

CLINICAL PRACTICE GUIDELINES

MOH/P/PAK/273.13(GU)

Management Of Osteoarthritis

(Second Edition)



Ministry of Health
Malaysia



Malaysian Society of
Rheumatology



Academy of
Medicine Malaysia

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<http://www.msr.my>

STATEMENT OF INTENT

These clinical practice guidelines (CPG) are meant to be guides for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not necessarily guarantee the best outcome in every case. Every healthcare provider is responsible for the management of his/her unique patient based on the clinical picture presented by the patient and the management options available locally.

These guidelines were issued in 2013 and will be reviewed in 2017 or sooner if new evidence becomes available.

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LEVELS OF EVIDENCE	
Level	Study design
I	Evidence from at least one properly randomised controlled trial
II -1	Evidence obtained from well-designed controlled trials without randomisation
II -2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or group
II -3	Evidence from multiple time series with or without intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence
III	Opinions of respected authorities based on clinical experience; descriptive studies and case reports; or reports of expert committees

SOURCE: US / CANADIAN PREVENTIVE SERVICES TASK FORCE

GRADES OF RECOMMENDATION	
A	At least one meta analysis, systematic review, or RCT, or evidence rated as good and directly applicable to the target population
B	Evidence from well conducted clinical trials, directly applicable to the target population, and demonstrating overall consistency of results; or evidence extrapolated from meta analysis, systematic review, or RCT
C	Evidence from expert committee reports, or opinions and /or clinical experiences of respected authorities; indicates absence of directly applicable clinical studies of good quality

SOURCE: MODIFIED FROM THE SCOTTISH INTERCOLLEGiate GUIDELINES NETWORK (SIGN)

Note: The grades of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

GUIDELINES DEVELOPMENT AND OBJECTIVES

GUIDELINES DEVELOPMENT

The members of the Development Group (DG) for these Clinical Practice Guidelines (CPG) were from the Ministry of Health (MoH) and Ministry of Higher Education. There was active involvement of a multidisciplinary Review Committee (RC) during the process of the CPG development.

The previous CPG entitled Management of Osteoarthritis 2002 was used as the basis for the development of the present guidelines. A literature search was carried out using the following electronic databases: Guidelines International Network (G-I-N); World Health Organization (WHO), Medline via Ovid, Pubmed, Cochrane Database of Systemic Reviews (CDSR) and International Health Technology Assessment websites (refer to **Appendix 1 for Example of Search Strategy**). The search was limited to literature published in the last ten years, on humans and in English. If the evidence was insufficient, the period of publication was extended for another ten years. In addition, the reference lists of all retrieved literature and guidelines were searched to further identify relevant studies. Experts in the field were also contacted to identify further studies. All searches were conducted from 27 October 2011 to 27 September 2012. Literature searches were repeated for all clinical questions at the end of the CPG development process allowing any relevant papers published before 31 July 2013 to be included. Future CPG updates will consider evidence published after this cut-off date. The details of the search strategy can be obtained upon request from the CPG Secretariat.

Reference was also made to other CPG on Osteoarthritis such as The National Collaborating Centre for Chronic Conditions (2008) & National Institute for Health and Clinical Excellence (2008) – Osteoarthritis: National Clinical Guideline for Care and Management in Adults. The CPG was evaluated using the Appraisal of Guidelines for Research and Evaluation (AGREE) II prior to them being used as references.

A total of 14 clinical questions were developed under different sections. Members of the DG were assigned individual questions within these sections. (Refer to **Appendix 2 for Clinical Questions**) The DG members met 28 times throughout the development of these guidelines. All literature retrieved were appraised by at least two DG members using Critical Appraisal Skill Programme checklist, presented in evidence tables and further discussed in each DG meetings. All statements and recommendations formulated after that were agreed

upon by both the DG and RC. Where evidence was insufficient, the recommendations were made by consensus of the DG and RC. These CPG are based largely on the findings of systematic reviews, meta-analyses and clinical trials, with local practices taken into consideration.

The literature used in these guidelines were graded using the US/Canadian Preventive Services Task Force Level of Evidence (2001), while the grading of recommendation was modified from grades of recommendation of the Scottish Intercollegiate Guidelines Network.

On completion, the draft guidelines were sent for review by external reviewers. It was also posted on the MoH Malaysia official website for feedback from any interested parties. The draft was finally presented to the Technical Advisory Committee for CPG, and the HTA and CPG Council MoH Malaysia for review and approval.

OBJECTIVES

The aim of these guidelines is to assist clinicians and other healthcare providers in making evidence-based decisions about appropriate management and treatment of Osteoarthritis (OA) specifically:-

- i. Early recognition and diagnosis,
- ii. Management,
- iii. Prevention and referral.

CLINICAL QUESTIONS

Refer to Appendix 2

TARGET POPULATION

Adults with OA

TARGET GROUP/USER

This document is intended to guide healthcare professionals and relevant stakeholders in all healthcare settings including:-

- | | |
|----------------------------------|--------------------------------------------------------|
| i. Doctors | iv. Medical students and healthcare trainees |
| ii. Pharmacists | v. Professional societies |
| iii. Allied health professionals | vi. Patients and carers/non-governmental organisations |

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Outpatient, inpatient and community settings

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The draft guidelines were reviewed by a panel of experts from both public and private sectors. They were asked to comment primarily on the comprehensiveness and accuracy of the interpretation of evidence supporting the recommendations in the guidelines.

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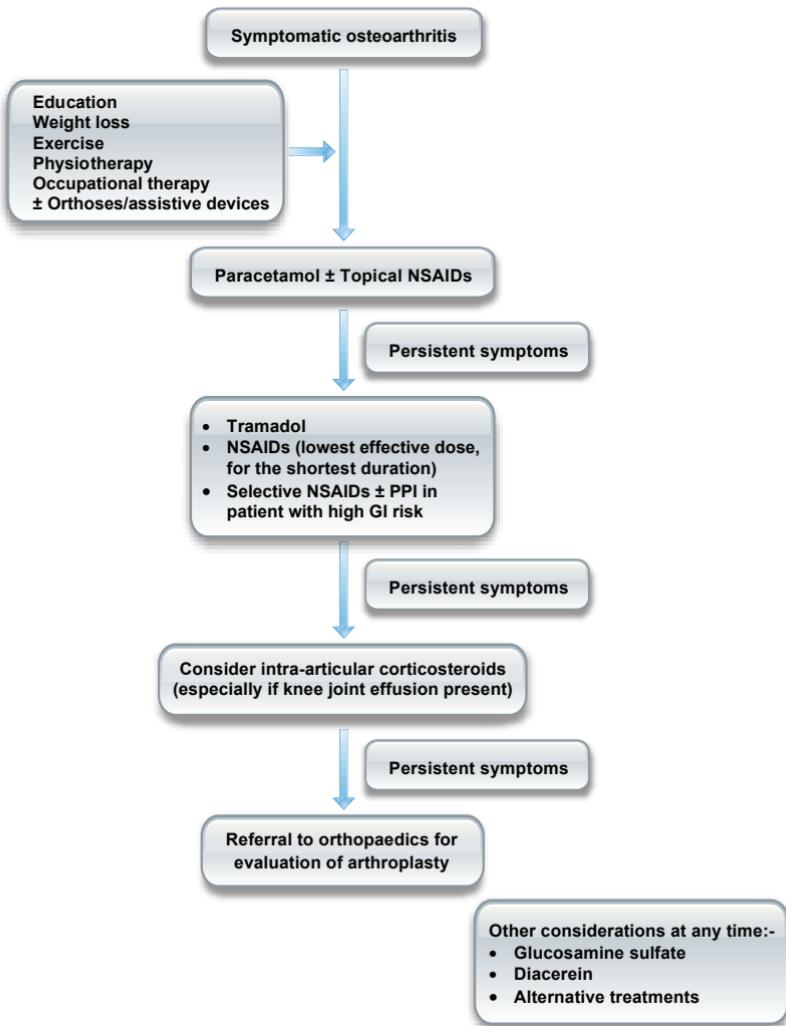
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ALGORITHM ON MANAGEMENT OF KNEE & HIP OSTEOARTHRITIS



Refer to **Appendix 9** for checklist on management of OA.

1. INTRODUCTION

Osteoarthritis (OA) is a progressive joint disease due to failure in repair of joint damage. This may arise as a result of biomechanical, biochemical and/or genetic factors. The process may involve one or multiple joints.

In the Global Burden of Disease 2010 Study, it was estimated that 251 million people suffered from knee OA worldwide. Musculoskeletal diseases which included OA was the second greatest cause of disability as measured by years lived with disability.¹

OA is prevalent in the ageing population. In 2010, WHO estimated that 524 million people were aged 65 or older and this number is expected to triple which represents 16% of the world's population by 2050.²

In view of its potential public health burden and emergence of more recent advances in the management of OA, it is timely to update the CPG on Management of OA 2002 using evidence-based methodology. It is hoped that this CPG serves as a useful guide in the daily practice of health care providers in various disciplines from the public, academic and private sectors.

2. EPIDEMIOLOGY & RISK FACTORS

2.1 Epidemiology

There is wide variability of OA prevalence depending on age, gender of population studied and case definition used. The most commonly used case definition is radiographic OA, symptomatic OA and self-reported OA. Symptomatic OA is defined as the presence of the radiographic features of OA in combination with symptoms attributable to it. Not all individuals with radiographic OA have concomitant symptoms; thus radiographic OA has the highest prevalence.^{3, level III}

a. Hand OA

In the Framingham Osteoarthritis Hand OA study, the mean baseline age was 58.9 years. The age-standardised prevalence of hand OA was higher in women (44.2%) than men (37.7%). The prevalence was even higher in erosive (9.9% vs 3.3%) and symptomatic (15.9% vs 8.2%) hand OA. Majority of women (96.4%) and men (91.4%) with hand OA at baseline showed progression at 9-year follow up.^{4, level II-2}

b. Hip OA

The prevalence of symptomatic hip OA in United States of America (USA) was 9.2% among adults age >45 with a slight female preponderance.^{5, level III} In another study, the crude prevalence of radiographic hip OA in Chinese aged 60 - 89 years was 0.9% in women and 1.1% in men. Hip OA was 80 - 90% less frequent in the Chinese than white persons in the USA.^{6, level III}

c. Knee OA

In the Johnston County OA Project of USA, the lifetime risk of developing symptomatic knee OA in at least one knee was 44.7% (95% CI 40.0% to 49.3%) by age 85 years. The lifetime risk is higher in those with history of knee injury and increased BMI.^{7, level II-2}

The prevalence of symptomatic knee OA was 4.9% among adults age >26 years in the Framingham study,^{5, level III} 16.7% among adults age >45 in the Johnston County study,^{7, level II-2} and 12.1% among adults aged >60 in the NHANES III study.^{5, level III}

In the Beijing Osteoarthritis Study of persons aged 60 years and above, the prevalence of radiographic knee OA was 42.8% in women and

21.5% in men. Symptomatic knee OA occurred in 15.0% of women and 5.6% of men. Compared with women of the same age in Framingham, women in Beijing had a higher prevalence of radiographic knee OA (prevalence ratio=1.45, 95% CI 1.31 to 1.60) and of symptomatic knee OA (prevalence ratio=1.43, 95% CI 1.16 to 1.75). The prevalence of knee OA in Chinese men was similar to that in their white USA counterparts (prevalence ratio of 0.90 for radiographic OA and 1.02 for symptomatic OA). Possible explanations for these differences range from genetic differences to heavy physical activity among Chinese.^{8, level III}

In the Community Orientated Program for the control of Rheumatic Disease (COPCORD) study in Malaysia which was initiated by ILAR and WHO, 9.3% of adult Malaysians had knee pain and more than half of those examined had clinical evidence of OA. The prevalence ranged from 1.1% to 5.6% in the various ethnic groups. This prevalence is likely to be an underestimate as the study only included those with pain in the past week and not all subjects with knee pain attended the subsequent medical examination. Hip pain was less common, with only 2.2% of the study population affected.^{9, level III}

To better understand the burden of disease, further epidemiological studies are needed to obtain the prevalence and incidence of OA in Malaysia.

2.2 Risk Factors

Multiple risk factors have been associated with the development and progression of OA. The risk factors can be categorised as the following:-

a. Non-modifiable

- Advancing age^{10, level II-2}
- Female [OR=1.8, 95% CI 1.3 to 2.5 (case-control studies), OR=1.9, 95% CI 1.6 to 2.3 (cohort studies)]^{10, level II-2}
- Genetic influence on hand and knee OA in women ranges from 39% to 65% ($p<0.001$)^{11, level II-2}
- Presence of Heberden's nodes in hand OA increase the risk for future knee OA, OR=1.4, 95% CI 1.1 to 1.8^{10, level II-2}

b. Modifiable

- Body mass index (BMI)^{10, level II-2}
 - overweight (BMI 25 to 30 kg/m²) [OR=2.6, 95% CI 2.2 to 3.0 (case-control studies), OR=2.0, 95% CI 1.8 to 2.1 (cohort studies)]

- obese (BMI >30 kg/m²) [OR=5.5, 95% CI 4.3 to 7.1 (case-control studies), OR=2.4, 95% CI 2.1 to 2.6 (cohort studies)]
- Previous knee injury [OR=4.7, 95% CI 3.5 to 6.4 (case-control studies), OR=2.8, 95% CI 1.8 to 4.2 (cohort studies)]¹⁰, level II-2
- Malalignment contributes to the progression of knee OA, however the results are mixed on whether it contributes to the incidence of the disease¹², level II-2

Identifying the modifiable risk factors mentioned above may help in prevention of OA and its progression.

3. CLASSIFICATION

There are various methods of classifying OA. The disease can be classified by the joint involved such as hand, hip and knee. It can also be classified by aetiology as shown below:-

a. Primary or Idiopathic

Primary OA includes generalised OA, a condition associated with Heberden's nodes and polyarticular disease. It occurs especially in the hand, with a female preponderance and has a high prevalence in first degree relatives.¹³

b. Secondary

- i. Metabolic such as acromegaly, haemachromatosis and chondrocalcinosis
- ii. Anatomic such as slipped femoral epiphysis, Legg-Perthes disease, congenital dislocation of the hip, leg length inequality, hypermobility syndromes and avascular necrosis
- iii. Trauma such as joint injury and fracture through a joint or osteonecrosis
- iv. Inflammatory such as rheumatoid arthritis, psoriatic arthropathy and septic arthritis

4. DIAGNOSIS

OA is frequently diagnosed by an overall clinical impression. However, there are diagnostic criteria by American College of Rheumatology and European League Against Rheumatism which can be used as a guide.

4.1 Clinical Features

Clinical features of OA depend on the extent of the disease. Patients may have radiological evidence of OA without clinical symptoms.

Symptoms of OA include:-

- i. Joint pain - Pain is the most common presenting complaint. It is usually insidious in onset, of variable intensity through the day, may be intermittent and relapsing, increased by joint use and impact and relieved by rest. Night pain may occur in severe OA. Refer to **Appendix 3** for possible mechanisms of pain in OA.
- ii. Stiffness - Stiffness may be defined as a sensation of tightening of the involved joint that usually occurs after inactivity, such as in the morning or when arising after sitting for a prolonged period. In contrast to inflammatory arthritis such as rheumatoid arthritis, stiffness in OA usually lasts only a few minutes and almost always less than 30 minutes.
- iii. Swelling - There may be fullness and swelling of the joint with or without associated warmth and loss of function.
- iv. Gait disturbance - OA of weight-bearing joints if significant is associated with gait disturbance, increased muscle spasm and a reduced quality of life. An affected knee or hip can produce a prominent limp. Impaired function of a weight-bearing joint will cause added stress on the contralateral weight-bearing joints, for example a patient with impaired right knee function and pain will have difficulty with the left hip and vice versa.
- v. Bony swelling - In hand OA, hypertrophic bone formation in the interphalangeal joint may result in reduced dexterity and difficulty in performing fine movements such as sewing. OA of the first carpometacarpal (CMC) joint may result in writing difficulties.
- vi. Loss of muscle bulk - Inactivity secondary to pain, for example in knee OA, may lead to significant weakness and loss of quadriceps muscle bulk.
- vii. Limb deformity - Enlargement of the knee joints may occur resulting in increasing deformity of the knees, such as 'knock knees' (valgus) or 'bowing' (varus).
- viii. Clicking or grinding sensation - There may be a clicking or grinding sensation with joint motion resulting in discomfort or pain.

- ix. Instability - The sensation of instability in the knee or hip may cause the patient to seek assistance in ambulation, such as using a cane or crutch.

Signs of OA include:-

- i. Gait - OA of weight-bearing joints, for example the hip, knee, ankle and/or foot leads to altered gait patterns.
- ii. Tenderness - Tenderness of soft tissues such as synovium, capsule, bursae and periarticular muscles, or periosteum at the insertion of capsule or ligaments may be present.
- iii. Joint swelling - Enlargement of the joint may be due to synovitis, synovial effusion or bone enlargement.
- iv. Crepitus - Grinding, crunching or cracking may be present over a joint with OA.
- v. Limitation of motion - There may be loss of function with reduced motion as a result of synovitis/effusion or periarticular soft tissue contractures.
- vi. Deformity - Deformity may be present in any of the peripheral joints with OA. However, it is most notable in the interphalangeal joints of the hands with enlargement and subluxation, the first CMC joint, the knees (varus/valgus) or the hips (shortened extremity). Deformity may be associated with joint fusion or instability.

4.2 Diagnostic Criteria

The diagnostic criteria for classification of OA are based on the American College of Rheumatology (ACR) criteria. These criteria were formulated according to the affected anatomic areas which include the knee, hand and hip as below:-

a. Hand OA

Table 1. The Diagnostic Criteria for Classification of Idiopathic OA of the Hand Based on the American College of Rheumatology 1990 Criteria¹⁴, level III

Diagnosis Criteria	Clinical only 1,2,3 + 4a or 4b
1	Hand pain, aching or stiffness
2	Hard tissue enlargement of ≥2 of 10 selected joints (2 nd and 3 rd DIP, 2 nd and 3 rd PIP, 1 st CMC joints of both hands)
3	Fewer than 3 swollen MCP joints
4a	Hard tissue enlargement of ≥2 of DIP joints OR
4b	Deformity of ≥2 of 10 selected joints
Sensitivity	92%
Specificity	98%

DIP=distal interphalangeal MCP=metacarpophalangeal PIP=proximal interphalangeal CMC=carpometacarpal

b. Hip OA

Table 2. The Diagnostic Criteria for Classification of Idiopathic OA of the Hip Based on the American College of Rheumatology 1991 Criteria¹⁵, level III

Diagnosis Criteria	Clinical, Laboratory and Radiographic
	Must have hip pain + at least 2 from 3 of the following
1	ESR <20 mm/hr
2	Femoral and acetabular osteophytes on X-ray
3	Axial joint space narrowing on X-ray
Sensitivity	89%
Specificity	91%

c. Knee OA

Table 3. The Diagnostic Criteria for Classification of Idiopathic OA of the Knee Based on the American College of Rheumatology 1986 Criteria¹⁶, level III

Diagnosis Criteria	Clinical and laboratory	Clinical and radiographic	Clinical only
Must have	Knee pain + At least 5 of 9 of the following	Knee pain + Osteophytes on x-ray + At least 1 of 3 of the following	Knee pain + At least 3 of 6 of the following
1	Age >50 years	Age >50 years	Age >50 years
2	Stiffness <30 min	Stiffness <30 min	Stiffness <30 min
3	Crepitus	Crepitus	Crepitus
4	Bony tenderness		Bony tenderness
5	Bony enlargement		Bony enlargement
6	No palpable warmth		No palpable warmth
7	ESR <40		
8	RF <1: 40		
9	SF OA		
Sensitivity	92%	91%	95%
Specificity	75%	86%	69% (if 3/6) 84% 89% (if 4/6)

ESR=erythrocyte sedimentation rate

RF=rheumatoid factor

SF OA=synovial fluid signs of OA (clear, viscous, or white blood cell count <2,000/mm³)

Knee OA can also be diagnosed using evidence-based recommendations by European League Against Rheumatism (EULAR) as shown in **Figure 1**.¹⁷, level III

- background risk (the population prevalence of knee OA)
- risk factors (such as age, gender, BMI and occupation)
- symptoms (persistent knee pain, brief morning stiffness and functional limitation)
- physical examination (crepitus, restricted movement and bony enlargement)
- plain radiographs as an adjunct

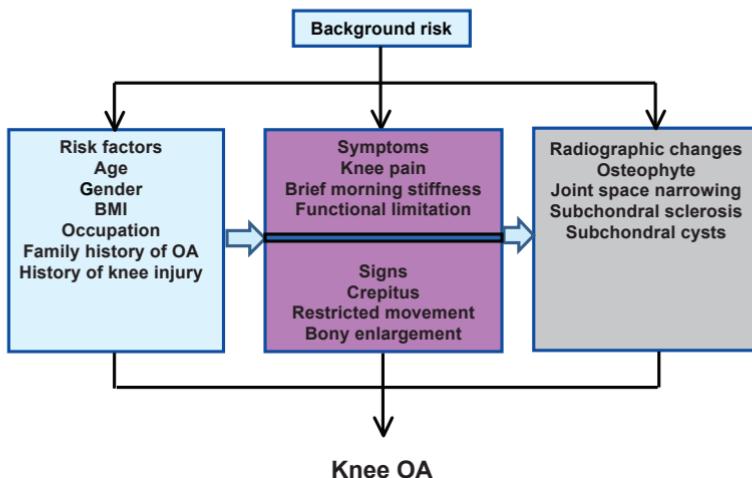


Figure 1. Diagnosis of Knee OA

5. INVESTIGATIONS

Diagnosis of OA is mainly clinical. Blood investigations and synovial fluid analysis are seldom required except to exclude other diagnosis such as septic, inflammatory and crystal arthropathy. There are various imaging techniques available now; however plain radiography is still the standard imaging for assessment of OA.

5.1 Laboratory Investigations

There are no specific laboratory investigations for diagnosis of OA. Inflammatory markers (ESR, CRP) are likely to be normal or only mildly elevated. Synovial fluid analysis is essentially normal in OA. Refer to **Table 4** for interpretation of synovial fluid analysis.

Table 4. Categories of Synovial Fluid Based upon Clinical and Laboratory Findings

Measure	Normal	Noninflammatory	Inflammatory	Septic	Haemorrhagic
Volume, mL (knee)	<3.5	Often >3.5	Often >3.5	Often >3.5	Usually >3.5
Clarity	Transparent	Transparent	Translucent opaque	Opaque	Bloody
Colour	Clear	Yellow	Yellow to opalescent	Yellow to green	Red
Viscosity	High	High	Low	Variable	Variable
WBC, per mm ³	<200	200-2,000	2,000-10,000	>100,000*	200-2,000
PMNs, percent	<25	<25	≥50	≥75	50-75
Culture	Negative	Negative	Negative	Often positive	Negative
Total protein, g/dL	1-2	1-3	3-5	3-5	4-6
LDH (compared to levels in blood)	Very low	Very low	High	Variable	Similar
Glucose, mg/dL	Nearly equal to blood	Nearly equal to blood	>25, much lower than blood	>25, much lower than blood	Nearly equal to blood

Adapted: 2013 UpToDate, Graphic 76506 version 2069.0 (available at <http://www.uptodate.com>)

5.2 Imaging

Plain radiography of the affected joint may be useful to support the diagnosis and assess severity of OA. When radiography is required in hip and knee OA, it should be done in weight bearing position (AP, standing). **Figure 2** and **3** shows an example of an osteoarthritic knee and hip respectively.



Figure 2. Knee Osteoarthritis - Anteroposterior (AP) Standing View



Figure 3. Hip Osteoarthritis - Anteroposterior (AP) Standing View

The Kellgren-Lawrence grading system is the most widely used radiological classification to identify and grade OA (refer to **Table 5**).

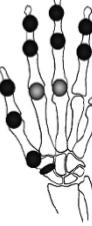
Table 5. Kellgren-Lawrence Grading System

Grade	Description
Grade I	Doubtful narrowing of the joint space, possible osteophytic lipping
Grade II	Definite osteophytes, possible narrowing of the joint space
Grade III	Moderate multiple osteophytes, definite joint space narrowing, some sclerosis, possible deformity of bone ends
Grade IV	Large osteophytes, marked joint space narrowing, severe sclerosis and definite bony end deformity.

Adapted: KELLGREN JH, LAWRENCE JS. Radiological assessment of osteo-arthritis. Ann Rheum Dis. 1957 Dec; 16(4):494-502.

In hand OA, plain radiography may also be useful to distinguish between various types of arthritis as shown in **Table 6**.

Table 6. Radiographic Changes of Interphalangeal Joints and Target Sites Involvement of OA and Other Arthritis

	Osteoarthritis	Erosive OA	Psoriatic Arthritis	Rheumatoid Arthritis
X-Ray changes	 Focal narrowing, marginal osteophyte, sclerosis, osteochondral bodies	 Subchondral erosion	 Proliferative marginal erosion, retained or increase bone density	 Non-proliferative marginal erosion, osteopenia
Target sites	 ● Common	 ● Uncommon	 ● Common	 ● Common

● Common

● Uncommon

Classical features of OA on plain radiograph includes:-

- narrowed joint space
- subchondral bone sclerosis
- osteophytes
- subchondral cysts

In addition to the above findings, centrally located erosions with osteophyte formation in the interphalangeal joints of the hand (gull-wing appearance) may occur (refer to **Figure 4** and **Figure 5**).



Figure 4. Gull-wing Appearance



Figure 5. Erosion with Osteophytes

Other imaging modalities such as magnetic resonance imaging and musculoskeletal ultrasonography (US) are seldom indicated for diagnosis of OA. However, US may be useful in early arthritis of the hands as it allows direct visualisation and quantification of cartilage.^{18, level III} In addition, US may demonstrate synovial inflammation in symptomatic OA of the hands and knees.^{19, level III; 20, level II-2; 21, level III}

Recommendation 1

- Osteoarthritis should be diagnosed clinically. (**Grade C**)
 - Plain radiographs may be used to support the diagnosis. (**Grade C**)
 - Laboratory investigations may be done to exclude other inflammatory joint diseases. (**Grade C**)

6. MANAGEMENT

The management of OA involves a multidisciplinary approach with the aim to relieve symptoms and improve joint function. It involves non-pharmacological and pharmacological treatment. Refer to **Appendix 9** for checklist on management of OA.

6.1 Non-Pharmacological Treatment

a. *Education*

Patient education is an important non-pharmacological approach in the management of OA. There are various types of patient education programmes and they have to be tailored according to the individual needs, goals and functional capabilities. It should include information of the diagnosis, nature of the disease, therapeutic options and the importance of ongoing patient participation in the disease management.^{22 - 25, level I} Patients who have an understanding of the disease tend to cope better and report less pain.²⁶ The most important goal is to instill a positive attitude.

Recommendation 2

- Patient education should form an integral part of osteoarthritis management. (**Grade A**)

b. *Lifestyle Modification*

Lifestyle medicine is defined as the application of environmental, behavioural, medical and motivational principles to the management of lifestyle related health problems.^{27, level III}

Lifestyle modification involves initiating and maintaining lifestyle changes. In hip and knee OA, behavioural changes focus on weight reduction and physical activity or exercise.

i. **Weight Reduction**

Obesity is an important modifiable risk factor for the development and progression of knee OA. Weight reduction is beneficial in pain reduction and improvement of function.^{28 - 30, level I} In a RCT done by Messier et al., each unit of weight loss will result in 4-fold reduction in the load exerted on the knee per step during daily activities.^{31, level I} There is no evidence available to support the effect of weight loss in hip OA.³²

Recommendation 3

- Weight reduction should be emphasised in the management of patients with knee osteoarthritis and who are overweight. (**Grade A**)

ii. Physical Activity

Exercise is effective in reducing pain in hip and knee OA. The frequency, intensity, duration and rate of progression of exercise can vary. The amount and intensity of exercise required is uncertain. In order to improve adherence, the following are suggested:-

- i. Individualised exercise programme
- ii. Graded type activity
- iii. Amount of activity based on personal goal setting
- iv. Feedback on progress
- v. Appropriate positive reinforcement
- vi. Problem solving skills incorporated

The EULAR 2013 Recommendations on the Non-Pharmacologic Treatment for Hip and Knee OA recommends that the intensity and duration of exercise should increase over time.³²

In hip and knee OA, pacing of activities and/or integrating Activities of Daily Living (ADL) as part of the exercise regime is more effective than usual care but not comparable to standardised exercise.³²

In knee OA, aerobic training (walking) is effective in reducing pain (ES=0.48, 95% CI 01.13 to 0.43) and improving physical function (ES=0.35, 95% CI 0.11 to 0.58).^{33, level I} The evidence for mixed exercise programmes, including strengthening, aerobic and flexibility components, in patients with knee OA is conflicting. One type of exercise has not been shown to be better than another (strength, aerobic or mixed exercises).³²

Regular non-competitive exercise does not exacerbate OA nor increase the likelihood of requiring joint replacement.

c. Physiotherapy

Physiotherapy can improve muscle strength, balance, coordination and joint mobility. It should be started as soon as possible to improve pain and physical capacity.

i. Exercise

Exercise programmes should be individualised while taking into consideration patient's preference and ability to perform the activities.

Land-based exercises include joint range of movement (ROM), muscle strengthening and low impact aerobic exercises. They should be supervised and done regularly (refer to **Appendix 4** and **Appendix 5**). Such exercise has short term benefits in reducing pain ($SMD = -0.40$, 95% CI -0.50 to -0.30) and improving physical function ($SMD = -0.37$, 95% CI -0.49 to -0.25) in knee OA.^{33, level I} However in hip OA, the benefit is only seen in pain reduction ($SMD = -0.38$, 95% CI -0.67 to -0.09) but not in physical function ($SMD = -0.10$, 95% CI -0.51 to 0.32).^{34, level I}

Aquatic exercise may be advantageous for OA patients. A Cochrane SR showed improvement in pain ($SMD = 0.19$, 95% CI 0.04 to 0.35) and quality of life ($SMD = 0.32$, 95% CI 0.03 to 0.61) for three months only in hip and knee OA. However, there was no statistically significant difference on walking ability.^{35, level I}

In the same review, aquatic exercise was better than land-based exercises in reducing pain in knee OA ($SMD = 0.86$, 95% CI 0.25 to 1.47). However, there was no effect on walking ability and stiffness.^{35, level I}

ii. Transcutaneous Electrostimulation (TENS)

There is a lack of evidence to support the use of transcutaneous electrostimulation for knee OA from the most recent Cochrane SR.^{36, level I} However, the ACR 2012 recommends the use of TENS for patients with chronic moderate to severe pain who are not suitable for total knee arthroplasty.³⁷

iii. Thermotherapy

Thermotherapy is commonly used in physical rehabilitation for OA patients. ACR recommends the use of thermal agents for hip and knee OA in combination with exercise supervised by a physiotherapist.³⁷

A SR showed that cold pack usage did not show a significant effect in pain reduction in knee OA ($WMD = -1.60$, 95% CI -4.53 to 1.33).^{38, level I}

iv. Therapeutic Ultrasound

Therapeutic ultrasound with high frequency vibrations is a modality used for pain relief in patients with hip and knee OA. However, in a Cochrane SR, the effectiveness of this modality in pain reduction and function was inconclusive.^{39, level I}

Recommendation 4

- Exercise programmes in hip and knee osteoarthritis must be individualised, supervised and done regularly. (**Grade C**)
- Land-based or aquatic exercise may be used for short-term benefit in osteoarthritis. (**Grade A**)

d. Occupational Therapy

Occupational therapy aims to improve health, prevent disability and help individuals to achieve their optimum functional level and independence in performing ADL.

The evidence suggests that people with pain, difficulty and frustration in performing daily activities and work tasks should be referred early to an occupational therapist for splinting, joint protection training and assistive device provision.⁴⁰

A NICE-commissioned CPG recommends that assistive devices such as walking sticks and tap turners should be considered as adjuncts to core treatment in OA patients with specific ADL problems.⁴⁰ The height of the walking stick handle should be at the wrist level when the user is standing. It is important to prescribe appropriate assistive device with proper training to the patients (refer to **Appendix 6**).

Joint protection and home exercises (JPE) are used in the treatment of hand OA. JPE increases grip strength significantly by 25% ($p<0.0005$) and global hand function by 65% ($p<0.05$).^{41, level I} Refer to **Appendix 7** for **Joint Protection Principles**. Thumb splints can help to reduce pain in the thumb and improve hand function.⁴⁰ Splinting and Joint Protection programme in hand OA can give significant decreases in pain and stiffness, and improvements in daily activities ($p<0.05$).^{42, level I} However, there is no evidence to support splinting in knee OA.

In a RCT, activity modification or instruction in ADL improved pain (MD= -3.21, 95 % CI -3.45 to -0.70) at 6 weeks.^{43, level I} Activity modification in performing ADL may be helpful in maintaining proper posture and thus reduce pain and disability (refer to **Appendix 7**).

Rest and relaxation may help in pain control. The beneficial therapies are:-

- Jacobson relaxation: improves pain at end of 8-week treatment ($p<0.05$) but the benefit is not sustained.^{44, level I} Jacobson's training procedure involves tensing and relaxing of muscles alternately, with the intent of developing awareness of the difference. The technique starts from the arm to face working downwards to the shoulders, chest, abdomen, legs and ends with the whole body in complete relaxation. The whole cycle can be performed under 20 minutes.
- Music therapy: improves pain at day 1, day 7 and at 2 weeks (end of treatment) (all $p=0.001$)^{45, level I}
- Guided Imagery Relaxation (GIR): increases Health Related Quality of Life in women with OA ($p=0.023$)^{46, level I}

Recommendation 5

- Early referral to occupational therapy may be considered for pain relief and improvement in activities of daily living in osteoarthritis. **(Grade A)**

e. Orthoses

Orthoses are defined as any medical device added to a person's body to support, align, position, immobilise, prevent or correct deformity, assist weak muscles or improve function. In knee OA, the general purpose is to decrease pain and improve physical function.

Walking shoes with neutral, contoured orthoses reduce pain and stiffness, and improve function in knee OA at one year ($p<0.001$).^{47, level I}

Knee braces for medial, lateral or patella-femoral OA have not been shown to reduce pain, improve function or quality of life, even though they are widely used.^{48 - 49, level I}

There is insufficient evidence to recommend the use of orthoses in hip OA.

Recommendation 6

- Walking shoes with neutral, contoured orthoses may be offered in:-
 - knee osteoarthritis **(Grade A)**
 - hip osteoarthritis **(Grade C)**
- Knee braces should not be offered in knee osteoarthritis. **(Grade A)**

6.2. Pharmacological Treatment

Pharmacological treatments are available in the form of oral, intra-articular and topical.

a. Oral Treatment

Oral treatment consists of:-

- i. Simple analgesics - paracetamol
- ii. Weak opioid analgesics - tramadol
- iii. Analgesics with anti-inflammatory properties - Non-steroidal Anti-inflammatory Drugs (NSAIDs) and Cyclo-oxygenase-2 (COX-2) Inhibitors
- iv. Nutraceutical - glucosamine, chondroitin, diacerein

i. Paracetamol

Paracetamol or acetaminophen is classified as a mild analgesic. In a SR of RCTs, paracetamol was superior to placebo in reduction of overall pain [SMD= -0.13 (95% CI -0.22 to -0.04), NNT=16]. However, NSAIDs were more efficacious than paracetamol in total WOMAC score (SMD= -0.25, 95% CI -0.39 to -0.11).^{50, level I}

Similarly, a meta-analysis showed that paracetamol was less efficacious than NSAIDs in overall pain using VAS at rest (WMD= -6.33mm, 95% CI -9.24 to -3.41) and on walking (WMD= -5.76mm, 95% CI -8.99 to -2.52).^{51, level I}

Paracetamol in the extended release formulation is significantly superior to placebo in reducing pain ($p=0.012$) and improving physical function ($p=0.016$).^{52, level I} Paracetamol in all formulations is well tolerated and safe.^{50 - 54, level I}

A combination tablet of ibuprofen/paracetamol confers no additional benefit to ibuprofen alone.^{53, level I}

Recommendation 7

- Paracetamol can be used in patients with osteoarthritis. (**Grade A**)
 - It should be used as first-line analgesic in mild to moderate pain. (**Grade C**)

ii. Tramadol

Tramadol is a synthetic opioid analgesic. In a meta-analysis, tramadol was more efficacious compared to placebo in reducing pain ($WMD = -8\text{mm}$, 95% CI -12.0 to -5.0), and improving stiffness and function ($WMD = -0.3$, 95% CI -0.5 to -0.2).^{55, level I}

Similarly, oral controlled-release tramadol is also more efficacious in reducing pain ($p=0.0009$) and improving physical function ($p=0.0205$) compared to placebo.^{56, level I} However, it is as efficacious as sustained-release diclofenac.^{57, level I}

In patients already on NSAIDs for at least 30 days, addition of tramadol/paracetamol combination tablets for 10 days duration is significantly efficacious in managing painful OA compared to those on placebo.^{58 - 59, level I}

Tramadol in all formulations show no major or significant adverse events.^{55 - 59, level I} Common side effects are dizziness, nausea, vomiting, constipation and drowsiness. This medication has to be used with caution in the elderly.

Recommendation 8

- Tramadol may be used alone or in combination with paracetamol in patients with osteoarthritis. **(Grade A)**

iii. NSAIDs and COX-2 Inhibitors

NSAIDs and COX-2 inhibitors reduce production of prostaglandin by inhibiting the enzyme cyclo-oxygenase. They vary in their selectivity for inhibiting different types of cyclo-oxygenase. They are a class of drugs that provide analgesic and anti-pyretic effects and in higher doses, anti-inflammatory effects. COX-2 inhibitors selectively inhibit COX-2 and thus improve gastro-intestinal tolerance.

In a meta-analysis, NSAIDs including COX-2 inhibitors were more efficacious than placebo in reducing short-term (2 - 13 weeks) pain intensity ($WMD=0.30$, 95% CI 0.24 to 0.39) and functional disability ($WMD=0.29$, 95% CI 0.18 to 0.40).^{60, level I}

Celecoxib 100 mg and 200 mg BID are as efficacious as diclofenac 50 mg BID and naproxen 500 mg BID in the treatment of hip, knee, or hand OA.^{61, level I}

In a study using OMERACT-OARSI responder criteria, those who responded within two weeks to etoricoxib 30 mg OD and celecoxib 200 mg OD are highly predictive of later response at 12 weeks.^{62, level I}

- **Gastrointestinal (GI) Safety**

The relative risks of upper GI complications of several NSAIDs and celecoxib compared to placebo analysed in a meta-analysis ranged from 1.45 to 4.14.^{63, level II-2}

Ulcer complications are seen significantly less frequent in COX-2 inhibitors compared to NSAIDs.^{61, level I; 64 - 66, level I} Comparing concomitant aspirin and non-aspirin users, the GI complications are significantly less in non-aspirin users ($p=0.007$).^{61, level I}

Proton pump inhibitors are effective in the prevention of NSAID-induced endoscopic duodenal (RR=0.19, 95% CI 0.09 to 0.37) and gastric ulcers (RR=0.40, 95% CI 0.32 to 0.51) at ≥ 12 weeks when compared to placebo.^{67, level I}

Lansoprazole significantly reduce the risk of gastroduodenal ulcers recurrence in patients with a definite history of GI ulcers requiring long-term NSAIDs therapy (HR=0.25, 95% CI 0.14 to 0.45)^{68, level I} or long-term low dose aspirin therapy (HR=0.10, 95% CI 0.04 to 0.23).^{69, level I}

The risk of GI events is lower in patients receiving celecoxib compared to diclofenac slow release plus omeprazole with HR of 4.3 (95% CI 2.6 to 7.0).^{70, level I} The risk of recurrent ulcer bleeding is also lower in the celecoxib 200 mg BD plus esomeprazole 20 mg BD group compared to the celecoxib 200 mg BD plus placebo group ($p=0.0004$).^{71, level I}

- **Cardiovascular (CV) Safety**

One of the main concerns among patients on long-term use of NSAIDs and COX-2 inhibitors is the increased risk of thrombotic CV events.

A meta-analysis showed that naproxen seemed to have the lowest Antiplatelet Trialists' Collaboration composite outcome of non-fatal myocardial infarction, non-fatal stroke or CV death among users of NSAIDs and COX-2 inhibitors (rate ratio=1.22, 95% CI 0.78 to 1.93).^{72, level I}

The numbers of CV thromboembolic events are low in both celecoxib and diclofenac or naproxen groups at 12 weeks.^{61, level I} Long-term etoricoxib use (20 months) is also associated with comparable CV events with that of diclofenac.^{73, level I}

- **Renal Safety**

In the Malaysian CPG on Chronic Kidney Disease (CKD) in Adults, there was conflicting evidence in the association between chronic NSAIDs usage and the development of CKD.⁷⁴ However, renal function should be monitored regularly in patients on chronic NSAIDs or COX-2 inhibitors treatment.

Recommendation 9

- Non-steroidal anti-inflammatory drugs (NSAIDs) or cyclooxygenase-2 (COX-2) inhibitors can be used in the treatment of osteoarthritis. (**Grade A**)
 - In patients with high risk of gastrointestinal (GI) complications, COX-2 inhibitors are preferred to non-selective NSAIDs with proton pump inhibitor (PPI) for primary ulcer prevention. (**Grade A**)
 - In patients with previous GI complications:
 - NSAIDs or COX-2 inhibitors should be avoided. (**Grade C**)
 - combination of COX-2 inhibitors and PPI may be offered for GI protection if indicated. (**Grade A**)
 - In patients with renal impairment, NSAIDs and COX-2 inhibitors should be used with caution. (**Grade C**)

- Combination therapy with more than one NSAID/COX-2 inhibitor should never be used. There is no benefit in combination therapy and the incidence of side effects may be additive.
- Caution is required when prescribing NSAIDs in the elderly and those with hypertension, cardiovascular disease, renal or hepatic impairment.
- Those who are allergic to one NSAID may also be allergic to others.

iv. Glucosamine and Chondroitin

Glucosamine is an amino sugar and a prominent precursor in the biochemical synthesis of glycosylated proteins and lipids, including glycosaminoglycans (GAG) which is a component of cartilage. Chondroitin sulfate is a sulfated GAG which is usually found attached to proteins as part of a proteoglycan. Glucosamine or chondroitin sulfate is required in the synthesis of the GAG component of cartilage, which provides the rationale for oral supplementation of these compounds in OA.

The glucosamine and chondroitin preparations available in Malaysia are in various combinations, strengths and purities which may affect their efficacy.

- **Glucosamine**

Glucosamine, in general, is not consistent in its effect as a structure modifier for OA. In terms of pain reduction, it is statistically more efficacious than placebo and can have similar efficacy with NSAIDs.^{75 - 77}, level I

Glucosamine hydrochloride or its combination with chondroitin sulfate is not efficacious as a structure or symptom modifier.^{75 - 76}, level I; ^{78 - 79}, level I

Glucosamine sulfate 1500 mg per day was statistically more efficacious in pain reduction when compared to placebo.^{76 - 77}, level I Pain relieving effect of glucosamine sulfate can be seen by three months after its initiation.⁸⁰, level I However, the evidence was from pharmaceutical-sponsored studies.

In terms of safety profile, glucosamine is well-tolerated and safe.^{75 - 78}, level I However, the effect of glucosamine on glucose metabolism needs further research.⁸¹, level I

Recommendation 10

- Glucosamine sulfate 1500 mg per day may be used as pain relief for knee osteoarthritis. (**Grade C**)
 - Evaluation on pain reduction should be done at three months after initiation of treatment before deciding on its continuation. (**Grade C**)

- **Chondroitin**

The evidence on efficacy of chondroitin sulfate in hip and knee OA for pain relief and its structure modifying effect is inconsistent.^{75 - 82}, level I

Chondroitin sulfate 800 mg as a single dose is more efficacious than placebo in pain reduction, improving hand function and morning stiffness in patients with hand OA.⁸³, level I However, its efficacy as a structural modifier is still debatable.^{84 - 86}, level I

In terms of safety profile, chondroitin sulfate is well-tolerated and safe.⁸³, level I

The efficacy of chondroitin in the treatment of hip or knee OA is inconclusive. It may be beneficial for symptomatic relief in hand OA.

v. Diacerein

Diacerein, a purified anthraquinone derivative, is a drug which inhibits production of interleukin (IL)-1beta, the major proinflammatory cytokine involved in articular cartilage destruction.

In a meta-analysis, diacerein was slightly more efficacious compared to placebo in reduction of pain [n-wtd pooled Glass score=1.31 (95% CI 0.49 to 2.14)] and improvement of joint function [n-wtd pooled Glass score=1.08 (95% CI 0.26 to 1.91)] in knee OA. In addition, diacerein had similar efficacy with NSAIDs in the reduction of pain in knee OA for duration of 16 weeks [(n-wtd pooled Glass score= -0.01 (95% CI -0.76 to 0.74)].^{87, level I}

Besides these, diacerein had significant carry-over effect in pain reduction in knee OA compared to placebo [(n-wtd pooled Glass score=2.71 (95% CI 1.32 to 4.10)] and NSAIDs [(n-wtd pooled Glass score=2.27 (95% CI 1.42 to 3.11)] for 16 weeks duration.^{87, level I}

In general, diacerein had an acceptable safety profile.^{87 - 90, level I} The incidence of adverse events such as diarrhea, abdominal pain, nausea and vomiting was higher compared to placebo ($p<0.01$), most were mild to moderate^{91, level I}

In view of modest efficacy and common adverse events, more studies are warranted to support the use of diacerein in OA.

Recommendation 11

- Diacerein may be used in the treatment of knee osteoarthritis. (Grade C)

b. Intra-articular Treatment

i. Corticosteroids

In a Cochrane systematic review of single/double blinded of 12 randomised controlled trials (n=653), the efficacy and safety of various preparations of intra-articular (IA) corticosteroid in the treatment of knee OA was evaluated.^{92, level I}

IA corticosteroid offered short-term pain relief at one week post-injection in patients with knee OA (WMD in VAS= -21.9 mm, 95% CI -29.9 to -13.9). The NNT calculated was three to four. The effect continued

to be seen at two weeks (RR=1.8, 95% CI 1.1 to 3.0) and three weeks (RR=3.1, 95% CI 1.6 to 6.0). However, it did not demonstrate improvement in function.^{92, level I}

There were no statistically significant differences detected in the total number of overall withdrawals including lack of efficacy, post-injection flare and local discomfort.^{92, level I}

Recommendation 12

- Intra-articular corticosteroid may be used for short-term pain relief in an acute exacerbation of knee osteoarthritis. (**Grade A**)

Oral corticosteroid have no role in the treatment of osteoarthritis.

ii. Viscosupplementation

Hyaluronic acid (HA) is a naturally occurring polysaccharide in the synovial fluid and is responsible for the elastoviscosity of synovial fluid. The quantity of HA in the synovial fluid is reduced in the patients who have OA. To improve biomechanical function, different hyaluronic acids were devised for intra-articular injection, commonly called viscosupplementation. There are now several different formulations of viscosupplements (hyaluronan and hylan) produced by different manufacturers and of widely differing molecular weights.

Two SRs showed that HA intra-articular injection may be beneficial in reducing pain, but the effect sizes were small when compared to placebo. In terms of improvement in physical function, the results were conflicting.^{93 - 94, level I} However, the pooled estimates in both SRs have to be interpreted cautiously because of different molecular weights of HA, different injection schedules and poor trial design despite large numbers of studies.

In a pharmacoconomics analysis by NICE, the above benefits may be offset by the frequency of the HA injections and other indirect costs. Thus, NICE does not recommend the use of viscosupplementation in treatment of knee OA.⁴⁰

Viscosupplementation is generally well-tolerated and with no significant difference in safety profile between it and placebo.^{94, level I} The risk of overall adverse events is insignificant.^{93, level I}

Due to a lack of supporting evidence, the CPG is unable to recommend the use of viscosupplementation in the treatment of osteoarthritis.

c. Topical Treatment

Topical treatment is an adjunct or alternative to oral NSAIDs for treatment of OA. The commonly used topical treatment includes NSAIDs, capsaicin and methylsalicylate. Topical analgesics can be in the form of gels, creams and transdermal patches.

Topical NSAIDs reduce knee OA pain at week 2 ($p<0.0001$), week 3 ($p<0.0002$)^{95, level I} and at week 4 to 12 (SMD= -0.33, 95% CI -0.48 to -0.18)^{96, level I} compared to placebo.

It is also more efficacious than placebo in reducing stiffness of knee OA (SMD in WOMAC stiffness at week 4 to 12= -0.30, 95% CI -0.45 to -0.15).^{96, level I}

Besides reducing pain and stiffness, physical function is also significantly improved with topical NSAIDs.^{95 - 97, level I}

Generally, topical NSAIDs were found to be safe in adults with OA in a SR of RCTs. The risk of minor skin dryness was higher in topical diclofenac compared to placebo (RR=1.74, 95% CI 1.37 to 2.22). Fewer severe gastrointestinal adverse events were reported in topical NSAIDs compared with oral NSAIDs.^{98, level I}

There were no recent studies found with regards to the usage of capsaicin and methylsalicylate in OA. However, the NICE CPG 2008 recommends that topical capsaicin should be considered as an adjunct to core treatment for knee or hand OA but does not recommend the use of topical methylsalicylate (rubefacients).⁴⁰

Recommendation 13

- Topical non-steroidal anti-inflammatory drugs may be offered in the treatment of osteoarthritis. **(Grade A)**
 - It may be used as adjunct therapy in mild to moderate pain. **(Grade C)**

7. ALTERNATIVE TREATMENT

Alternative treatments are extensively used in the treatment of OA however it is not based on evidence gathered using scientific methods.

Common alternative treatments that have shown positive results include acupuncture, avocado soybean unsaponifiables (ASU) and ginger.

- **Acupuncture**

Acupuncture is a traditional treatment which involves inserting needles into meridian points with the intention of influencing energy flow.

In a Cochrane SR, acupuncture significantly improved pain and function (as assessed by the WOMAC scale) in patients with knee OA compared to sham acupuncture:^{99, level I}

- SMD= -0.29 (95% CI -0.48 to -0.10) for pain at three months and
SMD= -0.10 (95% CI -0.21 to – 0.01) for pain at 26 weeks
- SMD= -0.29 (95% CI -0.49 to -0.08) for function at three months
- SMD= -0.29 (95% CI -0.50 to -0.09) for total score at three months

No serious adverse events were reported to be associated with acupuncture. Minor side effects were bruising and haematoma.

- **Avocado Soybean Unsaponifiables (ASU)**

ASU provided pain relief and improvement of function compared to placebo in chronic stable OA of the hip and knee in a Cochrane SR:^{100, level I}

- SMD= -8.06 (95% CI -11.3 to -4.60) for VAS pain score
- SMD= -1.69 (95% CI -2.41 to -0.98) for Lequesne index
- SMD=0.71 (95% CI 0.57 to 0.89) for resumption of NSAIDs

ASU had minimal gastrointestinal disturbances and no other serious side effect.

Another meta-analysis supported the above findings with improvement in pain in OMERACT III scale (SMD=0.39, 95% CI 0.01 to 0.76) and function in Lequesne index (SMD=45, 95% CI 0.21 to 0.70).^{101, level I}

- **Ginger**

In a small RCT of short duration, ginger extract was significantly more efficacious than placebo but less than ibuprofen ($p<0.005$) in improving pain and function. It was safe without serious side effects.^{102, level I}

Recommendation 14

- Acupuncture and avocado soybean unsaponifiables may be used as an adjunct short-term therapy in osteoarthritis. **(Grade A)**

8. SURGICAL TREATMENT

Surgery is considered if the symptoms of the affected joints significantly affect the quality of patients' life and interfere with ADL. There are five identified key areas which surgeons use to assess the need for surgery:-

- pain (sleep interruption and while resting)
- limitations to ADL (walking and self-care)
- psychosocial health (psychological well-being)
- economic impact and
- recent deterioration

The types of surgery that can be offered are:-

- Arthroscopic Surgery
- High Tibial Osteotomy
- Total Joint Replacement
- Partial Joint Replacement
- Arthrodesis

8.1 Arthroscopic Surgery

Arthroscopic lavage with or without debridement has been used in the treatment of knee OA. Studies showed no additional benefit in terms of pain relief and improvement in joint function compared to optimised physical and medical therapy.^{103 - 104, level I} However, it is indicated in patients with OA associated with mechanical symptoms such as locking, catching or giving way of the joint caused by presence of loose bodies or flaps of meniscus or cartilage.

8.2 High Tibial Osteotomy (HTO)

HTO works best in patients with isolated medial compartment arthritis, particularly if they are younger than 50 years old and have at least 120 degrees of knee flexion. It is an operation where the tibial bone is osteotomised at its upper end and repositioned in order to realign the mechanical axis of the limb away from the diseased area. This allows the knee to glide freely and distribute weight evenly on a more normal compartment.

HTO relieves pain and may delay the progression of OA. However, the disadvantages of this procedure are that the knee may look asymmetrical and may pose a more technically challenging procedure if Total Knee Replacement (TKR) is eventually required.

8.3 Total Joint Replacement

Total Joint Replacement is indicated in patients with severe OA who have failed to respond to all other therapies. This may result in a dramatic reduction in pain and a significant improvement in ADL.^{105, level I} However, patients are still advised to avoid certain activities, including jogging and high-impact sports for the rest of their life following surgery to ensure longevity of the implant.

a. *Total Knee Replacement (TKR)*

In the Canadian Joint Replacement Registry, 94% of TKR was due to degenerative OA.^{106, level III} Active infection is an absolute contraindication whereas young age <55 years, poor compliance, regional pain disorders and unrealistic expectations are relative contraindications. The rate of joint revision ranged between 0% and 13% in studies that reported more than five years follow-up.^{105, level I}

b. *Total Hip Replacement (THR)*

Indication for THR is similar to TKR. In the Canadian Joint Replacement Registry, 81% of THR was due to degenerative OA.^{106, level III} However, with the advancement in implant design, metallurgy and surgical techniques, THR is also advocated for the younger patient with severe hip OA.

8.4 Partial Joint Replacement

The advantages of partial knee replacement over total knee replacement are less blood loss intraoperatively and less pain post-surgery with faster recovery and better range of motion. The disadvantages include slightly less predictable pain relief and the potential need for subsequent surgery.

a. *Unicondylar Knee Replacement (UKR)*

UKR differs from TKR in that only a portion of the knee is replaced. It is indicated for patients with knee OA that affect either the medial or lateral compartment and have significant pain on weight bearing. The survival of UKR at 10 years is about 85%.^{107, level I; 108}

b. *Patellofemoral Knee Arthroplasty*

This surgery is an alternative to TKR for elderly patients with isolated advanced patellofemoral OA.

c. Bicompartamental Knee Arthroplasty

This type of surgery is an alternative to TKR when advanced medial or lateral compartment OA is associated with significant patellofemoral OA.

8.5 Arthrodesis

The aim of arthrodesis or joint fusion is to fuse the diseased joint in an optimal position. This would make the joint stiff but stable. The most common indication for knee arthrodesis is pain and significant ligamentous instability in an unreconstructable knee following an infection at the site of a knee arthroplasty. Arthrodesis of the knee can provide a stable, painless extremity for young active patients.

In general, arthrodesis is not the preferred surgical option in OA.

Recommendation 15

- Arthroscopic lavage and debridement should not be offered as a treatment in osteoarthritis (OA) of the knee except in selected conditions*. (**Grade A**)
- Joint Replacement should be offered to patients with severe OA. (**Grade A**)

*Refer to 8.1

8.6 Recent Advances in Osteoarthritis

a. Intra-articular Stem Cells

Stem cells have the capacity to produce all cell types in an unlimited fashion. Emerging evidence indicates that direct intra-articular injection of stem cells may boost the normally limited reparative process and limit the destructive process.

Malaysian Health Technology Assessment Section (MaHTAS) technology review showed that there was limited evidence on the benefits of stem cells in articular cartilage repair.¹⁰⁹

More evidence-based studies are needed before its recommendation as a standard treatment for OA.

b. Autologous Chondrocyte Implantation (ACI)

Autologous chondrocyte implantation is an approach that has been used to treat symptomatic knee cartilage defects. The aim of this treatment is to replenish cartilage through the recruitment of progenitor cells as potential cartilage precursors, allowing the development into chondrogenic cells and finally cartilage.^{110, level I}

Most of the studies on usage of ACI were done on younger age patients with articular cartilage damage due to secondary causes of OA such as sports injury or trauma. Hence, there is a lack of evidence presently to recommend the use of ACI in the treatment of primary OA.

c. Platelet Rich Plasma (PRP)

Platelet rich plasma (PRP) is a natural concentrate of autologous blood growth factors studied in different fields of medicine in order to test its potential to enhance tissue regeneration.

The preliminary short-term results within 3 to 6 months indicate that treatment with autologous PRP intra-articular injections may be useful for early OA, aiming to reduce pain and improve knee function and quality of life.^{111, level III} However, there is no further improvement after 6 months.^{111, level III; 112, level II-2}

Due to a lack of available evidence, the CPG is unable to recommend the use of intra-articular stem cells, autologous chondrocyte implantation or platelet-rich plasma in the treatment of osteoarthritis.

9. REFERRAL

9.1 Rheumatology Referral

Osteoarthritis is one of the major causes of disability in adults. Early diagnosis and intervention are important to minimise the impact of short-term and long-term morbidity. Rheumatology opinion should be sought for evaluation of arthritis with unclear diagnosis.

9.2 Orthopaedic Referral

Referral to the orthopaedic surgeon should be made when the patient does not experience satisfactory improvement in terms of pain, stability or function despite adequate pharmacological and non-pharmacological treatment. The patients should be made to understand the reason for referral.

Recommendation 16

- Referral of osteoarthritis cases to either rheumatology or orthopaedic clinic should provide the following information:-
 - Diagnosis
 - Severity and its impact on activity of daily living
 - Co-morbidities that might require further medical assessment
 - Relevant investigation results and current medications (**Grade C**)

10. PRIMARY PREVENTION

Identifying and modifying the risk factors can help in preventing OA and its progression. Many of these risk factors are of particular importance in weight-bearing joints. Prevention of obesity, weight reduction in the obese and health education pertaining to joint protection techniques including avoidance of trauma to the joints are recommended as measures for primary prevention. Currently, there is no evidence available to recommend the intake of any medication to prevent OA. An important aspect of primary prevention is to identify those individuals at risk.

11. IMPLEMENTING THE GUIDELINES

It is important to standardise the management of OA at all healthcare levels in Malaysia using an evidence-based CPG in order to manage OA appropriately. It is therefore crucial for healthcare providers to understand the disease as it is a common disease which may result in significant disabilities.

11.1 Facilitating & Limiting Factors

Existing facilitators for application of the recommendations in the CPG include:-

1. Wide dissemination of the CPG to healthcare providers (hard and soft copies)
2. Regular rheumatology update for healthcare providers

Existing barriers for application of the recommendations of the CPG are:-

1. Poor understanding/limited knowledge of OA
2. Insufficient resources in the management of OA particularly in rehabilitation
3. Variation in treatment practice and preferences

11.2 Potential Resource Implications

To implement the CPG, there must be strong commitment to:-

1. Ensure widespread distribution of the CPG to healthcare providers via printed and electronic copies.
2. Re-enforce training (with adequate funding) of healthcare providers by regular seminars or workshops to ensure information is up-to-date
3. Availability of rehabilitation services and trained manpower in OA management including multidisciplinary team at different levels of healthcare
4. Ensure availability of recommended drugs in primary care setting
5. Ensure patient empowerment via patient education materials

To assist in the implementation of the CPG, the following is proposed as **clinical audit indicator for quality management**:-

$$\text{Percentage of OA patients referred to rheumatology or orthopaedic clinic with proper documentation} = \frac{\text{Number of OA patients referred to rheumatology or orthopaedic clinic with proper documentation within a period of time}}{\text{Number of OA patients referred to rheumatology or orthopaedic clinic in the same period of time}} \times 100\%$$

$$\text{Percentage of patients with symptomatic OA at risk of GI complications* prescribed with NSAIDs alone} = \frac{\text{Number of patients with symptomatic OA at risk of GI complications prescribed with NSAIDs alone within a period of time}}{\text{Number of patients with symptomatic OA at risk of GI complications in the same period of time}} \times 100\%$$

*Those at high risk of GI complications (such as ulceration, bleeding, perforation and obstruction) are:-

- i. age more than 65 years old or
- ii. on high dose of NSAIDs, aspirin, corticosteroid or anticoagulant or
- iii. previous history of upper GI complications

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Appendix 1**EXAMPLE OF SEARCH STRATEGY**

The following MeSH terms or free text terms were used either singly or in combination, search was limit to English, human and 2001 to current:-

Paracetamol

1. osteoarthritis/
2. osteoarthritis.tw.
3. degenerative arthritis.tw.
4. 4.1 or 2 or 3
5. acetaminophen/
6. acetaminophen.tw.
7. paracetamol.tw.
8. 5 or 6 or 7
9. 4 and 8
10. limit 9

Tramadol

1. osteoarthritis/
2. osteoarthritis.tw.
3. degenerative arthritis.tw.
4. 1 or 2 or 3
5. tramadol/
6. tramadol.tw.
7. tramadol hydrochloride.tw.
8. 5 or 6 or 7
9. 4 and 8
10. limit 9

Intra-articular corticosteroids

1. osteoarthritis/
2. osteoarthritis.tw.
3. degenerative arthritis.tw.
4. 1 or 2 or 3
5. corticosteroid/
6. corticosteroid*.tw.
7. glucocorticoid*.tw.
8. 5 or 6 or 7
9. 4 and 8
10. limit 9

NSAIDs & COX-2 inhibitor

1. osteoarthritis/
2. osteoarthritis.tw.
3. degenerative arthritis.tw.
4. 1 or 2 or 3
5. non-steroidal anti-inflammatory agents/
6. non-steroidal anti-inflammatory agent*.tw.
7. NSAID*.tw.
8. 5 or 6 or 7
9. cyclooxygenase 2 inhibitors/
10. cyclooxygenase 2 inhibitor*.tw.
11. COX-2 inhibitor*.tw.
12. 9 or 10 or 11
13. 8 or 12
14. 4 and 13
15. limit 14

Glucosamine and Chondroitin

1. osteoarthritis/
2. osteoarthritis.tw.
3. degenerative arthritis.tw.
4. 1 or 2 or 3
5. glucosamine/
6. glucosamine.tw.
7. glucosamine sulphate.tw.
8. glucosamine hydrochloride.tw.
9. 5 or 6 or 7 or 8
10. chondroitin/
11. chondroitin.tw.
12. chondroitin sulphate.tw.
13. 10 or 11 or 12
14. 9 or 13
15. 4 and 14
16. limit 15

Viscosupplementation

1. osteoarthritis/
2. osteoarthritis.tw.
3. degenerative arthritis.tw.
4. 1 or 2 or 3
5. hyaluronic acid/
6. (hyaluronic adj1 acid).tw.
7. (sodium adj1 hyaluron*)tw.
8. viscosupplementation/
9. viscosupplement*.tw.
10. 5 or 6 or 7 or 8 or 9
11. 4 and 10
12. limit 11

Diacerein

1. osteoarthritis/
2. osteoarthritis.tw.
3. degenerative arthritis.tw.
4. 1 or 2 or 3
5. diacerein.mp.
6. diacerein.tw.
7. 5 or 6
8. 4 and 7
9. limit 8

Topical therapy

1. osteoarthritis/
2. osteoarthritis.tw.
3. degenerative arthritis.tw.
4. 1 or 2 or 3
5. topical NSAIDS.mp.
6. capsaicin.tw.
7. methylsalicylate.tw.
8. 5 or 6 or 7
9. 4 and 8
10. limit 9

Appendix 2**CLINICAL QUESTIONS**

1. What is the epidemiology of OA?
2. What are the risk factors of OA?
3. What are the signs and symptoms of OA?
4. How is OA diagnosed and classified?
5. What are the effective diagnostic tests in OA?
6. What are the effective & safe non-pharmacological modalities/lifestyle modifications in OA?
7. What are the effective & safe pharmacological treatments in OA?
8. What are the effective & safe alternative treatments in OA?
9. What are the effective & safe surgical modalities in OA?
10. What is the role of intra-articular stem cells, autologous chondrocyte implantation and platelet-rich plasma in OA?
11. When should OA patients be referred for rheumatology/orthopaedic services?
12. What are the primary preventive measures for OA?

Appendix 3**RELATIONSHIP BETWEEN ANATOMICAL SITE AND POSSIBLE PHYSIOLOGICAL MECHANISM FOR PAIN IN OSTEOARTHRITIS**

Anatomical site	Mechanism
Cartilage (defective or loss)	<i>Synovial:</i> inflammation induced by cartilage 'char' fragments, cartilage crystal shedding, cartilage release of cytokines (e.g. interleukin-1), enzymes (e.g. metalloproteinases) <i>Subchondral bone:</i> mechanical stress (see below) <i>Instability:</i> stress on capsule
Menisci	Tear or degeneration: stretch at insertion to the joint capsule, catch between surfaces
Synovial cavity	Stretch of joint capsule, transport of inflammatory mediators between synovium and cartilage
Synovium	Inflammation
Subchondral bone	Ischemia with increased pressure, decreased oxygen tension and increased pH Avascular necrosis Regeneration or repair of infarcted bone
Osteophytes	Periosteal elevation Neural impingement
Joint capsule	Stretch from joint distension Stress at insertion to periosteum and bone
Ligaments	Stress at insertion to periosteum and bone
Bursae	Inflammation, with or without calcification
Muscle	Spasm Nocturnal myoclonus
Central nervous system	Mild chronic depression, mild mood fluctuation, fibromyalgia Ethnic, cultural, coping skills

Appendix 4**QUADRICEPS STRENGTHENING EXERCISE****Figure A**

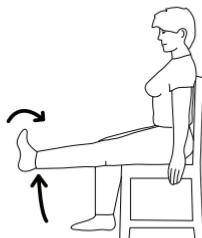
Lie flat in bed with your legs straight. Bend your ankles and push the back of your knees down firmly against the bed. Hold for five seconds, then return to the original position and relax.

**Figure B**

Sit on a firm flat surface with one leg bent and keep the other leg straight. Bend your ankle and push the back of your knee down firmly against the bed. Hold for five seconds, then return to the original position and relax.

**Figure C**

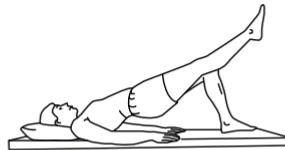
Lie flat in bed with a rolled towel/small cushion under your knee. Bend your ankle and push the back of your knee down firmly against the rolled towel/small cushion (keep knee on the towel/cushion). Hold for five seconds, then return to the original position and relax.

**Figure D**

Sit on a chair. Straighten your knee and bend your ankle. Hold for five seconds, then return to the original position and relax.

Appendix 5**HIP STRENGTHENING EXERCISE****Figure A**

Stand straight holding to a chair. Bring your leg backwards, keeping your knee straight (do not lean forwards). Hold for five seconds, then return to the original position and relax.

**Figure B**

Lie on your back with both knees bent. Then, lift your hips up and straighten one leg while shifting the weight over to the bent leg. Hold for five seconds, then return to the original position and relax.

**Figure C**

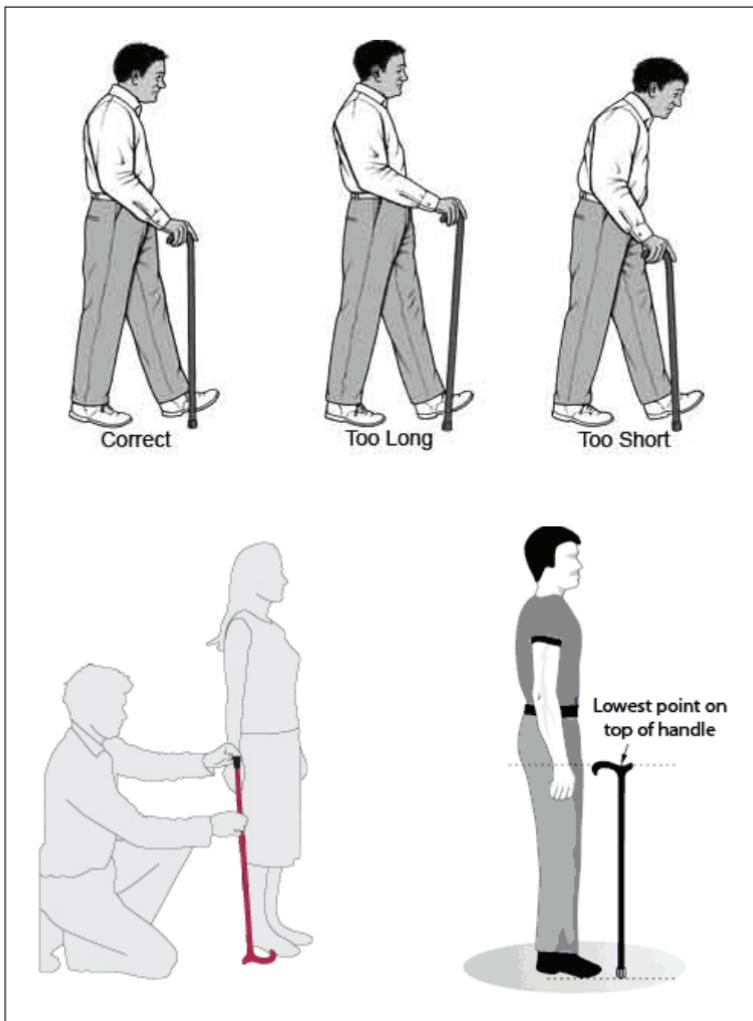
Lie on your back with knees bent. Squeeze your buttocks together and lift your bottom off the floor. Hold for five seconds, then return to the original position and relax.

**Figure D**

Lie face down. Lift one leg up while keeping the other leg straight on the floor. Hold for five seconds, then return to the original position and relax.

Appendix 6

APPROPRIATE MEASUREMENT FOR WALKING STICK



Appendix 7**JOINT PROTECTION PRINCIPLES**

Joint protection principles include:-

- Resting inflamed joints by reducing load, duration of use and repetitive movement
- Using the largest unaffected muscles and joints to perform a task
- Using proper movement techniques for lifting, sitting, standing, bending and reaching
- Using assistive devices and modifications for home equipment to minimise stress on joints
- Plan and organise activities ahead
- Using biomechanics and ergonomics to best effect
- Simplifying tasks
- Recruiting others to help
- Making exercise a part of everyday life including exercises which improve joint range of movement, stamina and strength
- Exercise should also be for cardiovascular fitness and to maintain or improve balance

Source: National Collaborating Centre for Chronic Conditions. Osteoarthritis: national clinical guideline for care and management in adults. London: Royal College of Physicians; 2008

ACTIVITY MODIFICATION IN PERFORMING ADL

- To use walking stick on the opposite hand of the affected knee / more painful knee joint during walking
- To climb stairs, use the railing of the stairs, climb slowly and the body weight should be transferred to the railing by the hand opposite to the affected knee
- To bathe in standing or sitting position with a shower and use high commode in bathroom
- To cook in standing position and if necessary to sit on a chair for a while and use dining table for eating
- To avoid high heeled shoes, sitting on low stool and prolonged walking/sitting/running
- To avoid performing activity in squatting position

Source: Shakoor MA, Taslim MA, Hossain MS. Effects of activity modification on the patients with osteoarthritis of the knee. Bangladesh Med Res Cunc Bull. 2007 Aug;33(2):55-9

Appendix 8

SUGGESTED MEDICATION DOSAGES AND SIDE EFFECTS

Drug Class	Drug	Recommended Dosages	Side Effects	Caution and Contraindications	Comments
Simple analgesic	Paracetamol	0.5 – 1 gm, 6 – 8-hourly Max: 4 gm/day	Rare but hypersensitivity including skin rash may occur	Hepatic impairment Alcohol dependence	Preferred drug particularly elderly patients
Non-selective NSAIDs	Ibuprofen	400 – 800 mg, 6 – 8-hourly Max: 3200 mg/day	Peptic ulcer GI bleed	Gastroduodenal ulcer Asthma Bleeding disorder Renal dysfunction	Physicians and patients should weigh the benefits and risks of NSAIDs therapy
	Mefenamic acid	250 – 500 mg, 6 – 8-hourly Max: 1500 mg/day	Platelet dysfunction Renal impairment	Ischaemic heart disease Cerebrovascular disease Inflammatory bowel disease	
	Diclofenac sodium	50 – 150 mg daily, 8 – 12-hourly	Hypertension		
		Max: 150 mg/day	Allergic reaction in susceptible individuals		
	Meloxicam	7.5 – 15 mg daily Max: 15 mg/day	Increase in CV/S events		
	Naproxen	250 – 500 mg, 12-hourly Max: 1500 mg/day			
	Naproxen sodium	275 – 550 mg, 12-hourly Max: 1650 mg/day			
	Piroxicam	10 – 20 mg daily, in single or divided doses Max: 20 mg/day			
Selective COX-2 inhibitors	Celecoxib	200 mg daily Max: 200 mg/day (Recommended daily maximum dose is 200 mg for OA and 400 mg for inflammatory arthritis)	Renal impairment Allergic reaction in susceptible individuals Increase in CV/S events	Ischaemic heart disease Cerebrovascular disease Contraindicated in hypersensitivity to sulphonamides	Associated with a lower risk of serious upper GI side effects
	Etoricoxib	60 mg daily Max: 90 mg/day	Hypertension Renal impairment Increase in CV/S events	Uncontrolled hypertension Ischaemic heart disease Cerebrovascular disease	Current data suggest that increased CV risk may be an effect of the NSAIDs/coxib class
					Physicians and patients should weigh the benefits and risks of coxib therapy

Drug Class	Drug	Recommended Dosages	Side Effects	Caution and Contraindications	Comments
Weak opioid	Tramadol	50 – 100 mg, 6 – 8-hourly Max: 400 mg/day	Dizziness Nausea Vomiting Constipation Drowsiness	Risk of seizures in patients with history of seizures and with high doses In elderly, start at lowest dose (50 mg), and maximum of 300 lowest dose (50 mg), and maximum of 300 mg daily	Interaction with Tricyclic Antidepressant Selective Serotonin Reuptake Inhibitor and Serotonin Norepinephrine Receptor Inhibitor
Combination of opioid and paracetamol	Paracetamol 325 mg + tramadol 37.5 mg (Ultracet®)	1 – 2 tablets, 6 – 8-hourly Max: 8 tablets/day	Nausea Vomiting Drowsiness	Hepatic impairment Renal impairment Alcohol dependence Epilepsy	-

Nutraceuticals

Drug	Recommended Dosages	Side Effects	Caution and Contraindications	Comments
Glucosamine sulfate	1500 mg in single or divided doses Max: 1500 mg/day	Nausea Dyspepsia Heartburn Vomiting Constipation Diarrhoea Headache Skin erythema Pruritus	Contraindicated in patients with • allergy and hypersensitivity to shellfish or its products • phenylketonuria • Asthmatic patients may be at risk for an asthma exacerbation when taking the combination of glucosamine and chondroitin Special precaution in diabetes	-
Chondroitin sulfate	800 – 1200 mg daily or divided doses Max: 1200 mg	Dyspepsia Nausea Vomiting	Asthmatic patients may be at risk for an asthma exacerbation when taking chondroitin Avoid in patients with prostate cancer	-

Drug	Recommended Dosages	Side Effects	Caution and Contraindications	Comments
Diacelein	50 mg 12-hourly	Diarrhoea Epigastric pain Nausea Vomiting Intense yellow colouring of urine Skin reactions	or are at high risk for developing prostate cancer Special precaution in diabetes when used in combination with glucosamine sulfate Hypersensitivity to anthraqinone derivatives Inflammatory bowel disease (ulcerative colitis, Crohn's disease), intestinal obstruction or partial obstruction, severe liver failure	Creatinine clearance >30 ml/min. dosage recommendation is 25 mg daily Antacid use may decrease diacelein absorption, so it is advised to take antacids after an interval of two hours
Avocado soybean unsaponifiables	300 mg daily	Diarrhoea Epigastric pain Extremely rare cases of liver disorders including increased transaminases, alkaline phosphatases, bilirubin and gamma-glutamyl transpeptidase	Previous history of allergic reaction to any of the ingredients	Inrequent lipid-scented regurgitation which may be avoided by taking the capsule during a meal

Sources:

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Appendix 9**CHECKLIST OF OA MANAGEMENT**

1. Education

- | | | |
|------------------------------------------------|------------------------------|-----------------------------|
| • Nature of OA | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| • Prognosis | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| • Treatment option - medication & side effects | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| • Self-management | <input type="checkbox"/> Yes | <input type="checkbox"/> No |

2. Lifestyle modification

- | | | |
|-------------------|------------------------------|-----------------------------|
| • Weight loss | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| • Dietary advice | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| • Exercise | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| • Footwear | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| • Pacing activity | <input type="checkbox"/> Yes | <input type="checkbox"/> No |

3. Referral where applicable

<input type="checkbox"/> Yes	<input type="checkbox"/> No
------------------------------	-----------------------------

LIST OF ABBREVIATIONS

ACI	autologous chondrocyte implantation
ACR	American College of Rheumatology
ADL	activities of daily living
AP	anteroposterior
ASU	avocado soybean unsaponifiable
BMI	body mass index
CI	confidence interval
CKD	chronic kidney disease
CMC	carpometacarpal
COPCORD	Community Oriented Program for the Control of Rheumatic Disease
COX-2	cyclo-oxygenase-2
CPG(s)	clinical practice guidelines
CRP	C-reactive protein
CV	cardiovascular
DG	Development Group
DIP	distal interphalangeal
ESR	erythrocyte sedimentation rate
EULAR	The European League Against Rheumatism
g	gram
GAG	glycosaminoglycans
GI	gastrointestinal
HA	hyaluronic acid
HR	hazard ratio
HTO	high tibial osteotomy
IA	intra-articular
JPE	Joint Protection Exercise
LDH	lactate dehydrogenase
MCP	metacarpophalangeal
max	maximum
MD	mean difference
mg	milligram
mL	milliliter
mm	milimeter
MoH	Ministry of Health
NICE	National Institute for Health and Clinical Excellence
NNT	number needed to treat
NSAIDs	non-steroidal anti-inflammatory drugs
n-wtd	non-weighted
OA	osteoarthritis
OD	once daily
OR	odds ratio
PIP	proximal interphalangeal
PMN	polymorphonucleocytes
PPI	proton pump inhibitor
PRP	platelet-rich plasma
RC	Review Committee

RCT(s)	randomised controlled trial(s)
RF	rheumatoid factor
ROM	range of movement
RR	relative risk
SF	synovial fluid
SMD	standardised mean difference
SR	systematic review
TENS	transcutaneous electrostimulation
THR	total hip replacement
TKR	total knee replacement
UKR	unicondylar knee replacement
VAS	Visual Analogue Scale
WBC	white blood cells
WHO	World Health Organization
WMD	weighted mean difference
WOMAC	The Western Ontario and McMaster Universities Arthritis Index

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