.

The working group discussed that, in the context of low-quality to very low-quality studies, despite potential beneficial effects, it is prudent to use caution and advocate that further research is needed before a firm recommendation on *Boswellia serrata* can be made.

Harms

There is limited data on safety available on the use of *Boswellia serrata*. In two RCTs with follow-up of 30–90 days pooled (n = 117), there was no significant increase in adverse events over placebo (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

| 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 |

What is it?

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. Curcuma products are readily available in Australia.

Rationale

Three small RCTs found significant short-term (ie six to eight weeks) benefits in pain and function; however, these are all industry-sponsored trials, raising concern about possible bias. Additionally, there were inconsistency in the results. All of the studies involved knee OA, so extrapolation to hip or other OA requires additional caution.

The working group discussed that in the context of low-quality to very low-quality studies, despite potential beneficial effects, it is prudent to use caution and advocate that further research is needed before a firm recommendation on curcuma can be made.

Harms

There is limited data on safety available on the use of curcuma. In two RCTs with follow-up of six to eight weeks pooled (n = 113), there was no significant increase in serious adverse events over placebo; however, there was a non-statistically significant increase in gastrointestinal adverse events of 15.8% versus 7.1% in placebo (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|--|---|--------------------------------------|------------------------------|
| Pine bark extract – Knee and/or hip | We are unable to recommend either for or against the use of pine bark extract for people with knee and/or hip OA. | Conditional (neutral) recommendation | Low (knee) Very low (hip) |

What is it?

A pine bark, *Pinus pinaster* (synonym *Pinus maritima*) extract. The doses used in the reviewed RCTs were 100–150 mg of pine bark extract daily.

Rationale

Three small RCTs found short-term benefits in pain and function; however, these could not be pooled because of heterogeneity and reporting weaknesses. All three trials were industry-sponsored, with the larger trial at very high risk of bias. Evidence is based on studies of knee OA, so extrapolation to hip or other OA requires additional caution. The working group discussed that in the context of low-quality to very low-quality studies, despite potential beneficial effects, it is prudent to use caution and advocate that further research is needed before a firm recommendation on the use of pine bark extract.

Harms

There is limited data on safety available on the use of Pycnogenol®. In two RCTs with follow-up of up to three months (n = 137), there was no significant increase in serious adverse events over placebo (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

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 osteoarthritis (OA). | Conditional against recommendation | Very low (knee) Low (hip) |

What is it?

Glucosamine is a naturally produced sugar by the body, and one of the building blocks of cartilage. It comes in two forms – glucosamine sulfate and hydrochloride, and the usual dose is 1500 mg daily. Glucosamine supplements are usually made from crab, lobster or shrimp shells, although some supplements are made from a plant form of glucosamine. These are available as tablets or liquid, and often in combination with chondroitin.

Rationale

Overall, there is very low-quality evidence from a large number of randomised controlled trials (RCTs) that found 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, no benefit is demonstrated. There is only one RCT on 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 suggest no effect, the working group decided on a conditional against recommendation to increase awareness of the unlikely benefit of glucosamine and chondroitin. This discussion occurred in the context of the costs associated with ongoing supplement use, competing treatment priorities where this might be prioritised over more effective interventions, and the possible influence of direct-to-consumer marketing of supplements. If someone who is taking glucosamine or chondroitin 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 these supplements.

Harms

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 participants with those conditions more carefully than usual practice (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

| 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 |

What is it?

Chondroitin is a component of connective tissues and bone, which 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.

Rationale

There are a large number of trials on the use of chondroitin (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*), where at least seven are 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 three months), which lessens to clinically not significant by six to 12 months, and no effect is demonstrated at 24 months. However, when the analysis is restricted to studies of higher quality or free of industry sponsorship, no benefit is demonstrated.

There are some moderate-term to long-term (12–24 months) benefits on joint space narrowing, but these are not clinically meaningful (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). The studies are all on participants with knee OA, so extrapolation to OA of 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 suggest no effect, the working group decided on a conditional against recommendation to increase awareness of the unlikely benefit of widespread use of glucosamine and chondroitin. This discussion occurred in the context of the costs associated with ongoing supplement use, competing treatment priorities where this might be prioritised over more effective interventions, and current use as a consequence of direct-to-consumer marketing that may be inconsistent with the scientific evidence. If someone who is taking glucosamine or chondroitin 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 these supplements.

Harms

Pooled data from six trials with more than 1000 participants found that the risk of adverse events is comparable to placebo.

| 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 |

What is it?

Glucosamine and chondroitin are often marketed in a combination at the same doses as individual components. There does not appear to be any beneficial drug–drug synergistic interaction.

Rationale

With pooling (where possible) of results from the nine available RCTs, no benefit for pain, function or joint space narrowing was demonstrated. Participants in all trials had knee OA, so extrapolation to hip OA needs additional caution (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

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 suggest no effect, the working group decided on a conditional against recommendation to increase awareness of the unlikely benefit of widespread use of glucosamine and chondroitin. This discussion occurred in the context of the costs associated with ongoing supplement use, competing treatment priorities where this might be prioritised over more effective interventions, and current use as a consequence of direct-to-consumer marketing which may be inconsistent with the scientific evidence. If someone who is taking glucosamine or chondroitin 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 these supplements.

Harms

As with the individual components, the reported rates of adverse events were similar to placebo.

| 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) |

What is it?

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 the studies analysed, a daily dose of 800–2000 IU, or a monthly dose of 50,000–60,000 IU, were used.

Rationale

There were four RCTs (one to three years' duration), all without serious risk of bias. However, there was very serious inconsistent 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 (standardised mean difference [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 participants who were vitamin D deficient also failed to show clinically meaningful beneficial effects (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Participants in all studies had knee OA, so extrapolation to OA of hip or other joints requires additional caution.

Harms

Vitamin D is relatively safe; however, there is a non-statistically significant increase in hypercalciuria. There is no clinical effect or safety concern.

| 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 |

What is it?

Omega-3 polyunsaturated fatty acids are mainly produced by marine organisms (eg oil from whole fish, seal, mussels). This is widely available, and the usage is generally varied by region and disease (usual dose is 1–2 g/day).

Rationale

Pooled data from five RCTs (15–26 weeks) demonstrated no benefits on pain and function in people with 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 and mussel extracts. High heterogeneity was expected from pooling different sources of omega-3 fatty acids, and measures within each outcome (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). The optimal type of omega-3 fatty acids could not be established in OA because only a few trials included marine oil from sources other than whole fish. There are high variations in doses of eicosapentaenoic acid (EPA; 0.01–1.7 g/day), and doses of docosahexaenoic acid (DHA; 0.01–1.10 g/day).

A controlled trial that was not included found no additional benefit of high dose fish oil (4.5 g/day), compared with low dose fish oil (0.45 g/day).

Harms

Side effects are usually minor and uncommon.

| 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) |

What is it?

There are many types of collagen and collagen-related derivatives, which can be extracted from chicken cartilage, pork skin and bovine bone. These are sometimes available in hydrolysed form to help absorption and distribution to joint tissues. There is insufficient research to recommend a particular dose.

Rationale

Pooled results from six studies found short-term (13–26 weeks) clinical benefits in pain; however, there have been very serious inconsistent results across the studies (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). Available data from four studies found 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.

Harms

Collagen use is relatively safe; however, there is a non-statistically significant increase in adverse gastrointestinal events.

| Intervention | Recommendation | Strength of recommendation | Quality of evidence |
|---|---|--------------------------------------|---------------------|
| Methylsulfonylmethane (MSM) – Knee and/or hip | We are unable to recommend either for or against the use of MSM for people with knee and/or hip OA. | Conditional (neutral) recommendation | Very low |

What is it?

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.

Rationale

There are three trials with short study durations (12–13 weeks), and pooled data found statistically and clinically significant benefits in pain. Even larger effects were found in function, but with very serious inconsistent results and high heterogeneity across studies. One trial had a high risk of bias because of inappropriate randomisation technique; while the other had potential reporting bias (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*). The doses in the trials ranged from 1.5–6 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.

Harms

The use of MSM for OA is relatively safe. Minor side effects were recorded, including gastrointestinal adverse events, fatigue and headaches; however, these were not statistically significant compared with placebo.

| 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 |

What is it?

Diacerein is purified compound with an anthraquinone structure that interferes with pro-inflammatory interleukin-1 (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 50 mg twice a day.

Rationale

Five trials were included, with time durations ranging from eight weeks to 12 months, all receiving high risk of bias because of 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 this did not reach the clinically meaningful threshold. Analysis of one study demonstrated no benefit in reducing joint space narrowing (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*).

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.

Harms

Adverse events were significantly increased after using diacerein, mainly diarrhoea (relative risk [RR]: 3.50; 95% confidence interval [CI]: 1.95, 6.27). There is an increase in rash, but the between-group difference was not significant.

3.4 Surgical interventions

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

What is it?

Arthroscopic surgery in people with knee OA is widely available and commonly occurs. It allows the surgeon to visualise the interior joint space. Arthroscopic joint lavage uses saline irrigation to remove particulate material, (eg cartilage fragments, 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.

Rationale

There is very low-quality evidence that there is no apparent benefit in terms of pain, function or quality of life (Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*) 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 past few years.

In the context of an intervention where there is a 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 OA. The Australian Orthopaedic Association and the Knee Society position statement (www.kneesociety.org.au/resources/aks-arthroscopy-position-statement.pdf) strongly states that arthroscopy is not indicated for the treatment of knee OA. In the infrequent instance where exercise fails to release the locked knee, arthroscopy could be indicated.

Harms

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.

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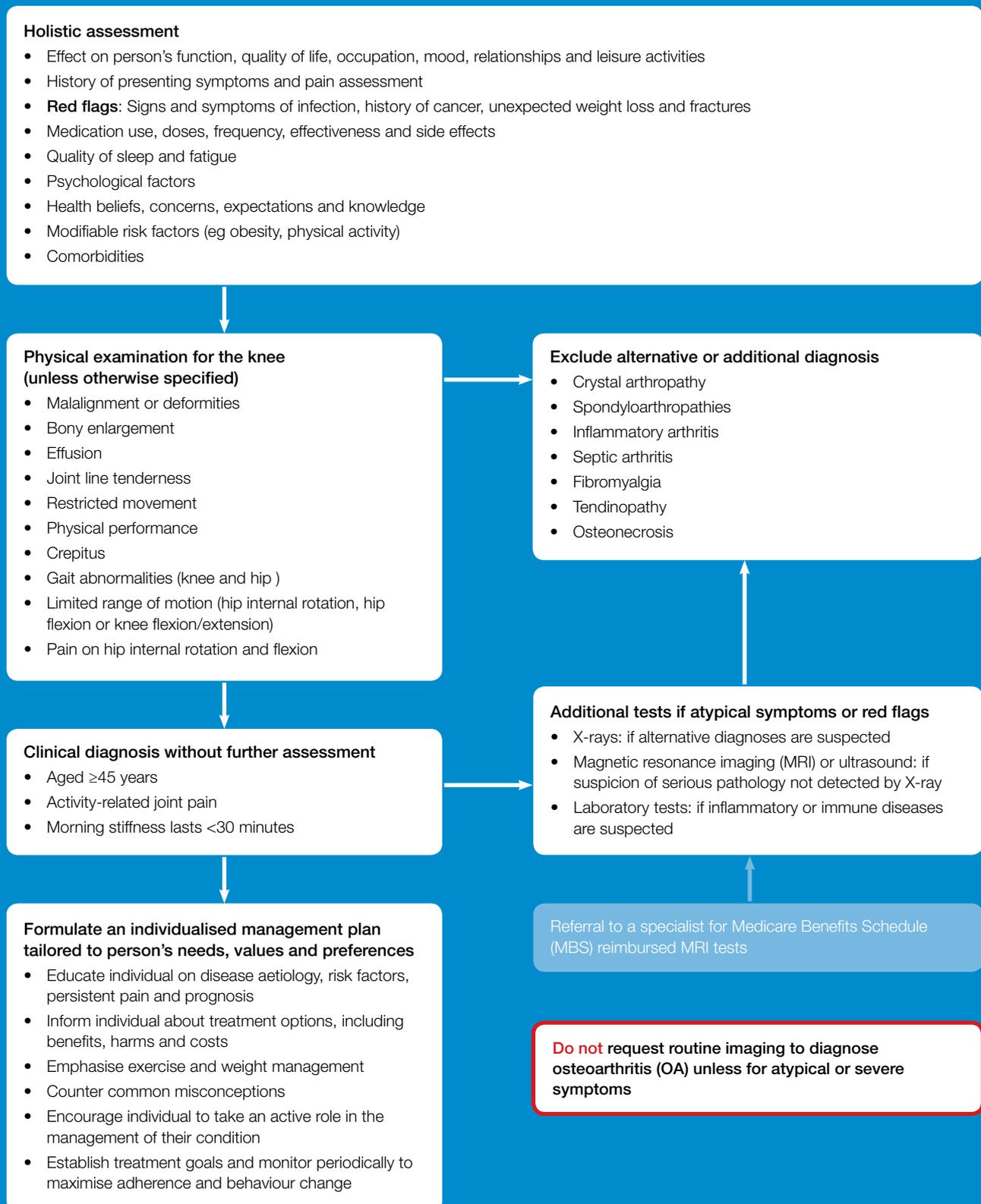
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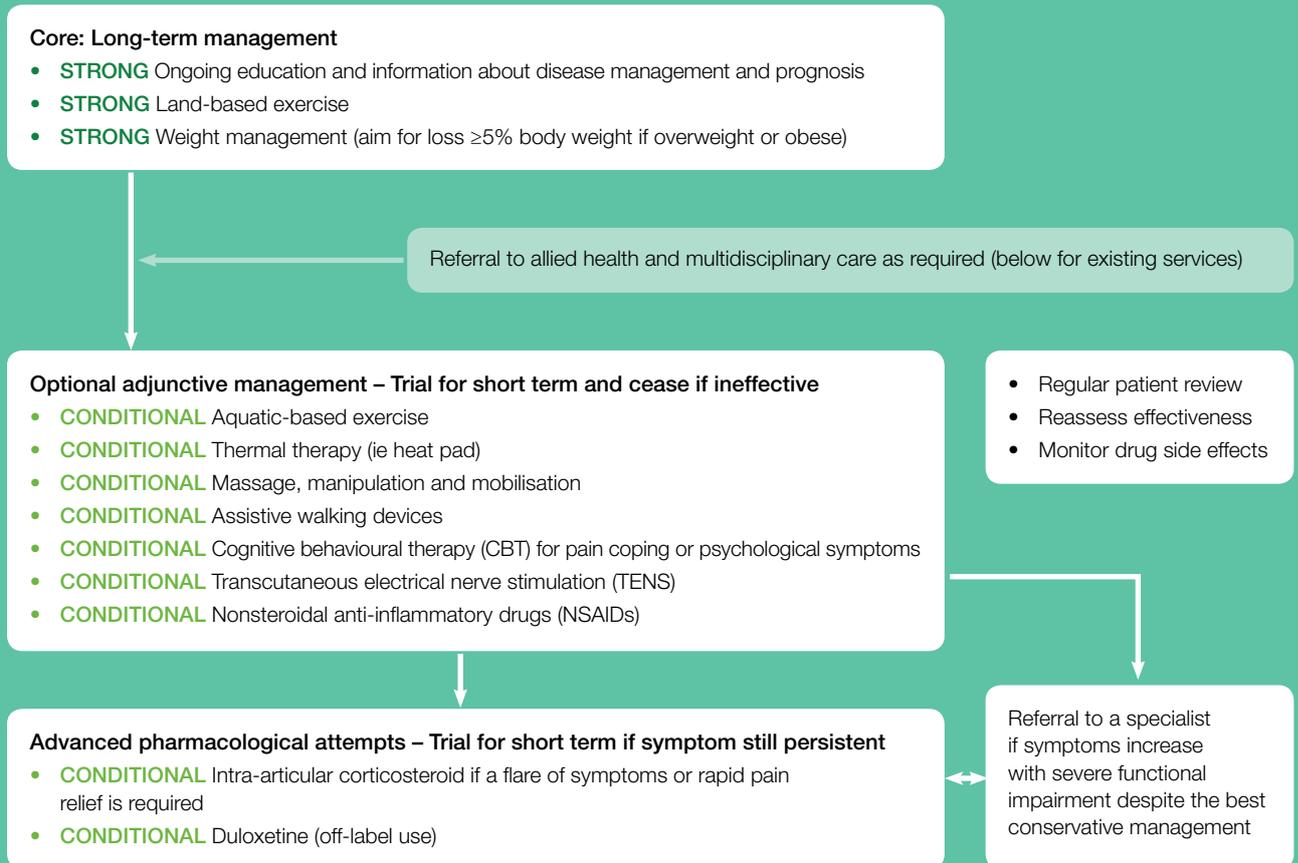
Appendix 1. Algorithm – Holistic assessment, diagnosis and management of knee and/or hip osteoarthritis

Assessment and diagnosis



Management

Non-surgical management for knee and/or hip OA



Surgical management for knee and/or hip OA



For detailed services and prescribing information

- Victoria Osteoarthritis Hip and Knee Service (www2.health.vic.gov.au/hospitals-and-health-services/patient-care/specialist-clinics/osteoarthritis-hip-knee-service)
- NSW Osteoarthritis Chronic Care Program (www.aci.health.nsw.gov.au/resources/musculoskeletal)
- NSW Pain management services (www.health.nsw.gov.au/pharmaceutical/doctors/Pages/pain-management-services.aspx)
- Get Healthy Service (www.gethealthynsw.com.au)

Appendix 2. PICO

PICO (patient/population/problem, intervention, comparison/control, outcome) questions

PICO questions are numbered in accordance with the relevant Grading of Recommendations Assessment, Development and Evaluation (GRADE) evidence tables in Appendix 5 of the *Guideline for the management of knee and hip osteoarthritis: Technical document*.

PICO questions for knee OA

Section 1. Non-pharmacological interventions (37 questions)

- 1.1. What are the benefits and harms of self-management education programs in the management of patients with knee osteoarthritis (OA)?
- 1.2. What are the benefits and harms of decision aids in the management of patients with knee OA? – excluded
- 1.3. What are the benefits and harms of cognitive behavioural therapy in the management of patients with knee OA?
- 1.4. What are the benefits and harms of all land-based exercise in the management of patients with knee OA?
- 1.5. Specific form of land-based exercise
 - 1.5.1. What are the benefits and harms of muscle strengthening in the management of patients with knee OA?
 - 1.5.2. What are the benefits and harms of walking in the management of patients with knee OA?
 - 1.5.3. What are the benefits and harms of stationary cycling in the management of patients with knee OA?
 - 1.5.4. What are the benefits and harms of Tai Chi in the management of patients with knee OA?
 - 1.5.5. What are the benefits and harms of Hatha yoga in the management of patients with knee OA?
- 1.6. What are the benefits and harms of aquatic exercise/hydrotherapy in the management of patients with knee OA?
- 1.7. Manual therapy
 - 1.7.1. What are the benefits and harms of massage in the management of patients with knee OA?
 - 1.7.2. What are the benefits and harms of manipulation and mobilisation in the management of patients with knee OA?
- 1.8. What are the benefits and harms of weight management in the management of patients with knee OA?
- 1.9. Thermotherapy
 - 1.9.1. What are the benefits and harms of local hot application in the management of patients with knee OA?
 - 1.9.2. What are the benefits and harms of local cold application in the management of patients with knee OA?
- 1.10. Orthotic braces
 - 1.10.1. What are the benefits and harms of varus unloading/re-alignment braces in the management of patients with knee OA?
 - 1.10.2. What are the benefits and harms of valgus unloading/re-alignment braces in the management of patients with knee OA?
 - 1.10.3. What are the benefits and harms of realigning patellofemoral braces in the management of patients with knee OA?

1.11. Insoles

1.11.1. What are the benefits and harms of medial wedged insoles in the management of patients with knee OA?

1.11.2. What are the benefits and harms of lateral wedge insoles in the management of patients with knee OA?

1.11.3. What are the benefits and harms of shock-absorbing insoles in the management of patients with knee OA?

1.11.4. What are the benefits and harms of arch supports in the management of patients with knee OA?

1.12. Shoes

1.12.1. What are the benefits and harms of unloading shoes in the management of patients with knee OA?

1.12.2. What are the benefits and harms of minimalist footwear in the management of patients with knee OA?

1.12.3. What are the benefits and harms of rocker-sole shoes in the management of patients with knee OA?

1.13. Taping

1.13.1. What are the benefits and harms of kinesio taping in the management of patients with knee OA?

1.13.2. What are the benefits and harms of patellar taping in the management of patients with knee OA?

1.14. What are the benefits and harms of walking cane/stick in the management of patients with knee OA?

1.15. Electromagnetic therapy

1.15.1. What are the benefits and harms of pulsed electromagnetic/shortwave therapy in the management of patients with knee OA?

1.15.2. What are the benefits and harms of shockwave therapy in the management of patients with knee OA?

1.16. Electrical stimulation

1.16.1. What are the benefits and harms of transcutaneous electrical nerve stimulation (TENS) in the management of patients with knee OA?

1.16.2. What are the benefits and harms of inferential currents in the management of patients with knee OA?

1.17. What are the benefits and harms of ultrasound in the management of patients with knee OA?

1.18. What are the benefits and harms of laser in the management of patients with knee OA?

1.19. Acupuncture

1.19.1. What are the benefits and harms of traditional acupuncture with manual stimulation in the management of patients with knee OA?

1.19.2. What are the benefits and harms of laser acupuncture in the management of patients with knee OA?

1.19.3. What are the benefits and harms of electroacupuncture in the management of patients with knee OA?

Section 2. Pharmacological interventions (35 questions)

2.1. Oral analgesics

2.1.1. What are the benefits and harms of oral paracetamol in the management of patients with knee OA?

2.1.2. What are the benefits and harms of oral nonsteroidal anti-inflammatory drugs (NSAIDs) including cyclooxygenase-2 (COX-2) inhibitors in the management of patients with knee OA?

2.1.3. What are the benefits and harms of oral opioids in the management of patients with knee OA?

2.2. Topical analgesics

2.2.1. What are the benefits and harms of topical NSAIDs in the management of patients with knee OA?

2.2.2. What are the benefits and harms of transdermal opioids in the management of patients with knee OA?

2.2.3. What are the benefits and harms of topical capsaicin in the management of patients with knee OA?

2.3. Herbal therapies

- 2.3.1. What are the benefits and harms of avocado/soybean unsaponifiables (ASU) in the management of patients with knee OA?
- 2.3.2. What are the benefits and harms of *Boswellia serrata* in the management of patients with knee OA?
- 2.3.3. What are the benefits and harms of curcuma in the management of patients with knee OA?
- 2.3.4. What are the benefits and harms of pycnogenol in the management of patients with knee OA?

2.4. Nutraceuticals

- 2.4.1. What are the benefits and harms of glucosamine in the management of patients with knee OA?
 - 2.4.2. What are the benefits and harms of chondroitin in the management of patients with knee OA?
 - 2.4.3. What are the benefits and harms of glucosamine and chondroitin in compound form in the management of patients with knee OA?
 - 2.4.4. What are the benefits and harms of vitamin D in the management of patients with knee OA?
 - 2.4.5. What are the benefits and harms of (omega-3/6) poly-unsaturated fatty acids in the management of patients with knee OA?
 - 2.4.6. What are the benefits and harms of collagen preparations in the management of patients with knee OA?
 - 2.4.7. What are the benefits and harms of methylsulfonylmethane in the management of patients with knee OA?
 - 2.4.8. What are the benefits and harms of diacerein in the management of patients with knee OA?
- 2.5. What are the benefits and harms of duloxetine in the management of patients with knee OA?
- 2.6. What are the benefits and harms of doxycycline in the management of patients with knee OA?
- 2.7. Anti-osteoporosis (anti-resorptive bone-acting) drugs
- 2.7.1. What are the benefits and harms of bisphosphonates in the management of patients with knee OA?
 - 2.7.2. What are the benefits and harms of calcitonin in the management of patients with knee OA?
 - 2.7.3. What are the benefits and harms of strontium ranelate in the management of patients with knee OA?
- 2.8. Investigational disease-modifying osteoarthritis drugs (DMOADs) (symptomatic or inflammatory modification)
- 2.8.1. What are the benefits and harms of interleukin-1 (IL-1) inhibitors in the management of patients with knee OA?
 - 2.8.2. What are the benefits and harms of tumour necrosis factor alpha (TNF-alpha) inhibitors in the management of patients with knee OA?
 - 2.8.3. What are the benefits and harms of anti-nerve growth factor (NGF) therapy in the management of patients with knee OA?
 - 2.8.4. What are the benefits and harms of fibroblast growth factor (FGF) therapy in the management of patients with knee OA?
 - 2.8.5. What are the benefits and harms of colchicine in the management of patients with knee OA?
 - 2.8.6. What are the benefits and harms of methotrexate in the management of patients with knee OA?
 - 2.8.7. What are the benefits and harms of statins in the management of patients with knee OA? – excluded
- 2.9. Intra-articular injections
- 2.9.1. What are the benefits and harms of corticosteroids in the management of patients with knee OA?
 - 2.9.2. What are the benefits and harms of viscosupplementation in the management of patients with knee OA?
 - 2.9.3. What are the benefits and harms of platelet-rich plasma (PRP) in the management of patients with knee OA?
 - 2.9.4. What are the benefits and harms of stem cell therapy in the management of patients with knee OA?
 - 2.9.5. What are the benefits and harms of dextrose prolotherapy in the management of patients with knee OA?

Section 3. Surgical interventions (non-arthroplasty) (three questions)

- 3.1. What are the benefits and harms of arthroscopic lavage and debridement interventions in the management of patients with knee OA?
- 3.2. What are the benefits and harms of arthroscopic meniscectomy interventions in the management of patients with knee OA?
- 3.3. What are the benefits and harms of arthroscopic procedures for cartilage repair interventions in the management of patients with knee OA?

Section 4. Combination therapies (four questions)

- 4.1. What are the benefits and harms of combination weight management and exercise interventions compared to exercise in patients with knee OA?
- 4.2. What are the benefits and harms of combination weight management and exercise interventions compared to weight management in patients with knee OA?
- 4.3. What are the benefits and harms of combination exercise and cognitive behavioural interventions compared to exercise in patients with knee OA?
- 4.4. What are the benefits and harms of combination exercise and cognitive behavioural interventions compared to cognitive behavioural interventions in patients with knee OA?

PICO questions for hip OA

Section 1. Non-pharmacological interventions (25 questions)

- 1.1. What are the benefits and harms of self-management education programs in the management of patients with hip OA?
- 1.2. What are the benefits and harms of decision aids in the management of patients with hip OA? – excluded
- 1.3. What are the benefits and harms of cognitive behavioural therapy (CBT) in the management of patients with hip OA?
- 1.4. What are the benefits and harms of all land-based exercise in the management of patients with hip OA?
- 1.5. Specific form of land-based exercise
 - 1.5.1. What are the benefits and harms of muscle strengthening in the management of patients with hip OA?
 - 1.5.2. What are the benefits and harms of walking in the management of patients with hip OA?
 - 1.5.3. What are the benefits and harms of stationary cycling in the management of patients with hip OA?
 - 1.5.4. What are the benefits and harms of Tai Chi in the management of patients with hip OA?
 - 1.5.5. What are the benefits and harms of Hatha yoga in the management of patients with hip OA?
- 1.6. What are the benefits and harms of aquatic exercise/hydrotherapy in the management of patients with hip OA?
- 1.7. Manual therapy
 - 1.7.1. What are the benefits and harms of massage in the management of patients with hip OA?
 - 1.7.2. What are the benefits and harms of manipulation and mobilisation in the management of patients with hip OA?
- 1.8. What are the benefits and harms of weight management in the management of patients with hip OA?
- 1.9. Thermotherapy
 - 1.9.1. What are the benefits and harms of local hot application in the management of patients with hip OA?
 - 1.9.2. What are the benefits and harms of local cold application in the management of patients with hip OA?

- 1.10. What are the benefits and harms of hip orthotics in the management of patients with hip OA?
- 1.11. What are the benefits and harms of kinesio taping in the management of patients with hip OA?
- 1.12. What are the benefits and harms of walking cane/stick in the management of patients with hip OA?
- 1.13. Electromagnetic therapy
 - 1.13.1. What are the benefits and harms of pulsed electromagnetic/shortwave therapy in the management of patients with hip OA?
 - 1.13.2. What are the benefits and harms of shockwave therapy in the management of patients with hip OA?
- 1.14. Electrical stimulation
 - 1.14.1. What are the benefits and harms of TENS in the management of patients with hip OA?
 - 1.14.2. What are the benefits and harms of inferential currents in the management of patients with hip OA?
- 1.15. What are the benefits and harms of therapeutic ultrasound in the management of patients with hip OA?
- 1.16. What are the benefits and harms of laser in the management of patients with hip OA?
- 1.17. What are the benefits and harms of acupuncture in the management of patients with hip OA?

Section 2. Pharmacological interventions (35 questions)

- 2.1. Oral analgesics
 - 2.1.1. What are the benefits and harms of paracetamol in the management of patients with hip OA?
 - 2.1.2. What are the benefits and harms of oral NSAIDs including COX-2 inhibitors in the management of patients with hip OA?
 - 2.1.3. What are the benefits and harms of oral opioids in the management of patients with hip OA?
- 2.2. Topical analgesics
 - 2.2.1. What are the benefits and harms of topical NSAIDs in the management of patients with hip OA?
 - 2.2.2. What are the benefits and harms of transdermal opioids in the management of patients with hip OA?
 - 2.2.3. What are the benefits and harms of topical capsaicin in the management of patients with hip OA?
- 2.3. Herbal therapies
 - 2.4.1. What are the benefits and harms of ASU in the management of patients with hip OA?
 - 2.4.2. What are the benefits and harms of *Boswellia serrata* in the management of patients with hip OA?
 - 2.4.3. What are the benefits and harms of curcuma in the management of patients with hip OA?
 - 2.4.4. What are the benefits and harms of pycnogenol in the management of patients with hip OA?
- 2.4. Nutraceuticals
 - 2.4.1. What are the benefits and harms of glucosamine in the management of patients with hip OA?
 - 2.4.2. What are the benefits and harms of chondroitin in the management of patients with hip OA?
 - 2.4.3. What are the benefits and harms of glucosamine and chondroitin in compound form in the management of patients with hip OA?
 - 2.4.4. What are the benefits and harms of vitamin D in the management of patients with hip OA?
 - 2.4.5. What are the benefits and harms of (omega-3/6) poly-unsaturated fatty acids in the management of patients with hip OA?
 - 2.4.6. What are the benefits and harms of collagen preparations in the management of patients with hip OA?
 - 2.4.7. What are the benefits and harms of methylsulfonylmethane (MSM) in the management of patients with hip OA?
 - 2.4.8. What are the benefits and harms of diacerein in the management of patients with hip OA?

- 2.5. What are the benefits and harms of duloxetine in the management of patients with hip OA?
- 2.6. What are the benefits and harms of doxycycline in the management of patients with hip OA?
- 2.7. Anti-osteoporosis (anti-resorptive bone-acting) drugs
 - 2.7.1. What are the benefits and harms of bisphosphonates in the management of patients with hip OA?
 - 2.7.2. What are the benefits and harms of calcitonin in the management of patients with hip OA?
 - 2.7.3. What are the benefits and harms of strontium ranelate in the management of patients with hip OA?
- 2.8. Investigational DMOADs (symptomatic or inflammatory modification)
 - 2.8.1. What are the benefits and harms of IL-1 inhibitors in the management of patients with hip OA?
 - 2.8.2. What are the benefits and harms of TNF-alpha inhibitors in the management of patients with hip OA?
 - 2.8.3. What are the benefits and harms of anti-NGF therapy in the management of patients with hip OA?
 - 2.8.4. What are the benefits and harms of FGF therapy in the management of patients with hip OA?
 - 2.8.5. What are the benefits and harms of colchicine in the management of patients with hip OA?
 - 2.8.6. What are the benefits and harms of methotrexate in the management of patients with hip OA?
 - 2.8.7. What are the benefits and harms of statins in the management of patients with hip OA? - excluded
- 2.9. Intra-articular injections
 - 2.9.1. What are the benefits and harms of corticosteroids in the management of patients with hip OA?
 - 2.9.2. What are the benefits and harms of viscosupplementation in the management of patients with hip OA?
 - 2.9.3. What are the benefits and harms of PRP in the management of patients with hip OA?
 - 2.9.4. What are the benefits and harms of stem cell therapy in the management of patients with hip OA?
 - 2.9.5. What are the benefits and harms of dextrose prolotherapy in the management of patients with hip OA?

Section 3. Surgical interventions (non-arthroplasty) (two questions)

- 3.1. What are the benefits and harms of arthroscopic lavage and debridement interventions in the management of patients with hip OA? – excluded
- 3.2. What are the benefits and harms of arthroscopic procedures for cartilage repair interventions in the management of patients with hip OA? – excluded

Section 4. Combination therapies (four questions)

- 4.1. What are the benefits and harms of combination weight management and exercise interventions compared to exercise in patients with hip OA?
- 4.2. What are the benefits and harms of combination weight management and exercise interventions compared to weight management in patients with hip OA?
- 4.3. What are the benefits and harms of combination exercise and cognitive behavioural interventions compared to exercise in patients with hip OA?
- 4.4. What are the benefits and harms of combination exercise and cognitive behavioural interventions compared to cognitive behavioural interventions in patients with hip OA?



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