### Levels of evidence and grades of recommendation

#### Levels of evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1+++</td>
<td>High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias.</td>
</tr>
<tr>
<td>1+</td>
<td>Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.</td>
</tr>
<tr>
<td>1−</td>
<td>Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias</td>
</tr>
<tr>
<td>2+++</td>
<td>High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal</td>
</tr>
<tr>
<td>2+</td>
<td>Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal</td>
</tr>
<tr>
<td>2−</td>
<td>Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal</td>
</tr>
<tr>
<td>3</td>
<td>Non-analytic studies, e.g. case reports, case series</td>
</tr>
<tr>
<td>4</td>
<td>Expert opinion</td>
</tr>
</tbody>
</table>

#### Grades of recommendation

<table>
<thead>
<tr>
<th>Grade</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At least one meta-analysis, systematic review of RCTs, or RCT rated as 1+++ and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results</td>
</tr>
<tr>
<td>B</td>
<td>A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1+++ or 1+</td>
</tr>
<tr>
<td>C</td>
<td>A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++</td>
</tr>
<tr>
<td>D</td>
<td>Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+</td>
</tr>
<tr>
<td>GPP (good practice points)</td>
<td>Recommended best practice based on the clinical experience of the guideline development group.</td>
</tr>
</tbody>
</table>
CLINICAL PRACTICE GUIDELINES

Osteoarthritis of the Knees

Published by Ministry of Health, Singapore
16 College Road,
College of Medicine Building
Singapore 169854

Printed by Golden City Colour Printing Co. (Pte.) Ltd.

Copyright © 2007 by Ministry of Health, Singapore


**Statement of Intent**

These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient, in the light of the clinical data presented by the patient and the diagnostic and treatment options available.
## Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive summary of recommendations</td>
<td>1</td>
</tr>
<tr>
<td>1 Introduction</td>
<td>8</td>
</tr>
<tr>
<td>2 Diagnostic Approach to Joint Pain and Osteoarthritis</td>
<td>10</td>
</tr>
<tr>
<td>3 Analgesics in Osteoarthritis of the Knees</td>
<td>13</td>
</tr>
<tr>
<td>4 Glucosamine/Chondroitin in the Treatment of Osteoarthritis</td>
<td>19</td>
</tr>
<tr>
<td>5 Intra-articular Injections</td>
<td>21</td>
</tr>
<tr>
<td>6 Topical Non-Steroidal Anti-inflammatory Drugs (NSAIDs) and Medications</td>
<td>23</td>
</tr>
<tr>
<td>7 Non-pharmacological Management</td>
<td>24</td>
</tr>
<tr>
<td>8 Surgery</td>
<td>30</td>
</tr>
<tr>
<td>9 Cost-effectiveness Issues</td>
<td>32</td>
</tr>
<tr>
<td>10 Clinical Quality Improvement</td>
<td>33</td>
</tr>
<tr>
<td>References</td>
<td>34</td>
</tr>
<tr>
<td>Self-assessment (MCQs)</td>
<td>44</td>
</tr>
<tr>
<td>Workgroup Members</td>
<td>48</td>
</tr>
</tbody>
</table>
Foreword

Osteoarthritis is characterized by focal areas of loss of articular cartilage within synovial joints, leading to pain and gradual loss of function. It can affect any joint but is most common in the knee and hip.

Globally, osteoarthritis is the commonest joint disorder, and the WHO estimated that as much as 40% of the people over the age of 70 years suffer from osteoarthritis of the knee. It accounts for 14.8 million disability adjusted life years (DALYs) lost, with 80% percent of those afflicted having some degree of limitation of movement and 25% being unable to perform the major activities of daily living. As the incidence and prevalence of osteoarthritis increase with age, the DALYs lost due to this disease are expected to increase by 40% by 2030.

In Singapore, 17,000 DALYs lost are attributable to osteoarthritis. As our population ages, the burden of disease due to osteoarthritis increases correspondingly. It is timely to develop the first national guidelines on osteoarthritis of the knees in order to enable our doctors to deal effectively with this disease. A multidisciplinary expert committee has reviewed the latest scientific evidence and combined the evidence with their expertise to develop guidelines appropriate for our population.

I hope these guidelines will assist doctors, especially primary care physicians, in managing their patients with osteoarthritis of the knees.

PROFESSOR K SATKU
DIRECTOR OF MEDICAL SERVICES
Executive Summary of Recommendations

Diagnostic Approach to Joint Pain and Osteoarthritis

**GPP** The diagnosis of osteoarthritis is made clinically based on history and physical examination, with laboratory and radiologic investigations selectively undertaken to exclude inflammatory arthritis, secondary osteoarthritis, and non-articular causes of joint pain (pg 10).

**GPP**

Analgesics in Osteoarthritis of the Knees

**A** Paracetamol (acetaminophen) should be considered as the first line of treatment for relieving pain and improving physical functioning in osteoarthritis (pg 13).

*Grade A, Level 1+

**A** Non-selective non-steroidal anti-inflammatory drugs should be used for the acute relief of pain and improvement in function for as short a period as possible. The benefits of using non-steroidal anti-inflammatory drugs should be weighed against the potential adverse reactions, especially with long-term use, in individuals at risk (pg 13).

*Grade A, Level 1+

**GPP** The selection of a non-steroidal anti-inflammatory drug for prescription for osteoarthritis knee should be based upon relative safety, patient acceptability and cost effectiveness (pg 13).

**GPP** Patients who develop hypersensitivity reactions to non-selective non-steroidal anti-inflammatory drugs are usually able to tolerate cyclo-oxygenase 2 selective inhibitors. These should preferably be prescribed following demonstration of tolerance through supervised drug provocation tests (pg 14).

**GPP**

**A** Patients with moderately high risk for gastroduodenal bleeds should receive concomitant gastroprotective agents (GPA) when using non-selective non-steroidal anti-inflammatory drugs (pg 14).
Risk factors for gastrointestinal complications include:

- age greater than 60 years
- previous history of gastrointestinal events (e.g. peptic ulcer disease)
- concomitant corticosteroid use.

Grade A, Level 1+

A Recommended prophylactic gastroprotective agents (GPA) against gastroduodenal ulcers include (pg 15):

- standard dose of proton-pump inhibitors (omeprazole 20 mg once daily)
- misoprostol 400-800 mcg/day
- double dose of H2-receptor antagonists (famotidine 40 mg bd, ranitidine 300 mg bd)

Grade A, Level 1+

A Cyclo-oxygenase 2 selective inhibitors may be used acutely in the reduction of pain from osteoarthritis of the knees. Although these drugs have relatively lower risk of gastroduodenal adverse effects, long-term use has been associated with myocardial and cerebral infarction (pg 16).

Grade A, Level 1+

GPP When non-steroidal anti-inflammatory drugs (including both cyclo-oxygenase 2 selective and non-selective non-steroidal anti-inflammatory drugs) are needed for the management of an individual patient, they should be prescribed at the lowest effective dose. The duration of treatment should be periodically reviewed and kept as short as possible (pg 16).

GPP All non-steroidal anti-inflammatory drugs should not be prescribed in patients who have recently undergone coronary artery bypass graft (CABG) surgery and revascularization procedures (pg 16).

GPP The benefits and risks of celecoxib and etoricoxib should be carefully assessed before they are prescribed to any individual patient, taking into consideration other available therapeutic options (pg 16).
Celecoxib or etoricoxib should not be prescribed for patients with established ischaemic heart disease, stroke or congestive heart failure (pg 16).

Caution should be exercised when prescribing celecoxib or etoricoxib to patients who have the following risk factors: hypertension, hyperlipidaemia, diabetes and smoking, as well as patients with peripheral arterial disease (pg 17).

Etoricoxib should not be prescribed for patients with hypertension whose blood pressure has not been adequately controlled (pg 17).

Meloxicam and nimesulide are two non-steroidal anti-inflammatory drugs with preferential cyclo-oxygenase 2 inhibition which may be used in the short term relief of pain from osteoarthritis of the knees (pg 17).

Tramadol may be used as an alternative to non-steroidal anti-inflammatory drugs for pain relief and improvement in physical functioning, especially where the risks of adverse effects from non-steroidal anti-inflammatory drugs outweigh the benefits (pg 18).

Oral corticosteroids are not indicated for management of knee osteoarthritis (pg 18).

Glucosamine/chondroitin in the Treatment of Osteoarthritis

Patients who have failed to respond to analgesics and non-pharmacologic measures and want to try glucosamine may be given glucosamine sulphate 1500 mg once daily as pharmacologic studies suggest that maximal benefit is better achieved at this dose (pg 20).
Patients who are already taking glucosamine and report improvement in symptoms may discontinue after a period of 6 months as evidence suggests that regular use for more than 6 months is no more effective than placebo in the relief of joint pain (pg 20).

Grade B, Level 1+

Patients allergic to shellfish should be warned about possible allergic reactions to glucosamine (pg 20).

Intra-articular Injections

Viscosupplementation can be used for treatment of osteoarthritis of the knee, where general measures or systemic therapies have failed or are contraindicated. It is effective with beneficial effects on pain, function and patient global assessment; and at different post injection periods but especially at the 5 to 13 week post injection period when compared with placebo (pg 21).

Grade B, Level 1+

In Singapore, data on effectiveness are too limited to allow any conclusions to be drawn regarding cost-effectiveness of viscosupplementation. However, in view of the relative high cost of viscosupplementation and its comparable efficacy with other forms of systemic intervention, it should be considered only if general measures and systemic therapies have failed or are contraindicated (pg 21).

Regular use of intra-articular steroids is not recommended for osteoarthritis of the knees in the general practice setting (pg 22).
Topical non-steroidal anti-inflammatory drugs (NSAIDs) and medications

A Topical non-steroidal anti-inflammatory drugs (NSAIDs) can be considered for the short-term symptomatic relief of pain in osteoarthritis. Side effects of topical NSAIDs are usually minor (pg 23).

Grade A, Level 1+

A Topical capsaicin may also be considered in relieving pain due to osteoarthritis. Transient local burning sensation may occur at the site of application (pg 23).

Grade A, Level 1+

Non-pharmacological Management

A Regular knee strengthening and aerobic exercises should be encouraged and taught to patients with osteoarthritis of the knees, as these improve functional ability, aerobic and endurance capacity and reduce knee pain (pg 24).

Grade A, Level 1+

A Weight loss can result in significant changes in knee joint biomechanics with improved knee function for stair climbing and other daily activities. It is most effectively achieved by a combination of exercise and dietary control (pg 25).

Grade A, Level 1+

A Regular water-based exercise or exercises in the pool are recommended as these exercises reduce pain and improve physical function in patients with osteoarthritis of the knees (pg 25).

Grade A, Level 1++

B Transcutaneous electrical nerve stimulation, in the form of strong burst mode with high frequency, should be used to provide short-term relief of osteoarthritis of the knee pain, reduce stiffness and improve knee range of motion, with effects lasting for 4 weeks (pg 26).

Grade B, Level 1+
**B** Interferential current may be used to reduce pain and increase in knee range of motion for osteoarthritis of the knee patients (pg 26).

**Grade B, Level 1+**

**A** Taping may be used to shift the patella medially and provide effective relief of pain in osteoarthritis of the knee (pg 26).

**Grade A, Level 1++**

**B** Lateral wedge insoles (tilt angle of 8.5 to 11 degrees) should be used to provide pain relief for osteoarthritis of the knee with medial osteoarthritis symptoms (pg 27).

**Grade B, Level 1+**

**B** Valgus knee brace and knee sleeves may be used to provide significant improvement in functional tasks and unloading of varus deformity (pg 27).

**Grade B, Level 1+**

**A** Manual therapy applied to the knee together with an exercise programme may be used to improve knee function and pain relief for patients with osteoarthritis of the knee (pg 27).

**Grade A, Level 1+**

**A** Needle electro-acupuncture may be used as an adjunct for symptomatic relief of pain and improvement of knee function (pg 28).

**Grade A, Level 1++**

**Surgery**

**GPP** A referral to the orthopaedic surgeon should be made when conservative management mentioned previously has failed (pg 30).

**GPP**

**Cost-effectiveness Issues**

**GPP** Pain medications are important in managing osteoarthritis symptoms and should be used concurrently with nutritional, physical, and educational interventions. Doctors should consider efficacy, adverse side effects, dosing frequency, and cost to the patient when recommending osteoarthritis treatments (pg 32).

**GPP**
For mild to moderate osteoarthritis pain, paracetamol is the drug of choice as it is cost-effective and has minimal side-effects. In treating moderate to severe osteoarthritis pain, the use of non-steroidal anti-inflammatory drugs and COX-2 specific inhibitors (for a patient who is at high risk of adverse upper gastrointestinal events) should be considered only if the patient is not responding to paracetamol (pg 32).

Grade C, Level 2+

For patients who have failed medical therapy and who are suitable for surgical interventions, both unicompartmental and total knee arthroplasty are cost effective in terms of quality of life gain (pg 32).

Grade C, Level 2+
1 Introduction

1.1 Aim and scope of guideline

Rheumatic diseases are a common cause of morbidity. In a local survey rheumatic pain was the second most common symptom which led a patient to see the family doctor. The scope of arthritis and rheumatism is very broad ranging from fibromyalgia and tennis elbow to multiorgan related systemic lupus and catastrophic antiphospholipid syndrome.

Osteoarthritis affects older people and the demography of the population shows that in 2030 there will be a rise from 19% currently to 26% who are over the age of 60. Osteoarthritis is also the rheumatic disease which is the most commonly managed by the family doctor. The main focus is on osteoarthritis of the knee as it is one of the most common forms of osteoarthritis in Singapore. Thumboo et al found that in a consecutive cohort of patients with osteoarthritis of the knee and hip seen in the rheumatology department of a tertiary institution, 94% had osteoarthritis of the knee.\(^1\) In Singapore the use of SF-36 and the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) has been validated.\(^1\) Studies showed that in multiple regression analysis, less pain was associated with a younger age, shorter duration of symptoms, more years of education, working, and Chinese ethnicity. Better physical function was associated with more years of education, less learned helplessness, less bodily pain, and less severe osteoarthritis.

We have therefore chosen to confine the topic for this set of guidelines to the management of osteoarthritis of the knees.

1.2 Target group

Management of osteoarthritis is multidisciplinary, involving the rheumatologist, orthopaedic surgeon, physiotherapist, occupational therapist, podiatrist and specialist nurses. We hope that this set of guidelines will benefit all doctors involved in the care of patients with osteoarthritis and form the basis of good, practical and evidence based care to osteoarthritis patients in the community.
1.3 **Guideline development**

These guidelines have been produced by a committee comprising rheumatologists, an orthopaedic surgeon, a family physician and a physiotherapist appointed by the Ministry of Health. They were developed using the best available current evidence and expert opinion.

Some treatments which are widely available suffer from a paucity of good clinical evidence for efficacy and safety. These include the use of glucosamine, chondroitin and other nutraceutical products as well as alternative therapies such as acupuncture and reflexology. However where data does exist, the workgroup has stated recommendations which hopefully will be beneficial to the clinician.

1.4 **Review of guidelines**

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supercede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review five years after publication, or if new evidence appears that requires substantive changes to the recommendations.
2 Diagnostic Approach to Joint Pain and Osteoarthritis

**GPP** The diagnosis of osteoarthritis is made clinically based on history and physical examination, with laboratory and radiologic investigations selectively undertaken to exclude inflammatory arthritis, secondary osteoarthritis, and non-articular causes of joint pain.

A practical diagnostic approach to a patient presenting with joint pain, which is suspected to be due to osteoarthritis is to ask 3 questions:

1) Is the source of pain articular or non-articular?

2) If articular, is the pathology osteoarthritis?

3) If osteoarthritis, is the pathogenesis idiopathic (primary) or secondary?

1) **Is it articular or non-articular pain?**

Palpation is key in evaluation. Non-articular sources of joint pain include:

- **Peri-articular soft tissue pain:**
  - Ligament (tear/strain)
  - Tendon (tendonitis, enthesitis)
  - Muscle (myositis, myofascial pain, disuse atrophy, tight hamstrings)
  - Fascia (fasciitis, iliotibial band syndrome)
  - Bursa (bursitis)
  - Plica
  - Fat pad (Hoffa’s syndrome)
  - Blood vessel (aneurysm, varicose veins)
  - Bone (avascular necrosis, tumour)
  - Nerve (neuroma).

- **Referred pain, e.g. knee pain due to:**
  - Hip pathology
  - Myofascial piriformis pain
  - Prolapsed lumbar disc with sciatica.
• Central pain:
  ▪ Fibromyalgia
  ▪ Restless Leg Syndrome
  ▪ Complex regional pain syndrome (Sudeck’s dystrophy).

2) Is it osteoarthritis?

As osteoarthritis has no specific clinical characteristic or diagnostic laboratory test, and radiographic findings may not correlate with clinical severity, the diagnosis is made clinically based on history and physical examination, with laboratory and radiologic tests selectively undertaken to exclude inflammatory arthritis, secondary osteoarthritis, and non-articular causes of joint pain.2

The table below lists “red-flags” to alert physicians to seriously reconsider the diagnosis of osteoarthritis as the main reason for the patient’s symptomatology:

| Clinical | Significant early morning stiffness >30 min  
Nocturnal pain disturbing sleep  
Referred pain  
Fever / chills / weight loss  
Soft tissue swelling with warmth  
Focal tenderness  
Numbness/tingling, especially if aggravated by neck / back movement  
Neurological deficit (weakness, sensory deficit)  
Erythema / cyanosis / nailfold infarcts  
Claudication  
Weak /absent peripheral pulses |
|-----------------|--------------------------------------------------|
| Laboratory      | ESR>40 mm/1st hour  
Elevated C-reactive protein  
Anaemia  
Thrombocytosis |
| Radiological    | Periarticular osteopaenia  
Presence of erosions / joint ankylosis  
Fracture  
Joint dislocation |
3) **Is it primary or secondary osteoarthritis?**

Primary/idiopathic osteoarthritis has a symmetrical predilection for joints of the fingers (distal interphalangeal joint, proximal interphalangeal joint, 1st carpometacarpal joint), hips, knees and spine. Involvement of other joints should prompt an evaluation for secondary causes of osteoarthritis:

- Trauma, Charcot’s (neuropathic) joint, Avascular necrosis
- Inflammatory arthritis
  - Crystal arthropathy
  - Rheumatoid arthritis
  - Septic arthritis
- Congenital/developmental

**The pattern of the joint involvement**

Primary osteoarthritis can be further subdivided into localized or generalized, the latter involving 3 or more sets of joints. The more common joints involved in osteoarthritis are shown shaded in the figure below:
3 Analgesics in Osteoarthritis of the Knees

3.1 Oral paracetamol

A Paracetamol (acetaminophen) should be considered as the first line of treatment for relieving pain and improving physical functioning in osteoarthritis.\textsuperscript{3-5}

Grade A, Level 1+

Paracetamol is effective in relieving pain and improving physical function in osteoarthritis.\textsuperscript{3} When compared to non-steroidal anti-inflammatory drugs (NSAIDs), although it was less effective than NSAIDs in pain reduction\textsuperscript{6} and global assessment, it was as effective as NSAIDs in the improvement in physical functioning. Gastrointestinal discomfort was more frequent with NSAIDs than with paracetamol.\textsuperscript{6} The evidence supports current European League Against Rheumatism (EULAR)\textsuperscript{4} and American College of Rheumatology (ACR)\textsuperscript{5} guidelines which recommend paracetamol as the first line oral analgesic for patients with knee osteoarthritis in view of its efficacy, safety profile and lower cost.

3.2 Non-selective non-steroidal anti-inflammatory drugs (NSAID)

A Non-selective non-steroidal anti-inflammatory drugs should be used for the acute relief of pain and improvement in function for as short a period as possible. The benefits of using non-steroidal anti-inflammatory drugs should be weighed against the potential adverse reactions, especially with long-term use, in individuals at risk.\textsuperscript{7}

Grade A, Level 1+

GPP The selection of a non-steroidal anti-inflammatory drug for prescription for osteoarthritis knee should be based upon relative safety, patient acceptability and cost effectiveness.

GPP

Non-selective NSAIDs can reduce pain in osteoarthritis of the knees in the short term only slightly better than placebo. When compared to acetaminophen, NSAIDs appear superior for improving hip and knee pain, but not for improving function for up to 6 weeks’ duration.\textsuperscript{7}
There is no substantial evidence demonstrating differences in the relative efficacy of individual NSAIDs when used in the management of osteoarthritis of the knee. This is because of the paucity of randomised control trials, design errors in randomised control trials comparing 2 or more NSAIDs particularly the use of inequivalent dose comparisons. The selection of an NSAID for prescription for osteoarthritis of the knee should be based upon relative safety, patient acceptability and cost.7

Side effects that are clinically important include:

- gastrointestinal (gastroduodenal perforations, ulcers and bleeds, small bowel perforations)
- renal (hyperkalaemia, hypertension, oedema, acute renal insufficiency)
- hypersensitivity reactions including periorbital angioedema, urticaria, rhinitis or attacks of asthma.

Emerging evidence suggests that there are cardiovascular risks associated with non-selective NSAIDs as well8,9 although this could not be conclusively demonstrated in a recent meta-analysis.10

**GPP** Patients who develop hypersensitivity reactions to non-selective non-steroidal anti-inflammatory drugs are usually able to tolerate cyclo-oxygenase 2 selective inhibitors. These should preferably be prescribed following demonstration of tolerance through supervised drug provocation tests.

**GPP**

**A** Patients with moderately high risk for gastroduodenal bleeds should receive concomitant gastroprotective agents (GPA) when using non-selective non-steroidal anti-inflammatory drugs.11

Risk factors for gastrointestinal complications include:11

- age greater than 60 years
- previous history of gastrointestinal events (e.g. peptic ulcer disease)
- concomitant corticosteroid use.

**Grade A, Level 1+**
Recommended prophylactic gastroprotective agents (GPA) against gastroduodenal ulcers include:¹²

- standard dose of proton-pump inhibitors (omeprazole 20 mg once daily)
- misoprostol 400-800 mcg/day
- double dose of H2-receptor antagonists (famotidine 40 mg bd, ranitidine 300 mg bd)

Grade A, Level 1+

Risk factors for nephrotoxicity include:¹³

- Concomitant diuretics, angiotension converting enzyme (ACE) inhibitors or angiotensin-1 (AT1) receptor blockers
- Volume depleted patients
- Elderly
- Congestive heart failure
- Underlying diabetes mellitus, or renal and liver insufficiency

Patients who develop periorbital swelling with NSAIDs (e.g. diclofenac, indomethacin, naproxen) often have NSAID sensitivity, which is an idiosyncratic, non-IgE mediated reaction. They may occasionally also develop urticaria, bronchospasm or anaphylaxis. Extremely sensitive individuals may also develop a similar reaction to topical NSAIDs. NSAID-sensitive individuals should avoid all other potentially cross-reacting NSAIDs. Individuals with a similar reaction to paracetamol should also avoid all NSAIDs.

Selective cyclo-oxygenase inhibitors (COX-2 selective inhibitors) are possible alternative treatments in NSAID sensitive individuals should paracetamol or tramadol be ineffective or result in adverse reactions e.g. nausea/giddiness with tramadol. As the COX-2 selective inhibitors may also result in a similar reaction in such individuals, supervised drug provocation tests by specialists trained in allergy/immunology are recommended before using these drugs in NSAID-sensitive individuals.
3.3 Cyclo-oxygenase 2 (COX-2) selective inhibitors

A Cyclo-oxygenase 2 selective inhibitors may be used acutely in the reduction of pain from osteoarthritis of the knees.\textsuperscript{14-16} Although these drugs have relatively lower risk of gastroduodenal adverse effects, long-term use has been associated with myocardial and cerebral infarction.\textsuperscript{17-19}

\textit{Grade A, Level 1+}

\textbf{GPP} When non-steroidal anti-inflammatory drugs (including both cyclo-oxygenase 2 selective and non-selective non-steroidal anti-inflammatory drugs) are needed for the management of an individual patient, they should be prescribed at the lowest effective dose. The duration of treatment should be periodically reviewed and kept as short as possible.

GPP

Coxibs, the class of NSAIDs that selectively inhibit cyclo-oxygenase 2 (COX-2), were designed to reduce joint pain and inflammation without causing the gastroduodenal adverse effects typical of nonselective NSAIDs, namely perforations, ulcers and bleeds.\textsuperscript{14-16}

Meta-analyses have shown that selective COX-2 inhibitors were not more effective than conventional NSAIDs and paracetamol in the relief of symptoms of osteoarthritis.\textsuperscript{20} Similarly, randomized controlled trials have shown that the clinical efficacy of lumiracoxib in patients with symptomatic osteoarthritis is similar to celecoxib.\textsuperscript{21}

\textbf{GPP} All non-steroidal anti-inflammatory drugs should not be prescribed in patients who have recently undergone coronary artery bypass graft (CABG) surgery and revascularization procedures.

\textbf{GPP} The benefits and risks of celecoxib and etoricoxib should be carefully assessed before they are prescribed to any individual patient, taking into consideration other available therapeutic options.

\textbf{GPP} Celecoxib or etoricoxib should not be prescribed for patients with established ischaemic heart disease, stroke or congestive heart failure.

\textbf{GPP}
Caution should be exercised when prescribing celecoxib or etoricoxib to patients who have the following risk factors: hypertension, hyperlipidaemia, diabetes and smoking, as well as patients with peripheral arterial disease.

Etoricoxib should not be prescribed for patients with hypertension whose blood pressure has not been adequately controlled.

The COX-2 selective inhibitors have recently been found to be associated with increased cardiovascular events, leading to the withdrawal of rofecoxib in Singapore in October 2004.

There was no significant difference between lumiracoxib versus combined comparator NSAIDs irrespective of aspirin use with regards to cardiovascular events contributing to myocardial infarction, stroke or cardiovascular death. The rates of thrombotic cardiovascular events in patients with osteoarthritis or rheumatoid arthritis on etoricoxib were found to be similar to those on diclofenac with long-term use of these drugs.

In addition to the increased cardiovascular risks, reports of severe cutaneous reactions (Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis) among patients taking valdecoxib resulted in the drug being removed from the market in several countries including Singapore in April 2005.

The nephrotoxicity of selective COX-2 inhibitors is no different from those of non-selective NSAIDs.

3.4 **NSAID with preferential COX-2 inhibition**

Meloxicam and nimesulide are two non-steroidal anti-inflammatory drugs with preferential cyclo-oxygenase 2 inhibition which may be used in the short term relief of pain from osteoarthritis of the knees.

Meloxicam, an NSAID with preferential but not selective COX-2 inhibition, has been shown to be comparable to piroxicam for acute
pain relief (over 28 days) in osteoarthritis of the knees but with better gastrointestinal tolerability. The superior gastrointestinal tolerability in symptomatic osteoarthritis over 28 days has also been demonstrated in comparison to diclofenac.\textsuperscript{27,28}

Nimesulide, another NSAID with preferential but not selective COX-2 inhibition, has been found to be effective in the acute relief of pain in osteoarthritis of the knees. It was reported to have rapid onset of action when compared to other selective COX-2 inhibitors with minimal adverse effects. Although it is indicated for the short-term relief of joint pain, there have been reports of elevated liver enzymes and hepatitis.\textsuperscript{29,30}

### 3.5 Tramadol

Tramadol may be used as an alternative to non-steroidal anti-inflammatory drugs for pain relief and improvement in physical functioning, especially where the risks of adverse effects from non-steroidal anti-inflammatory drugs outweigh the benefits.\textsuperscript{31,32}

**Grade A, Level 1+**

The American College for Rheumatology recommends tramadol for use in osteoarthritis where patients get an inadequate response with acetaminophen, COX-2 inhibitors or NSAIDS. The American Pain Society recommends tramadol alone or in combination with acetaminophen or NSAIDs at any time when NSAIDs alone produce inadequate pain relief. Tramadol ER at a dose of 200-400 mg/day has been shown to improve significantly the symptoms (pain, stiffness, physical functioning) in osteoarthritis of the knees.\textsuperscript{31,32}

### 3.6 Oral corticosteroids

**GPP** Oral corticosteroids are not indicated for management of knee osteoarthritis.

**GPP**

Osteoarthritis (unlike rheumatoid arthritis) is not a systemic inflammatory disease and the risks of side effects associated with the use of oral corticosteroids outweigh possible benefits.
Over the years, there have been several randomized controlled studies published evaluating the use of glucosamine in the treatment of osteoarthritis. Initial results suggested that glucosamine was superior to placebo in terms of pain reduction and function. However, these studies have been largely funded by pharmaceutical companies and are heterogenous in terms of study protocols as well as drug preparations and administration. High-quality systemic reviews undertaken by the Cochrane Collaboration and more recently; the largest, non-pharmaceutical driven randomized trial (GAIT: Glucosamine/chondroitin Arthritis Intervention Trial), have concluded that glucosamine sulphate or glucosamine hydrochloride did not demonstrate a clear and consistent benefit in improving WOMAC outcomes for pain, stiffness and function over that of placebo.\textsuperscript{33,34} Although subgroup analysis demonstrated that the Rotta preparation\textsuperscript{34} of glucosamine sulphate (1500 mg/daily) was superior to placebo in the treatment of pain and functional impairment in patients with symptomatic osteoarthritis and the subset of patients with moderate to severe knee osteoarthritis in GAIT that received combination glucosamine and chondroitin sulphate therapy demonstrated significant pain reduction and improved function over placebo\textsuperscript{33}; these results must be interpreted with caution as the former studies were manufacturer-driven and important study limitations existed in GAIT.

There has also been a well-documented wide variation in the active ingredients and in the quality of supplement products. In many countries, they are available over the counter and are classified as dietary supplements and not therapeutic products and so are not subject to stringent manufacturing regulations.

**Efficacy**

Neither glucosamine hydrochloride nor chondroitin sulfate alone has been shown to be more efficacious than placebo for the treatment of knee pain.\textsuperscript{33,34,34a}
Patients who have failed to respond to analgesics and non-
pharmacologic measures and want to try glucosamine may be given
glucosamine sulphate 1500 mg once daily as pharmacologic studies
suggest that maximal benefit is better achieved at this dose.\textsuperscript{35}

\textbf{Grade B, Level 2++}

Patients who are already taking glucosamine and report
improvement in symptoms may discontinue after a period of 6 months
as evidence suggest that regular use for more than 6 months is no
more effective than placebo in the relief of joint pain.\textsuperscript{36}

\textbf{Grade B, Level 1+}

There is no evidence for the use of glucosamine and/or chondroitin in
the primary prevention of osteoarthritis.

\textbf{Structural modification}

There is no clear evidence to date that glucosamine sulphate may
retard radiological progression of knee osteoarthritis.\textsuperscript{34,37,38} There is
also no evidence that these agents prevent osteoarthritis in healthy
persons or in persons with knee pain but normal radiographs.

\textbf{Pharmacokinetics}

There may be variable response with different preparations (Rotta and
non-Rotta) of glucosamine, and pharmacokinetic studies suggest that
maximal benefit is better achieved if glucosamine sulphate is taken at
a dose of 1500 mg once daily.\textsuperscript{35}

\textbf{Safety}

Glucosamine and/or chondroitin have a good safety profile with no
effect on glucose metabolism.\textsuperscript{34,39,40}

\textbf{GPP} Patients allergic to shellfish should be warned about possible
allergic reactions to glucosamine.

\textbf{GPP}
5 Intra-articular Injections

5.1 Viscosupplementation

Viscosupplementation can be used for treatment of osteoarthritis of the knee, where general measures or systemic therapies have failed or are contraindicated. It is effective with beneficial effects on pain, function and patient global assessment; and at different post injection periods but especially at the 5 to 13 week post injection period when compared with placebo.\textsuperscript{41}

\textbf{Grade B, Level 1+}

Patients with the most advanced radiographic stage of osteoarthritis (complete loss of the joint space) were less likely to benefit from intra-articular injection of hyaluronic acid.\textsuperscript{42}

Viscosupplements were comparable in efficacy to systemic forms of active intervention (e.g. NSAIDs), with more local reactions (post injection inflammation) but fewer systemic adverse events.\textsuperscript{41}

\textbf{GPP} In Singapore, data on effectiveness are too limited to allow any conclusions to be drawn regarding cost-effectiveness of viscosupplementation. However, in view of the relative high cost of viscosupplementation and its comparable efficacy with other forms of systemic intervention, it should be considered only if general measures and systemic therapies have failed or are contraindicated.

Hyaluronic acid products had more prolonged effects than intra-articular (IA) corticosteroids.\textsuperscript{41}

Sample-size restrictions preclude any definitive comment on the safety of the hyaluronic acid class of products. However, within the constraints of the trial designs employed, no major safety issues were detected.\textsuperscript{41}
5.2 Intra-articular (IA) corticosteroid

**B** In patients with knee osteoarthritis who are symptomatic despite general measures and systemic therapies, evidence supports short term (up to two weeks) improvement of symptoms from intra-articular corticosteroid injection.\(^{43}\)

*Grade B, Level 1-

**GPP** Regular use of intra-articular steroids is not recommended for osteoarthritis of the knees in the general practice setting.

*GPP*
6 Topical Non-steroidal Anti-inflammatory Drugs (NSAIDs) and Medications

A Topical non-steroidal anti-inflammatory drugs (NSAIDs) can be considered for the short-term symptomatic relief of pain in osteoarthritis. Side effects of topical NSAIDs are usually minor.

Grade A, Level 1+

Topical medications are often used for joint pain and muscle aches. Review of randomized controlled trials in osteoarthritis have shown that topical NSAIDs are more effective than placebo in relieving pain and they have relatively minor side effects.\(^44\-47\) However, the use of the topical NSAIDs usually provide only short term symptomatic relief of the osteoarthritis.

A Topical capsaicin may also be considered in relieving pain due to osteoarthritis. Transient local burning sensation may occur at the site of application.

Grade A, Level 1+

Topical capsaicin has also been shown to be more effective than placebo in short term trials but it may cause local burning sensation and this may limit its use in some patients.\(^48\,49\)

At present, there is insufficient evidence to determine the efficacy of topical glucosamine in osteoarthritis.

One published trial using a topical cream containing glucosamine sulfate, chondroitin sulfate and camphor for osteoarthritis of the knee was reported to show a greater reduction in pain compared to placebo. However, the active treatment contained camphor and peppermint oil gave rise to local burning sensation and smell, and thus the study was not truly blinded.\(^50\)
Non-pharmacological Management

The majority of the non-pharmaceutical management methods of osteoarthritis are physiotherapy techniques.\textsuperscript{51-55}

Physiotherapy of osteoarthritis of the knee usually encompasses the use of a wide range of techniques and modalities to:

1. eliminate pain sensation – relief may last as long as up to one year.
2. maintain and improve muscle strength, fitness and endurance to perform activities of daily living
3. maintain and improve range of motion in the knee and joint alignment in order to perform activities of daily living
4. reduce and delay the progression of joint destruction.

The techniques used in physiotherapy are termed treatment modalities. There are many physiotherapy modalities used in the treatment of osteoarthritis of the knee. However the key modalities that have been extensively researched with evidence from randomised controlled trials are listed below.

7.1 Exercise

A Regular knee strengthening and aerobic exercises should be encouraged and taught to patients with osteoarthritis of the knees, as these improve functional ability, aerobic and endurance capacity and reduce knee pain.

\textbf{Grade A, Level 1+}

Patients with osteoarthritis will benefit from appropriately prescribed exercises that will strengthen the muscles and improve endurance and cardiovascular fitness. Correct exercise prescription is important to provide a balance of strength, endurance and fitness to enable patients to maintain functional activities of daily living and for weight reduction. Exercise programmes usually consist of a series of simple knee extension or leg lifting home exercises, stationary cycling, aerobic walking and water-based exercise (hydrotherapy).\textsuperscript{56,57}
Studies show that regular exercise in the form of aerobic and strengthening weight training exercises are effective in improving function and reducing pain during walking for patients with osteoarthritis.\textsuperscript{56-58} These exercises also improved fitness and endurance during functional activities, like the 6-minute walk test, walking and stair climbing.\textsuperscript{56,57}

7.2 **Weight reduction**

A Weight loss can result in significant changes in knee joint biomechanics with improved knee function for stair climbing and other daily activities. It is most effectively achieved by a combination of exercise and dietary control.

**Grade A, Level 1+**

Obesity is a significant risk factor in the progression of osteoarthritis, and recent studies support that there are significant biomechanical joint changes and functional improvements with at least 6\% of body weight reduction for patients with osteoarthritis.\textsuperscript{59,60} These studies show that loss of weight will increase knee medial joint space, reduce knee joint compression\textsuperscript{60} and improve functional ability, stair climbing and fitness.\textsuperscript{60-62} Felson et al reported that the odds ratio for developing or progressing osteoarthritis in the knee can be significantly reduced by 50\% with a weight reduction of at least 5 kg.\textsuperscript{61} Many studies have shown that weight loss is most effectively achieved by a combination of exercise and dietary control.\textsuperscript{60}

7.3 **Hydrotherapy**

A Regular water-based exercise or exercises in the pool are recommended as these exercises reduce pain and improve physical function in patients with osteoarthritis of the knees.

**Grade A, Level 1++**

Hydrotherapy, is the use of (at least) knee-deep water in a pool to perform various functional exercises in a reduced weight-bearing environment. Water-based exercise programmes was found to reduce pain and improve physical function for patients with osteoarthritis of the knee, with effects lasting even at one year of follow up.\textsuperscript{63-65} The effectiveness of hydrotherapy is not surprising as it probably provides
another form of strengthening exercise in a non-weight bearing environment.

7.4 **Transcutaneous electrical nerve stimulation (TENS)**

**B** Transcutaneous electrical nerve stimulation, in the form of strong burst mode with high frequency, should be used to provide short-term relief of osteoarthritis of the knee pain, reduce stiffness and improve knee range of motion, with effects lasting for 4 weeks.

*Grade B, Level 1+*

Transcutaneous electrical nerve stimulation (TENS) is the use of low frequency electrical current to modify and reduce the pain sensation. There is evidence for the use of TENS to provide short term relief of osteoarthritis of the knee pain with effects lasting for about 4 weeks after the last application.\(^{53,66,67}\) In particular, strong burst mode at high frequency (70 to 100 Hz) TENS is beneficial to decrease stiffness and improve range of motion.\(^{68}\)

7.5 **Interferential current therapy**

**B** Interferential current may be used to reduce pain and increase in knee range of motion for osteoarthritis of the knee patients.

*Grade B, Level 1+*

Interferential current therapy, another form of electrical stimulation similar to TENS, but consisting of medium frequency currents, can also reduce morning stiffness, improve knee range of motion and increase the pain threshold.\(^{69,70}\)

7.6 **Taping**

**A** Taping may be used to shift the patella medially and provide effective relief of pain in osteoarthritis of the knee.

*Grade A, Level 1++*

A prospective randomised study found that taping (leukoplast tapes) was efficacious in the management of pain and disability in patients with osteoarthritis of the knee.\(^{71}\) When performed correctly and combined with strengthening exercises, taping offers effective pain relief. There is evidence for the use of taping to shift the patella
medially to provide effective relief of pain in osteoarthritis of the knees.\textsuperscript{71,72}

7.7 Braces and wedges

\textbf{B} Lateral wedge insoles (tilt angle of 8.5 to 11 degrees) should be used to provide pain relief for osteoarthritis of the knee with medial osteoarthritis symptoms.

\textit{Grade B, Level 1+}

\textbf{B} Valgus knee brace and knee sleeves may be used to provide significant improvement in functional tasks and unloading of varus deformity.

\textit{Grade B, Level 1+}

Lateral wedge insoles\textsuperscript{73,74} provide significant pain relief for osteoarthritis of the knee with varus deformity, while protective knee sleeve\textsuperscript{75} and Valgus knee braces\textsuperscript{76} can provide significant improvement during functional tasks (stair climbing, 6-minute walk test) by providing improved stability, proprioception and mechanical re-alignment of knee mechanics.

7.8 Manual therapy

\textbf{A} Manual therapy applied to the knee together with an exercise programme may be used to improve knee function and pain relief for patients with osteoarthritis of the knee.

\textit{Grade A, Level 1+}

Manual therapy in the treatment of osteoarthritis of the knee involves the use of specific hands-on techniques applied to soft tissue and joint structures around the knee, for the purpose of improving tissue extensibility, increasing joint range of motion, encouraging normal joint-play, and achieving pain relief. Its use in the treatment of osteoarthritis of the knees is recommended in conjunction with an exercise programme for significant improvement in function and pain relief.\textsuperscript{77,78}
7.9 Other treatment modalities

- Thermal therapy, especially heat, has a long traditional and anecdotal history for the relief of pain, muscle soreness, tightness and it encourages muscle relaxation. Diathermy or deep heating of tissues and joints is commonly used to reduce pain in osteoarthritis of the knees, however there is only one study that reported significantly reduced pain after 30 sessions of Shortwave diathermy.\(^7^9\) Superficial heating with infra-red and red laser, twice daily over 10 days was found to result in reduction of 39% on pain scale with pain relief lasting for 4 months.\(^8^0\)

- Similarly ice therapy is also found to be statistically beneficial to reduce pain hence improve quadricep strength in patients with osteoarthritis of the knee.\(^8^1\)

7.10 Other alternative therapies

**Needle electro-acupuncture may be used as an adjunct for symptomatic relief of pain and improvement of knee function.**

*Grade A, Level 1++*

Acupuncture, specifically electro-acupuncture, a form of Traditional Chinese Medicine, is supported in the literature as an effective adjunct for symptomatic relief of pain and improvement in function (daily activities) in osteoarthritis of knee joint.\(^8^2,8^3\)

There is insufficient support for the use of magnetic bracelets and pulsed electromagnetic pulses for the treatment of pain and improvement of range of motion for osteoarthritis of the knee\(^8^4-8^6\), as most of these studies did not standardise the type of equipment used in the study.

This is only one randomised control trial study showing that *Tai Chi* can significantly reduce pain and improve WOMAC scores.\(^8^7\) However effects were not sustained after detraining. There is no evidence to suggest that Tui Na therapy can help patients with knee osteoarthritis.
Summary

The literature has shown a strong support for the use of physiotherapy modalities in the management of pain, reduction of swelling and improvement of physical function and fitness for patients with osteoarthritis. The treatment of patients with osteoarthritis of the knee pain, muscle weakness and stiffness should include a regular exercise regime, on land or in water, with sufficient dietary control to reduce weight if necessary. For pain relief, a combination of TENS, taping, bracing, manual therapy, heat, ice, laser and knee strengthening exercises are found to be effective for most patients with osteoarthritis of the knee.

Alternative therapies are not strongly supported by research studies, except for acupuncture, which may be useful as an adjunctive treatment for pain relief, together with the above-mentioned physiotherapy modalities.
8 Surgery

8.1 Introduction

A referral to the orthopaedic surgeon should be made when conservative management mentioned previously has failed.

Failure of treatment means that the patient did not have satisfactory improvement of pain, stability or function despite adequate conservative (non-pharmacological and pharmacological) treatment.

8.2 Diagnosis specific surgical options

1) Bi- or Tri- compartmental osteoarthritis

a) Total knee arthroplasty
   Generally for patients above 55 years old
   Survivorship: >90% (10 years)

b) Fusion can be considered in young active high demand patients, especially those with severe knee instability.

2) Medial compartment osteoarthritis

Options include tibia osteotomy or unicompartmental arthroplasty.

a) Proximal tibia osteotomy
   i. Indications: young and active patients with varus alignment
   ii. Prerequisites
       1. range of motion greater than 5° to 90°
       2. maintenance of some articular cartilage medially
       3. minimal involvement of lateral or patello-femoral compartments
       4. minimal instability or lateral subluxation
   iii. Survivorship:
       1. 90% (5 years), 65% (10 years)
b) Medial unicompartmental arthroplasty  
   i. Indications: less active patients  
   ii. Prerequisites  
      1. well localized medial compartment pain  
      2. minimal involvement of lateral or patello-femoral compartments  
      3. reasonable weight  
      4. functional anterior cruciate ligament  
   iii. Survivorship: 85% (10 years)  

c) Total knee arthroplasty  
   i. If patients not suitable for (a) or (b) above.  

3) Lateral compartment osteoarthritis  

a) Distal femoral varus osteotomy for young active patients  
b) Total knee arthroplasty if patients not suitable for (a)  
c) Lateral compartment unicompartmental arthroplasty.  

4) Isolated patellofemoral osteoarthritis  

a) Young and active  
   i. Tibial tubercle elevation with or without autologous chondrocyte implantation  
   ii. Patelllectomy  
b) Older and less active  
   i. Total knee arthroplasty  
   ii. Patellofemoral arthroplasty  
c) Other procedures  
   i. Lateral retinacular release with or without partial facetectomy.  

5) Role of arthroscopic debridement and lavage  

a) Indicated for patients with degenerative arthritis and mechanical symptoms. Presence of loose bodies or flaps of meniscus or cartilage that are causing mechanical symptoms, especially locking, catching, or giving way of the joint.  
b) Not indicated for patients without mechanical symptoms.
9 Cost-effectiveness Issues

**GPP** Pain medications are important in managing osteoarthritis symptoms and should be used concurrently with nutritional, physical, and educational interventions. Doctors should consider efficacy, adverse side effects, dosing frequency, and cost to the patient when recommending osteoarthritis treatments.

**C** For mild to moderate osteoarthritis pain, paracetamol is the drug of choice as it is cost-effective and has minimal side-effects. In treating moderate to severe osteoarthritis pain, the use of non-steroidal anti-inflammatory drugs and COX-2 specific inhibitors (for a patient who is at high risk of adverse upper gastrointestinal events) should be considered only if the patient is not responding to paracetamol.\(^{88}\)

**Grade C, Level 2+**

**C** For patients who have failed medical therapy and who are suitable for surgical interventions, both unicompartmental and total knee arthroplasty are cost effective in terms of quality of life gain.\(^{89-91}\)

**Grade C, Level 2+**
The following clinical quality indicators are proposed:

1. Knee pain and function should be assessed yearly.

2. Exercise in the form of a directed or supervised muscle strengthening or aerobic exercise program should have been prescribed at least once and reviewed at least once per year in ambulatory patients with no contraindication to exercise.

3. Weight should be measured yearly. Weight reduction should be advocated for patients with body mass index of >25 kg/m². Obese patients with body mass index >30 kg/m² should be referred to a medically-supervised weight reduction programme.

4. Activities of daily living should be assessed and physiotherapy assessment for assisted devices made should ADL be impaired.
References


Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category III (Self-Study) of the SMC Online CME System. Before you login to claim the CME point, we encourage you to evaluate whether you have mastered the key points in the Guidelines by completing this set of MCQs. This is an extension of the learning process and is not intended to “judge” your knowledge and is not compulsory. The answers can be found at the end of the questionnaire.

Instruction: Choose “True” or “False.”

1. A 60-year-old man who is a sports teacher has progressively worsening pain in his knees upon walking in the past 2 weeks. The features alerting the treating physician to investigate further:
   A) Nocturnal pain disturbing sleep
   B) Early morning stiffness lasting no more than 15 minutes
   C) ESR 45 mm/hour
   D) Lost of medial joint spaces noted in the radiographs of the knees

2. A 50-year-old woman complained of pain in various joints. The areas commonly affected by osteoarthritis:
   A) Elbow
   B) Knees
   C) Hips
   D) Metacarpophalangeal joints

3. A 70-year-old woman who is active and exercises regularly has progressively worsening pain in her knees upon walking in the past 2 weeks. She has hypertension and hyperlipidaemia and no other medical problems.
   A) Paracetamol or tramadol would be the first drugs of choice in the acute relief of pain.
   B) Selective cyclooxygenase inhibitors are very safe for acute relief of pain provided the duration of treatment is less than 1 week.
   C) NSAID are contraindicated only if she has a history
of peptic ulcer disease or renal impairment.

D) Systemic corticosteroids like oral prednisolone and
dexamethasone are recommended alternatives for the
acute relief of pain.

4. A 50-year-old man with osteoarthritis of the knees has a
history of periorbital swelling with diclofenac, naproxen
and indomethacin.

A) Paracetamol and tramadol are alternative
medications that may safely be used.

B) Topical diclofenac and piroxicam may also trigger
periorbital swelling in extremely sensitive
individuals.

C) Selective cycloxygenase inhibitors are possible
alternative treatments in NSAID sensitive
individuals.

D) Selective cycloxygenase inhibitors may also result in
periorbital swelling in some NSAID sensitive
individuals.

5. Regarding glucosamine in the treatment of osteoarthritis of
the knees:

A) There is clear evidence that long-term use of
glucosamine will cause insulin resistance and
glucose intolerance.

B) Glucosamine is able to retard structural progression
in osteoarthritis.

C) Glucosamine may be effective in improving pain and
function in some patients with knee osteoarthritis.

D) The optimal daily dose of glucosamine is 1500
mg/day.

E) Glucosamine should be given prophylactically to
athletes and those with a family history of
osteoarthritis as it is helpful in primary prevention of
osteoarthritis.

6. A 40-year-old lady with bilateral anterior knee pain was
found to have bilateral isolated patellofemoral
osteoarthritis. The initial treatment is

A) Arthroscopic lateral release

B) Tibial tubercle elevation
C) Physiotherapy and oral analgesia
D) Arthroscopic debridement

7. A 55-year-old woman weighing 74 kg complains of pain in both knees especially when walking down stairs and raising from a chair. Besides medication, other treatments
A) Hydrotherapy
B) Weight loss and exercise
C) Rest from walking and exercises
D) Electrical stimulation

8. A middle aged man who exercises 3 times a week, complains of pain in the knees during and after a run/jog. Advice to the patient is
A) Stop running until the pain is gone
B) Weight loss and exercise
C) Patella taping, knee bracing and exercise to align the knee during the run
D) Acupuncture

9. Regarding topical medications for osteoarthritis
A) Compared to placebo, topical NSAIDs have been shown to be more effective in providing short term symptomatic relief of pain in patients with osteoarthritis of the knees.
B) Topical NSAIDs are generally safe and have minor side effects only.
C) The use of topical capsaicin in osteoarthritis should be avoided because it has not been proven to be effective.
D) There is good evidence to support the use of topical glucosamine in the treatment of osteoarthritis.

10. Modalities used by physiotherapists to reduce pain and improve knee function in patients with osteoarthritis of the knees
A) Hydrotherapy
B) Exercise
C) Lateral wedge insoles and valgus knee brace
D) Electrical stimulation
### Answer

<p>| | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 A)</td>
<td>T</td>
<td>Pg 11</td>
<td>6 A)</td>
<td>F</td>
<td>Pg 30,31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 B)</td>
<td>F</td>
<td></td>
<td>6 B)</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 C)</td>
<td>T</td>
<td></td>
<td>6 C)</td>
<td>T</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 D)</td>
<td>F</td>
<td></td>
<td>6 D)</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 A)</td>
<td>F</td>
<td>Pg 12</td>
<td>7 A)</td>
<td>T</td>
<td>Pgs 24-26</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 B)</td>
<td>T</td>
<td></td>
<td>7 B)</td>
<td>T</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 C)</td>
<td>T</td>
<td></td>
<td>7 C)</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 D)</td>
<td>F</td>
<td></td>
<td>7 D)</td>
<td>T</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 A)</td>
<td>T</td>
<td>Pgs 13-15, 18</td>
<td>8 A)</td>
<td>F</td>
<td>Pgs 26,27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 B)</td>
<td>F</td>
<td></td>
<td>8 B)</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 C)</td>
<td>F</td>
<td></td>
<td>8 C)</td>
<td>T</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 D)</td>
<td>F</td>
<td></td>
<td>8 D)</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 A)</td>
<td>T</td>
<td>Pg 15</td>
<td>9 A)</td>
<td>T</td>
<td>Pg 23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 B)</td>
<td>T</td>
<td></td>
<td>9 B)</td>
<td>T</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 C)</td>
<td>T</td>
<td></td>
<td>9 C)</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 D)</td>
<td>T</td>
<td></td>
<td>9 D)</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 A)</td>
<td>F</td>
<td>Pgs 19,20</td>
<td>10 A)</td>
<td>T</td>
<td>Pgs 25-27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 B)</td>
<td>F</td>
<td></td>
<td>10 B)</td>
<td>T</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 C)</td>
<td>T</td>
<td></td>
<td>10 C)</td>
<td>T</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 D)</td>
<td>T</td>
<td></td>
<td>10 D)</td>
<td>T</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 E)</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Workgroup members**

The members of the workgroup, who were appointed in their personal professional capacity, are:

**Chairperson**

Dr Leong Keng Hong  
Leong Keng Hong Arthritis and Medical Clinic  
Gleneagles Medical Centre

**Members**

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
<th>Department</th>
<th>Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Lau Tang Ching</td>
<td>Consultant</td>
<td>Dept of Rheumatology, Allergy &amp; Immunology</td>
<td>Tan Tock Seng Hospital</td>
</tr>
<tr>
<td>Dr Thong Yu Hor Bernard</td>
<td>Consultant</td>
<td>Dept of Rheumatology, Allergy &amp; Immunology</td>
<td>Tan Tock Seng Hospital</td>
</tr>
<tr>
<td>Dr Eugene Lim</td>
<td></td>
<td>Elim Rheumatic Centre (Bone, Joint, Rheumatism)</td>
<td>Gleneagles Medical Centre</td>
</tr>
<tr>
<td>A/Prof Fong Kok Yong</td>
<td>Senior Consultant</td>
<td>Dept of Rheumatology &amp; Immunology</td>
<td>Singapore General Hospital</td>
</tr>
<tr>
<td>Dr Koh Wei Howe</td>
<td>Consultant</td>
<td>Koh Wei Howe Arthritis &amp; Rheumatism Medical Clinic</td>
<td>Mt Elizabeth Medical Centre</td>
</tr>
<tr>
<td>Dr Ng Swee Cheng</td>
<td>Senior Consultant</td>
<td>Dept of Medicine</td>
<td>Alexandra Hospital</td>
</tr>
<tr>
<td>Dr Lo Ngai Nung</td>
<td>Senior Consultant &amp; Director</td>
<td>Adult Reconstruction Service and Deputy Head, Dept of Orthopaedic Surgery</td>
<td>Singapore General Hospital</td>
</tr>
<tr>
<td>Dr Celia Tan</td>
<td>Assistant Director</td>
<td>Allied Health Division</td>
<td>Singapore General Hospital</td>
</tr>
<tr>
<td>Dr Kong Kok Ooi</td>
<td>Consultant</td>
<td>Dept of Rheumatology, Allergy &amp; Immunology</td>
<td>Tan Tock Seng Hospital</td>
</tr>
<tr>
<td>Dr Adrian Ee Guan Liang</td>
<td>Director, Clinical Services</td>
<td>Div of Rheumatology</td>
<td>SingHealth Polyclinics</td>
</tr>
<tr>
<td>Dr Sheila Vasoo Sushilan</td>
<td>Consultant</td>
<td>Dept of Medicine, Div of Rheumatology</td>
<td>National University Hospital</td>
</tr>
<tr>
<td>Dr Tan Chyn Hong</td>
<td>Registrar</td>
<td>Dept of Orthopaedic Surgery</td>
<td>National University Hospital</td>
</tr>
</tbody>
</table>
Subsidiary editors:

Dr Pwee Keng Ho
Deputy Director (Health Technology Assessment)
Health Services Research & Evaluation Division
Ministry of Health

Dr Rajni Gupta
Executive (Health Technology Assessment)
Health Services Research & Evaluation Division
Ministry of Health

Acknowledgement:

Recommendations and grading of articles in chapter 7 were contributed by the following Physiotherapists:

Adon Chan | Ravi Chandran Visvanathan
Singapore General Hospital | Hallmark Physiotherapy Pte Ltd

Gigi Kuwan | Sairamkumar Balachandran
Tan Tock Seng Hospital | Back and Neck Centre

Jackson Yong | Shawn Soh
EconHealth Care | Rehab Asia

Kavita Bhojwani | Upendranath Reddy Potturi
Singapore General Hospital | Institute of Mental Health

Ong Hwee Kuan | Wong Mei Ching
Singapore General Hospital | Singapore General Hospital

Rachel Soh | Celia Tan
Tan Tock Seng Hospital | Singapore General Hospital
Acknowledgement:

Dr Edwin Chan Shih-Yen
Head of Evidence-Based Medicine
and
Director of the Singapore Branch, Australasian Cochrane Centre
Clinical Trials & Epidemiology Research Unit

Dr Miny Samuel
Senior Evidence-Based Medicine Analyst
and
Co-Director of the Singapore Branch, Australasian Cochrane Centre
Clinical Trials & Epidemiology Research Unit