Managing pain in osteoarthritis: focus on the person

KEY PRACTICE POINTS:

- Exercise and physical activity are core treatments; this includes muscle strengthening around the affected joint(s), maintaining the range of motion of affected joint(s) and general aerobic fitness
- Weight loss can result in significant improvements in symptoms in people with osteoarthritis of weight-bearing joints
- Topical NSAIDs (unsubsidised) or topical capsaicin (subsidised with Special Authority approval) can be used as a first-line treatment approach for patients with symptoms limited to specific areas such as the knee or finger joints
- Paracetamol, up to 4 g/day, is the recommended first-line oral medicine
- Oral NSAIDs produce greater improvement in pain, joint function and stiffness than paracetamol, but have a higher risk of adverse effects and may not be suitable for some patients
- Intra-articular injections of corticosteroids are useful for flares, providing a reduction in pain for up to one month

Osteoarthritis affects the joints, but impacts the whole person

Osteoarthritis is the most common form of arthritis, affecting 10% of all adults in New Zealand.[1] The knee joint is most frequently involved, followed by osteoarthritis of the hip, and then other joints such as the small joints of the hands.[1] The progression of osteoarthritis is variable. Functional decline and worsening of symptoms is not inevitable, and most people do not have symptoms severe enough to warrant joint replacement. People with osteoarthritis do, however, require ongoing management of pain, in the context of how this affects their daily living. In addition to pain, people with osteoarthritis often report loss of function, sleep disturbance, anxiety, depression and fatigue.[2]

A suggested framework for the assessment and management of patients with osteoarthritis is "the four P's". This highlights issues that are most significant for the patient, and can also be used to develop patient-specific goals for treatment:[3]

- **Pain:** ask open-ended questions about the nature and occurrence of pain, e.g. "describe how it feels" rather than "is it a stabbing pain?"

- **Performance and function:** ask how the pain affects the patient's daily living, sleep, ability to carry out work or recreational activities, mobility and self-care
- **Psychological:** ask about the emotional impact of any pain, e.g. depression, anxiety, affect on relationships and future thinking
- **Past medical history:** consider whether co-morbidities are adding to the patient's functional limitations or influencing treatment choices

Encourage patients to focus on maintaining function and achieving goals rather than reducing pain

Reducing pain is central to the management of osteoarthritis, but patients may lose motivation if the reduction in their pain is not what they had hoped for. Try to create expectations based around improving function and quality of life, and minimising disruption to this during flares. Highlighting that a treatment approach could help the patient to keep working or doing an activity they enjoy may help them to persevere with self-management.

Agree on a review schedule

Discuss with the patient a suitable length of follow-up for a review of their overall management strategy. An annual review may be appropriate for many patients, e.g. those taking regular medicines to manage pain, those with co-morbidities or those with osteoarthritis affecting more than one joint.[2] More, or less, frequent review may be appropriate for other patients, depending on their specific symptoms and clinical picture.

Core approaches to managing osteoarthritis are non-pharmacological

Exercise and physical activity are the cornerstones of treatment

Appropriate exercise and staying active is a key aim for all patients with osteoarthritis, irrespective of age, co-morbidity, pain severity or disability.[2] Exercise interventions have been shown to reduce pain and medicine use while improving physical functioning, muscle strength, balance, mood and quality of life.[2] Exercise also has other benefits, such as weight loss and reducing the risk of cardiovascular disease.

A variety of exercises and activities are beneficial

Exercise should ideally include muscle strengthening around the affected joint(s), e.g. quadriceps strengthening for osteoarthritis of the knee, and activities to maintain the range of motion as well as general aerobic fitness.[2] This could include walking, using a gym, riding a bike or swimming/aqua jogging. Including exercise in a class setting may produce greater improvements than if patients only exercise alone.[2]

Consider writing a green prescription; this may help patients feel they are not just being given general lifestyle advice but are being offered a specific evidence-based treatment for osteoarthritis.

A handout for patients with arthritis including information on staying active and a guide to specific exercises is available from: **www.arthritis.org.nz/wp-content/uploads/2014/03/ARTHRITIS-NZ-Exercise-Book-Nov-2011-FINAL-WEB.pdf**

Arthritis New Zealand also lists exercise classes for patients in some areas: **www.arthritis.org.nz/40228-2/**

Imaging is often not necessary

Imaging is not necessary to diagnose osteoarthritis but may provide clinicians with greater certainty in some cases.[4] The x-ray results can help distinguish whether symptoms are due to osteoarthritis or another diagnosis, such as suspected fracture or crystal arthropathy.[2, 4] Routine x-rays during follow-up for patients with early osteoarthritis are typically not necessary as they do not influence management.[4] However, x-rays can be useful if patients have a change in their condition, such as a sudden increase in the severity of symptoms or a lack of response to treatment.[2] In patients with more severe osteoarthritis who are potential candidates for joint replacement surgery, x-rays should be ordered prior to referral to secondary care.[4]

Reassure patients that pain in osteoarthritis does not necessarily equal harm

Patients may regard their experience of pain as a signal from the body to warn of damage. Focusing on pain can often lead to avoidance of exercise and other activities.[5] Explain to patients that the link between pain and harm is not as straightforward in conditions associated with chronic pain as it is in situations of acute pain.[5] This can help to reassure patients that it is safe to exercise, as long as any pain or discomfort they experience plateaus and they feel it is manageable.[5]

A pre-emptive dose of an analgesic prior to physical activity may be helpful for some patients. Discuss ways in which this can be done safely, e.g. ensuring that they do not exceed the maximum daily dose of their regular analgesia or scheduling doses to coincide with exercise sessions (see pharmacological treatment section below for further information on analgesia).

Encourage weight loss

Patients with osteoarthritis of weight-bearing joints who are overweight or obese should be supported to lose weight. A reduction of 5–10% of initial body weight can produce significant improvements in symptoms, with a weight loss of approximately 10% resulting in symptom improvement comparable to the effect of joint replacement surgery.[6,7] Weight loss primarily results in an improvement in physical function, but some patients may also experience a reduction in pain.[2]

Weight loss is also beneficial if a patient requires joint replacement surgery in the future; patients who are obese have greater risks associated with surgery, less improvement in function following joint replacement and higher rates of additional surgeries on the replaced joint.[8]

Pace activities throughout the day or week

Activity pacing is a strategy used for conditions associated with chronic pain. Patients should plan activities or exercises so they are divided into manageable portions which do not exacerbate their symptoms, e.g. completing a task over multiple short blocks of time throughout the day, rather than all at once in the morning.[5] When done effectively, this strategy can help patients gain confidence and feel in control, by being able to continue with their desired activities.[5]

A patient handout on managing chronic pain, including activity pacing, is available from: **www.tepou.co.nz/uploads/files/tehikuwai/tehikuwai-handout-chronicpain-fatigue.pdf**

Refer patients to a physiotherapist or occupational therapist

Referral to a physiotherapist can help patients learn techniques which can assist their balance and strength. A physiotherapist can also guide patients regarding appropriate footwear and orthotic devices, such as shoe wedges, and the use of walking aids, joint supports or bracing to correct any malalignment of joints.

An occupational therapist can provide guidance on assistance devices for patients with difficulty with tasks of daily living, such as shower or toilet rails, tap-turning, jar-opening and grabbing devices.[2] Assistive devices such as these can reduce pain and help patients to maintain function and independent living, and may help prevent hospitalisations due to falls.[9]

Pharmacological treatment options

Pharmacological approaches to managing osteoarthritis.[10]

First line treatments:

- Paracetamol:
  - Has limited effectiveness in some patients, but others may gain sufficient analgesia with paracetamol alone
  - Has a low risk of adverse effects when used in appropriate doses
  - May reduce the use of other medicines such as oral NSAIDs and weak opioids
- Topical analgesia for patients with few joints affected or localised pain:
  - Topical NSAIDs: diclofenac and ibuprofen gels or sprays are available unsubsidised
  - Topical capsaicin is available subsidised with Special Authority approval

Second-line treatments:

- Oral NSAIDs
- Intra-articular corticosteroid injections (for flares)

Third-line treatments:

- Weak opioids: codeine or tramadol

Paracetamol is first-line

Paracetamol is recommended as the initial oral pharmacological treatment for patients with osteoarthritis. Regular use is likely to provide the greatest benefit, although some patients may prefer to use paracetamol on an as-needed basis for intermittent pain relief.[11]

Paracetamol is not as effective in osteoarthritis as other oral medicines, such as NSAIDs, but has a better safety profile and less risk of adverse effects.[10,12] In clinical trials, patients with osteoarthritis taking regular paracetamol at a dose of 4 g/day had an average 18% reduction in pain and 15% improvement in function compared to patients taking placebo.[2,12,13] This is approximately half the benefit provided by oral NSAIDs in clinical trials.[12,13] However, these are averages across groups of patients and individual response can vary.

Patients can take up to 4 g/day of paracetamol, unless they

are malnourished, have a body weight less than 50 kg, are dehydrated or have a high alcohol intake; in these cases a maximum dose of 3 g/day is recommended to reduce the risk of hepatotoxicity.[14]

Advise patients taking paracetamol for the treatment of osteoarthritis to:

- Avoid over-the-counter products which contain paracetamol, such as cold and flu medicines
- Maintain their alcohol intake within recommended guidelines
- Use dosing aids such as pill boxes to assist with taking the correct doses at correct intervals

Pharmacists can assist by asking patients dispensed paracetamol if they are taking other over-the-counter products, and advising them to avoid products containing paracetamol.

Paracetamol and potential liver toxicity

When taken within recommended doses, hepatotoxicity due to paracetamol is rare.[15, 16] For example, in a randomised controlled trial including approximately 600 patients with osteoarthritis who took 4 g/day of paracetamol for six to 12 months, 98% of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) measures were within normal limits.[17] These patients did not have pre-existing liver disease and consumed alcohol within recommended limits.[17] However, if paracetamol is taken in excess of recommended doses, it results in accumulation of hepatotoxic metabolites which can cause liver failure and death. Paracetamol should be prescribed with caution to patients who may be at increased risk of liver toxicity, such as those with low body weight (under 50 kg), with reduced liver function or who regularly drink alcohol.[14]

Topical treatments are a first-line option for patients with localised pain

Guidelines increasingly emphasise the benefits of topical treatments for patients with mild to moderate osteoarthritis limited to specific areas, such as the knee or finger joints. This management strategy should be considered in particular for patients with localised pain who have contraindications to oral NSAID use.[18] There is a lack of clinical trials assessing whether topical treatments are efficacious for patients with hip osteoarthritis.[19] Cost is likely to be the main barrier for patients to using topical treatments; capsaicin is the only subsidised option (with restrictions).

Topical capsaicin (0.025%) is fully subsidised with Special Authority approval for patients with osteoarthritis who have not improved sufficiently with paracetamol and for whom oral NSAIDs are contraindicated. Topical capsaicin can also be purchased over-the-counter. Topical capsaicin is reported to reduce pain by 25-30% on average compared to applications of a placebo.[21] Patients should apply a small amount of cream to the affected joint, four times daily. A transient burning sensation is often experienced after application.[14] Advise patients to wash their hands after applying capsaicin cream to avoid transfer to other areas such as the eyes and mouth. Treatment may be required for one to two weeks before a reduction in pain is achieved.[14, 20] Application can then be reduced to twice daily.[21]

Topical NSAIDs available in New Zealand include diclofenac and ibuprofen gels or sprays (all unsubsidised). Topical NSAIDs are reported to reduce pain by approximately 30% on average compared to applications of a placebo.[2] Topical NSAIDs are absorbed systemically, however, the incidence of adverse effects such as gastrointestinal bleeding is lower compared to the use of oral NSAIDs.[22] Patients should apply 2 to 4 g of a topical NSAID gel to the affected joint three to four times daily.[14, 23] Significant improvements in symptoms can be expected within the first week of treatment, and there may be further improvement in the following week.[23] Patients may experience local adverse effects, such as erythema or pruritus.[14]

Oral NSAIDs: more effective than paracetamol but with a higher risk of adverse effects

Oral NSAIDs may be considered for patients with ongoing pain and discomfort despite non-pharmacological approaches and paracetamol use, or those with more severe symptoms at diagnosis, provided they do not have contraindications.[2] NSAIDs can be used instead of, or in addition to, oral paracetamol. The aim should be for patients to use oral NSAIDs at the lowest effective dose for the shortest possible time in order to minimise the risk of adverse effects, e.g. during a flare only.[2] Some patients may require ongoing use.

Evidence suggests all oral NSAIDs have similar efficacy for osteoarthritis

A range of non-selective NSAIDs are available subsidised in New Zealand, and celecoxib, a COX-2 selective NSAID, is also now fully subsidised. Oral NSAIDs reduce pain by 30–44%, which is approximately double the effect of paracetamol, as well as result in greater improvements in function and stiffness than paracetamol or placebo medicines.[12, 18] There is no clear evidence to suggest any one particular NSAID (including celecoxib) is superior in terms of efficacy for treating patients with osteoarthritis.[2] Therefore, the decision as to which NSAID to use can be based on the patient's response and preference, their risk of adverse effects and co-morbidities. Patients may need to trial more than one NSAID in order to find one which provides sufficient analgesia.

Dosing recommendations for prescribing NSAIDs for the treatment of osteoarthritis are available from: **www.nzf.org.nz/nzf_5476**

Sustained release formulations may be preferred by some patients

Sustained release formulations of ibuprofen, naproxen, diclofenac and ketoprofen are available and subsidised. There is no evidence that a sustained release formulation of a NSAID results in better outcomes for patients with osteoarthritis than an immediate release preparation. However, as sustained release preparations are designed to deliver the dose of NSAID gradually, this may avoid breakthrough pain, improve adherence and reduce peak dose adverse effects.

Once a patient has been stabilised on a daily NSAID regimen, this could be replaced with a sustained release preparation of a NSAID, usually once-daily. The main disadvantage of using a sustained release formulation is that "top-up" doses are usually not possible as this would exceed the recommended maximum daily dose, e.g. if extra analgesia is required prior to exercise. A sustained release formulation would therefore be less suitable for patients who experience variable levels of pain.

All NSAIDs have risks: consider the patient's risk of adverse effects before prescribing

All oral NSAIDs increase the risk of cardiovascular events and gastrointestinal bleeding to some extent, and are associated with a risk of nephrotoxicity and medicines interactions.
The baseline risk of cardiovascular events or gastrointestinal bleeds (i.e. in the absence of medicine use) increases with age, and therefore older patients are at greater risk of an adverse event with NSAID use.

Considerations prior to prescribing a NSAID include:

- Serious adverse effects, such as acute kidney injury, cardiovascular adverse effects and gastrointestinal bleeding, can occur within the first month of treatment[24–26]
- The risk of nephrotoxicity is increased in patients who are taking other nephrotoxic medicines, e.g. the "triple whammy" combination of an NSAID, ACE inhibitor and diuretic,[18]
- The risk of nephrotoxicity is also increased in patients with pre-existing renal disease, hypovolaemia, hypertension, atherosclerosis or who are aged over 65 years[14]
- The increased risk of gastrointestinal adverse effects with NSAID use is further increased if patients are also taking low dose aspirin[9]

Consider the use of a proton pump inhibitor (PPI) for gastrointestinal protection in patients prescribed NSAIDs who are aged 65 years and over or at increased risk of gastrointestinal adverse effects.[27] Celecoxib has a lower risk of gastrointestinal adverse effects than non-selective NSAIDS, and this risk is even lower when prescribed with a PPI.[28] Using a non-selective NSAID with a PPI is associated with a risk of gastrointestinal adverse effects comparable to using celecoxib alone.[28] Histamine receptor antagonists (e.g. ranitidine) do not provide sufficient reduction in the risk of gastrointestinal adverse effects with NSAID use and are therefore not recommended.[28] Dyspepsia is a common adverse effect regardless of COX-2 selectivity.

For further information about celecoxib, including a discussion of risks and benefits compared to other NSAIDs, see: "Celecoxib: the need to know for safe prescribing", **www.bpac.org.nz/2018/celecoxib.aspx**

Analgesics used for the treatment of neuropathic pain are not effective for osteoarthritis

Tricyclic antidepressants, gabapentin or pregabalin are not recommended for patients with osteoarthritis due to lack of efficacy or unfavourable balances of benefits to risks, unless there are other reasons for prescribing, e.g. the patient has pain with a neuropathic component.[2]

Escalating treatment during a flare of osteoarthritis

Patients who have ongoing symptoms or a flare can be stepped up to the next stage of treatment. For example, patients who have been otherwise well-controlled with paracetamol can be prescribed an oral NSAID during a flare.[18]

Also consider using a combination of medicines which have different mechanisms of action, e.g. topical NSAIDs combined with paracetamol, or oral NSAIDs with intra-articular corticosteroids (see below). This may produce better pain relief with fewer adverse effects than higher doses of a single medicine.[9]

Intra-articular corticosteroid injections may be useful for flares

Intra-articular corticosteroid injections produce short-term reductions in pain (e.g. one month), but do not improve joint function or stiffness.[2] They are therefore most likely to be useful for treating flares. A three month period between injections is recommended.[29] Intra-articular injections carry a very small risk of infection, with reported rates ranging from 1 in 3,000 to 1 in 50,000 injections.[30] Intra-articular injections must be given under aseptic conditions to minimise this.

Triamcinolone acetonide, dexamethasone phosphate and methylprednisolone acetate for injection are available fully subsidised, and betamethasone acetate + betamethasone sodium phosphate for injection available partly subsidised;

see the NZF for dosing recommendations: **www.nzf.org.nz/nzf_5565**. Up to five injections of dexamethasone phosphate are available on a practitioner's supply order.

Intra-articular hyaluronic acid injections are unlikely to be effective

Many clinical guidelines no longer recommend the use of intra-articular hyaluronic acid due to lack of efficacy.[10]

Patients with ongoing or severe symptoms

Many patients with osteoarthritis have flares and remissions, but overall their symptoms remain at the same intensity. However, some patients will experience a moderate to severe progression of symptoms, and therefore their pain management may need to be escalated.[31]

Clinical guidelines recommend that weak opioids, such as codeine or tramadol, should be reserved for use in patients who do not sufficiently improve, are unable to tolerate or have contraindications to paracetamol, topical treatments or oral NSAIDs.[10] Evidence suggests stronger opioids may have small to moderate benefits, however, this may not be sufficient to balance the risks of adverse effects associated with these medicines, such as falls, drowsiness, constipation and addiction.[10]

Referral to a Mobility Action Programme is recommended if patients have ongoing or severe symptoms despite the use of standard non-pharmacological and pharmacological approaches, or if they have contraindications to these treatments.

Further information on the Mobility Action Programme is available at: **www.health.govt.nz/our-work/preventative-health-wellness/mobility-action-programme**

Referral to an orthopaedic surgeon for joint replacement may be an option in patients with severe and continuing symptoms. Factors which contribute to this decision include the patient's level of pain, disruption of sleep, limitations to daily activities, and psychological impact of their symptoms and whether they can safely undergo surgery.[32]

Limited evidence for alternative treatment options for osteoarthritis

Complementary or alternative treatments are typically not recommended in the treatment of osteoarthritis, due to a lack of quality evidence or evidence that they are ineffective (see sections below). In order to guide discussions with patients regarding the use of alternative treatments, consider questions such as:

- Is the treatment recommended in a clinical guideline or is there evidence of efficacy?
- What is known about the adverse effects?
- Will it interact with other medicines the patient is taking?
- Will it reduce the need for conventional medicines?
- Will it compromise conventional medical treatment?
- What is the hoped outcome of use? How and when will the patient decide if the treatment has been of benefit?
- Is the cost prohibitive?

Treatments with mixed support in clinical guidelines

Clinical guidelines and evidence do not provide a strong mandate for the widespread use of these treatment options. Some patients may find them beneficial, possibly due to a placebo effect.

Acupuncture: Some guidelines recommend that acupuncture should not be used for treating patients with osteoarthritis, while others provide recommendations in favour of acupuncture or advise it could be used in specific circumstances, e.g. in patients with contraindications to conventional treatments.[10, 19] These diverse recommendations come from differing interpretations of the available evidence, which shows that acupuncture results in average improvements of 5% or less in patient ratings of pain and function compared to a sham treatment.[33]

Heat or cooling, e.g. a hot bath or cooling pack on the affected joint, are recommended in some guidelines.[10] There is little evidence regarding whether these methods are effective but they are often used by patients and have a low risk of adverse effects.

TENS (transcutaneous electrical nerve stimulation) may be effective at reducing pain and the need for analgesia and some guidelines include TENS as a possible treatment option to be used in addition to other approaches.[10] The evidence of benefit is mainly when TENS is administered in a healthcare setting; studies involving patients using TENS machines at home have not found benefit, suggesting clear instructions for use are essential.[2]

Glucosamine or chondroitin are not recommended for the treatment of osteoarthritis in the majority of guidelines.[10] However, many patients use these supplements and report beneficial effects. Glucosamine, chondroitin, or the two in combination have small effects on pain, with patients on average reporting pain scores which are up to 5% less than patients taking a placebo. Glucosamine and chondroitin have small but statistically significant effects on reducing the extent of joint space narrowing in patients with osteoarthritis after two to three years of use.[34, 35] In general, evidence is more supportive of the efficacy of glucosamine sulphate than glucosamine hydrochloride.[36] In clinical trials, rates of

adverse effects in groups of patients taking glucosamine and chondroitin have not differed from rates in groups of patients taking placebo medicines.[35] However, some reports suggest they have the potential to cause medicine interactions.[14]

Treatments which have a limited evidence base and are not recommended in guidelines

Clinical guidelines and evidence do not support the widespread use of these treatment options. Some patients may find them beneficial, possibly due to a placebo effect.

Arthrem contains the herb Artemisia annua which is used in Chinese medicine and is the original source of the anti-malarial medicine artemisinin. Arthrem has been assessed in one clinical trial, however, it did not produce significant improvements compared to a placebo medicine.[37]

Green-lipped mussel extract may produce benefit with at least four months of use, but this evidence is only from a single clinical trial.[37]

Topical rubefacients or herbal creams, e.g. Deep Heat, Anti-Flamme, are not recommended for the treatment of osteoarthritis in clinical guidelines and have either not been assessed in clinical trials or have been assessed in clinical trials and evidence suggests they are unlikely to be better than placebo treatments.[10, 38]

Further information on the effectiveness of complementary and alternative medicines in patients with osteoarthritis is available at the United States National Center for Complementary and Integrative Health: **https://nccih.nih.gov/health/arthritis/osteoarthritis**

Patient support and information about osteoarthritis is available from:

- Arthritis New Zealand: **www.arthritis.org.nz**, 0800 663 463; information and advice, brochures and webinars about osteoarthritis, exercises for improving joint function and treatment options.
- Health Navigator: **www.healthnavigator.org.nz/health-a-z/o/osteoarthritis/**; information, videos and brochures about the structure of joints, treatment options and living with osteoarthritis.

Acknowledgement: Thank you to **Dr Rebecca Grainger**, Rheumatologist and Head of Department of Medicine, University of Otago, Wellington for expert review of this article. N.B. Expert reviewers are not responsible for the final content of the article.

References:

1. Ministry of Health. Annual Update of Key Results 2015/16: New Zealand Health Survey. Ministry of Health NZ. Available from: www.health.govt.nz/publication/annual-update-key-results-2015-16-new-zealand-health-survey (Accessed Oct, 2017).
2. National Institute for Health Care Excellence (NICE). Osteoarthritis: care and management. NICE, 2014. Available from: www.nice.org.uk/guidance/cg177 (Accessed Oct, 2017).
3. Wan A. GP pain management: what are the 'Ps' and 'As' of pain management? Aust Fam Physician 2014;43:537–40.
4. Sakellariou G, Conaghan PG, Zhang W, et al. EULAR recommendations for the use of imaging in the clinical management of peripheral joint osteoarthritis. Ann Rheum Dis 2017;76:1484–94. doi:10.1136/annrheumdis-2016-210815
5. Booth J, Moseley GL, Schiltenwolf M, et al. Exercise for chronic musculoskeletal pain: A biopsychosocial approach. Musculoskeletal Care 2017; [Epub ahead of print]. doi:10.1002/msc.1191
6. Christensen R, Bartels EM, Astrup A, et al. Effect of weight reduction in obese patients diagnosed with knee osteoarthritis: a systematic review and meta- analysis. Ann Rheum Dis 2007;66:433–9. doi:10.1136/ard.2006.065904
7. Christensen R, Astrup A, Bliddal H. Weight loss: the treatment of choice for knee osteoarthritis? A randomized trial. Osteoarthr Cartil 2005;13:20–7. doi:10.1016/j.joca.2004.10.008
8. Martin JR, Jennings JM, Dennis DA. Morbid obesity and total knee arthroplasty: a growing problem. J Am Acad Orthop Surg 2017;25:188–94. doi:10.5435/JAAOS-D-15-00684
9. Abdulla A, Adams N, Bone M, et al. Guidance on the management of pain in older people. Age Ageing 2013;42 Suppl 1:i1-57. doi:10.1093/ageing/afs200
10. Nelson AE, Allen KD, Golightly YM, et al. A systematic review of recommendations and guidelines for the management of osteoarthritis: The chronic osteoarthritis management initiative of the U.S. bone and joint initiative. Semin Arthritis Rheum 2014;43:701–12. doi:10.1016/j.semarthrit.2013.11.012
11. American Geriatrics Society Panel on Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain in older persons. J Am Geriatr Soc 2009;57:1331–46. doi:10.1111/j.1532-5415.2009.02376.x
12. Bannuru RR, Schmid CH, Kent DM, et al. Comparative effectiveness of pharmacologic interventions for knee osteoarthritis: a systematic review and network meta-analysis. Ann Intern Med 2015;162:46–54. doi:10.7326/M14-1231
13. da Costa BR, Reichenbach S, Keller N, et al. Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis: a network meta-analysis. Lancet 2017;390:e21–33. doi:10.1016/S0140-6736(17)31744-0
14. New Zealand Formulary (NZF). NZF v64. 2017. Available from: www.nzf.org.nz (Accessed Oct, 2017).
15. Dart RC, Bailey E. Does therapeutic use of acetaminophen cause acute liver failure? Pharmacotherapy 2007;27:1219–30. doi:10.1592/phco.27.9.1219
16. Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine. Acute pain management: scientific evidence. Fourth Edition. 2015. Available from: http://fpm.anzca.edu.au/documents/apmse4_2015_final (Accessed Dec, 2017).
17. Temple AR, Benson GD, Zinsenheim JR, et al. Multicenter, randomized, double-blind, active-controlled, parallel-group trial of the long-term (6-12 months) safety of acetaminophen in adult patients with osteoarthritis. Clin Ther 2006;28:222–35. doi:10.1016/j.clinthera.2006.02.004
18. Bruyère O, Cooper C, Pelletier J-P, et al. An algorithm recommendation for

the management of knee osteoarthritis in Europe and internationally: a report from a task force of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). Semin Arthritis Rheum 2014;44:253–63. doi:10.1016/j.semarthrit.2014.05.014
19. Hochberg MC, Altman RD, April KT, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res (Hoboken) 2012;64:465–74.
20. Deal CL. The use of topical capsaicin in managing arthritis pain: A clinician's perspective. Semin Arthritis Rheum 1994;23:48–51. doi:10.1016/S0049-0172(10)80026-5
21. Schnitzer T, Morton C, Coker S. Topical capsaicin therapy for osteoarthritis pain: Achieving a maintenance regimen. Semin Arthritis Rheum 1994;23:34–40. doi:10.1016/S0049-0172(10)80024-1
22. Derry S, Conaghan P, Da Silva JAP, et al. Topical NSAIDs for chronic musculoskeletal pain in adults. Cochrane Database Syst Rev 2016;4:CD007400. doi:10.1002/14651858.CD007400.pub3
23. Niethard FU, Gold MS, Solomon GS, et al. Efficacy of topical diclofenac diethylamine gel in osteoarthritis of the knee. J Rheumatol 2005;32:2384–92.
24. Lapi F, Azoulay L, Yin H, et al. Concurrent use of diuretics, angiotensin converting enzyme inhibitors, and angiotensin receptor blockers with non-steroidal anti-inflammatory drugs and risk of acute kidney injury: nested case-control study. BMJ 2013;346:e8525.
25. Bally M, Dendukuri N, Rich B, et al. Risk of acute myocardial infarction with NSAIDs in real world use: bayesian meta-analysis of individual patient data. BMJ 2017;357:j1909.
26. Sostres C, Carrera-Lasfuentes P, Lanas A. Non-steroidal anti-inflammatory drug related upper gastrointestinal bleeding: types of drug use and patient profiles in real clinical practice. Curr Med Res Opin 2017;33:1815–20. doi:10.1080/03007995.2017.1338178
27. American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated Beers criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2015;63:2227–46. doi:10.1111/jgs.13702
28. Yuan JQ, Tsoi KKF, Yang M, et al. Systematic review with network meta-analysis: comparative effectiveness and safety of strategies for preventing NSAID-associated gastrointestinal toxicity. Aliment Pharmacol Ther 2016;43:1262–75. doi:10.1111/apt.13642
29. Law TY, Nguyen C, Frank RM, et al. Current concepts on the use of corticosteroid injections for knee osteoarthritis. Phys Sportsmed 2015;43:269–73. doi:10.1080/00913847.2015.1017440
30. McGarry JG, Livingston K, Daruwalla ZJ. Accurate intra-articular knee joint injection in the obese? 'Fat Chance!' - A clinical lesson and recommendations for secondary referral. Eur J Gen Pract 2011;17:124–8. doi:10.3109/13814788.2011.573548
31. Bastick AN, Wesseling J, Damen J, et al. Defining knee pain trajectories in early symptomatic knee osteoarthritis in primary care: 5-year results from a nationwide prospective cohort study (CHECK). Br J Gen Pract 2016;66:e32-39. doi:10.3399/bjgp15X688129
32. Royal Australian College of General Practitioners. Referral for joint replacement: a management guide for health providers. 2007. Available from: www.racgp.org.au/your-practice/guidelines/musculoskeletal/ (Accessed Jan, 2018).
33. Manheimer E, Cheng K, Linde K, et al. Acupuncture for peripheral joint osteoarthritis. Cochrane Database Syst Rev 2010;1:CD001977. doi:10.1002/14651858.CD001977.pub2
34. Lee YH, Woo J-H, Choi SJ, et al. Effect of glucosamine or chondroitin sulfate on the osteoarthritis progression: a meta-analysis. Rheumatol Int 2010;30:357–63. doi:10.1007/s00296-009-0969-5
35. Wandel S, Jüni P, Tendal B, et al. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis. BMJ 2010;341:c4675.
36. Wu D, Huang Y, Gu Y, et al. Efficacies of different preparations of glucosamine for the treatment of osteoarthritis: a meta-analysis of randomised, double-blind, placebo-controlled trials. Int J Clin Pract 2013;67:585–94. doi:10.1111/ijcp.12115
37. Liu X, Machado GC, Eyles JP, et al. Dietary supplements for treating osteoarthritis: a systematic review and meta-analysis. Br J Sports Med 2017; [Epub ahead of print]. doi:10.1136/bjsports-2016-097333
38. Derry S, Wiffen PJ, Kalso EA, et al. Topical analgesics for acute and chronic pain in adults - an overview of Cochrane Reviews. Cochrane Database Syst Rev 2017;5:CD008609. doi:10.1002/14651858.CD008609.pub2

This article is available online at:
www.bpac.org.nz/2018/osteoarthritis.aspx