

MANAGEMENT OF OSTEOARTHRITIS (SECOND EDITION)



Ministry of Health
Malaysia



Malaysian Society of
Rheumatology



Academy of
Medicine Malaysia

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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 2001

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

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Outpatient, inpatient and community settings

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REVIEW COMMITTEE

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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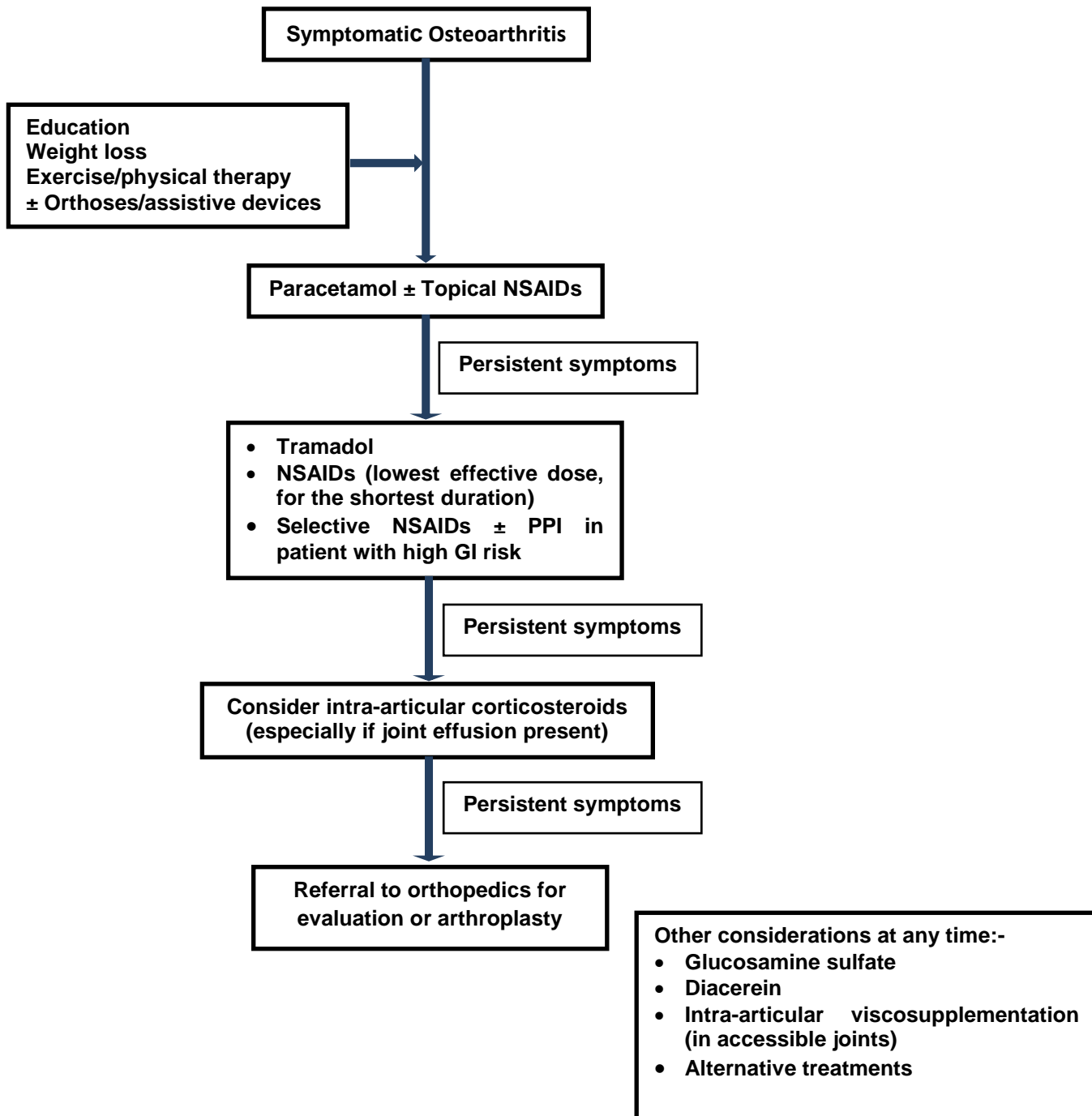
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The following external reviewers provided feedback on the draft:-

ALGORITHM ON MANAGEMENT OF OSTEOARTHRITIS



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

In symptomatic hip OA, the prevalence was 9.2% among adults age >45 with a slight female preponderance.^{Lawrence RC et al., 2008}

c. Knee OA

In the Johnston County OA Project in the US, 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.^{5, level II-2}

The prevalence of symptomatic knee OA was 4.9% among adults age >26 years in the Framingham study,^{ref} 16.7% among adults age >45 in the Johnston County study,^{5, level II-2} and 12.1% among adults aged >60 in the NHANES III study.^{6, 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.^{7, 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^{8, 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)]^{8, level II-2}
- Genetic influence on hand and knee OA in women ranges from 39% to 65% ($p<0.001$)^{9, level II-2}
- Presence of Heberden's nodes and/or hand OA increased the risk for future knee OA, OR=1.4, 95% CI 1.1 to 1.8^{8, level II-2}

Modifiable

- Body mass index (BMI)^{8, 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% C 1.8 to 4.2 (cohort studies)]^{8, 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 disease^{10, 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.^{11, 2002}

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. Traumatic such as major joint trauma, fracture through a joint or osteonecrosis, joint surgery arthritis, psoriatic arthropathy and septic arthritis
- iv. Inflammatory such as rheumatoid arthritis

4. DIAGNOSIS

OA is frequently diagnosed by an overall clinical impression.

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 4** 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 Criteria^{12, 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
4b	Deformity of ≥ 2 of 10 selected joints
Sensitivity	92%
Specificity	98%

DIP=distal interphalangeal
PIP=proximal interphalangeal

MCP=metacarpophalangeal
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 Criteria^{13, 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 Criteria^{14, 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%	84%
Specificity	75%	86%	69% (if 3/6)	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**:^{15, level III}

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

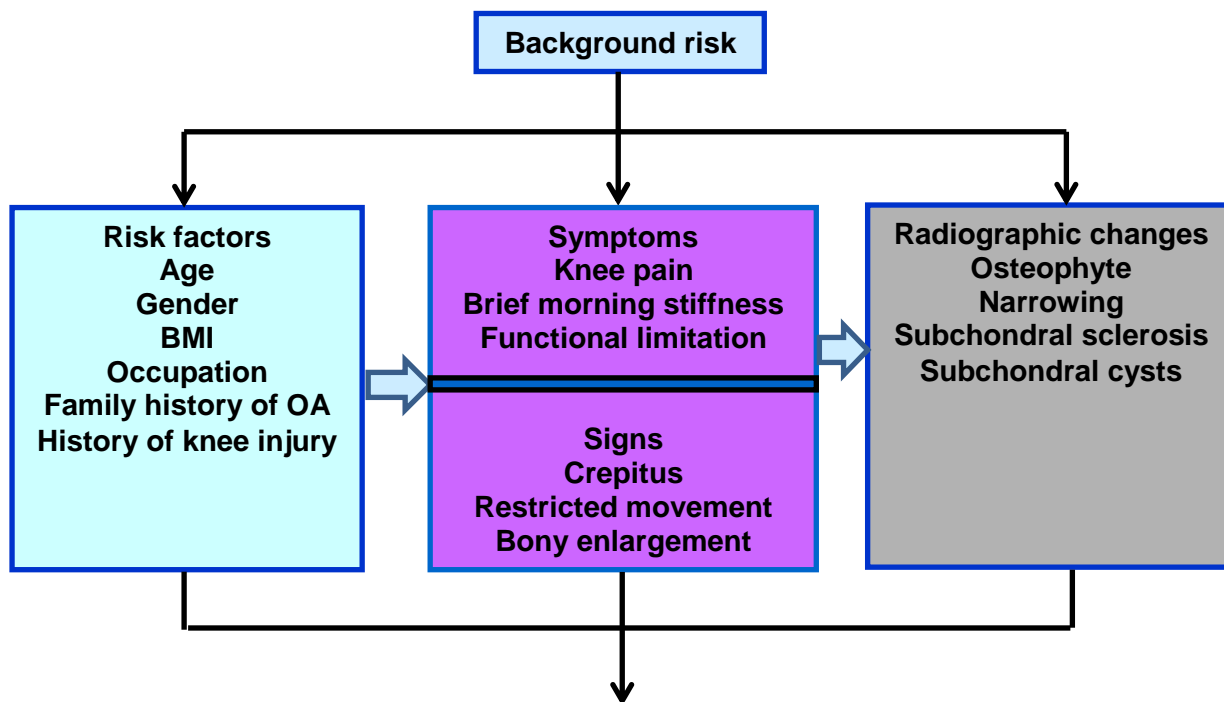


Figure 1: Diagnosis of Knee OA

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 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/home>)

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** shows an example of an osteoarthritic knee.



Figure 2: Knee 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**).

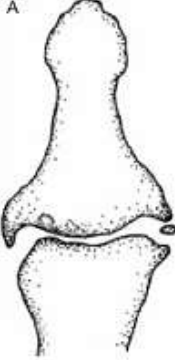

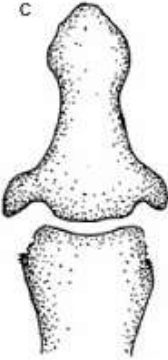

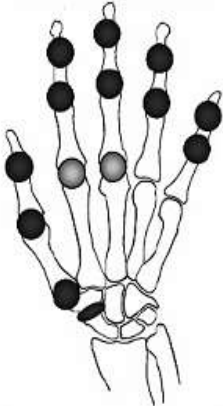
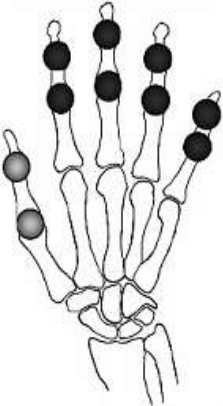
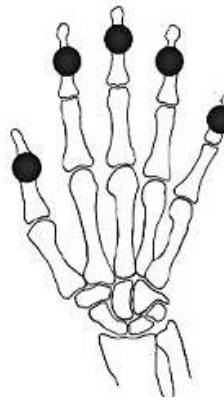

Table 5: Kellgren-Lawrence Grading System

Imaging					
		0	I	II	III
Radiographic Grade	0	I	II	III	IV
Classification	Normal	Doubtful	Mild	Moderate	Severe
Description	No features of OA	Minute osteophyte; doubtful significance	Definite osteophyte; normal joint space	Moderate joint space reduction	Joint space greatly reduced; subchondral sclerosis

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	 <p>Focal narrowing, marginal osteophyte, sclerosis, osteochondral bodies</p>	 <p>Subchondral erosion</p>	 <p>Proliferative marginal erosion, retained or increase bone density</p>	 <p>Non-proliferative marginal erosion, osteopenia</p>
Target sites				

● 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 3** and **Figure 4**).



Figure 3: Gull-wing Appearance



Figure 4: 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.^{16, level III} In addition, US may demonstrate synovial inflammation in symptomatic OA of the hands and knees.^{17, level III; 18, level II-2; 19, 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. NON-PHARMACOLOGICAL TREATMENT

6.1 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.^{20, level I; 21, level I; 22, level I; 23, level I} Patients who have an understanding of the disease tend to cope better and report less pain.²⁴ The most important goal is to instil a positive attitude.

Recommendation 2

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

6.2 Lifestyle Modification

Lifestyle medicine is defined as the application of environmental, behavioural, medical and motivational principles to the management of lifestyle related health problems.^{25, level III}

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

a. 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.^{26, level I; 27, level I; 28, 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.^{29, level I} There is no evidence available to support the effect of weight loss in hip OA.³⁰

Recommendation 3

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

b. Physical Activity

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

- i. The exercise programme is individualised
- ii. The activity is graded activity
- iii. The amount of activity is based on personal goal setting
- iv. There is feedback on progress
- v. Appropriate positive reinforcement is given
- vi. Problem solving skills are taught

The amount and intensity of exercise required is uncertain. 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.³⁰

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.³⁰

In knee OA, aerobic training (walking) is effective in reducing pain (ES=0.48, 95% CI 0.13 to 0.43) and improving physical function (ES=0.35, 95% CI 0.11 to 0.58).^{31, 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).³⁰

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

6.3 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.

a. Exercise

Exercise programmes should be individualised while taking into consideration patient 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.^{31, 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).^{32, 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.^{33, 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.^{33, level I}

b. 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.^{34, level I} However, the ACR 2012 Recommendations suggest the use of TENS for patients with chronic moderate to severe pain who are not suitable for total knee arthroplasty.³⁵

c. Thermotherapy

Thermotherapy is commonly used in physical rehabilitation for OA patients. ACR recommended the use of thermal agents for hip and knee OA in combination with exercise supervised by a physiotherapist.³⁵

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).^{36, level I}

d. Therapeutic Ultrasound

Therapeutic ultrasound with high frequency vibrations is a modality used in the rehabilitation of patients with hip and knee OA. However, in a Cochrane SR, the effectiveness of this modality in pain reduction and function was inconclusive.^{37, 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)**

6.4 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.³⁸

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.³⁸ 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% ($p < 0.05$).^{39, level I} Refer to **Appendix 7** for **Joint Protection Principles**. Thumb splints can help to reduce pain in the thumb and improve hand function.³⁸ Splinting and Joint Protection programme in hand OA can give significant decreases in pain and stiffness and improvements in daily activities ($p < 0.05$).^{40, 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.^{41, 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 related therapies are:-

- Jacobson relaxation: improves pain at end of 8-week treatment ($p < 0.05$) but the benefit is not sustained^{42, level I}
- Music therapy: improves pain at day 1, day 7 and at 2 weeks (end of treatment) (all $p = 0.001$)^{43, level I}
- Guided Imagery Relaxation (GIR): increases Health Related Quality of Life in women with OA ($p = 0.023$)^{44, 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)**

6.5 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 ($p < 0.001$).^{45, 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.^{46 - 47, 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 are should not be offered in knee osteoarthritis. **(Grade A)**

7. PHARMACOLOGICAL TREATMENT

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

7.1. 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 and Cyclo-oxygenase-2 Inhibitors
- iv. Nutraceutical - glucosamine, chondroitin, diacerein

a. Paracetamol

Paracetamol or acetaminophen is classified as a mild analgesia. 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).^{48, 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).^{49, level I}

Paracetamol in the extended release formulation is significantly superior to placebo in reducing pain ($p=0.012$) and improving physical function ($p=0.016$).^{50, level I} Paracetamol in all formulations is well tolerated and safe.^{48, level I; 49, level I; 50, level I; 51, level I; 52, level I}

A combination tablet of ibuprofen/paracetamol confers no additional benefit to ibuprofen alone.^{51, level I}

Recommendation 7

- Paracetamol can be used in patients with osteoarthritis. **(Grade A)**

b. Tramadol

Tramadol is a synthetic opioid analgesic. In a meta-analysis, tramadol was more efficacious compared to placebo in reducing pain (WMD= -8mm, 95% CI, -12.0 to -5.0) and improving stiffness and function (WMD= -0.3, 95% CI, -0.5 to -0.2).^{53, 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.^{54, level I} However, it is as efficacious as sustained-release diclofenac.^{55, 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.^{56 - 57, level I}

Tramadol in all formulations show no major or significant adverse events.^{53, level I; 54, level I; 55, level I; 56, level I; 57, 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)**

c. Non-steroidal Anti-inflammatory Drugs (NSAIDs) and Cyclo-oxygenase-2 (COX-2) Inhibitors

NSAIDs are a class of drugs that provide analgesic and anti-pyretic effects and in higher doses, anti-inflammatory effects, while COX-2 inhibitors are a type of NSAIDs which selectively inhibit COX-2 which is an enzyme responsible for inflammation and pain.

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).^{58, 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.^{59, level I}

The early response based on OMERACT-OARSI responder criteria within the first two weeks of treatment to etoricoxib 30 mg **OD** and celecoxib 200 mg **OD** are highly predictive of later response to the medications.^{60, level I}

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.^{61, level II-2}

Ulcer complications are seen significantly less frequent in COX-2 inhibitors compared to NSAIDs.^{59, level I; 62, level I; 63, level I; 64, level I} Comparing concomitant aspirin and non-aspirin users, the GI complications are significantly less in non-aspirin users ($p=0.007$).^{59, 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.^{65, 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)^{66, level I} or long-term low dose aspirin therapy (HR=0.10, 95% CI 0.04 to 0.23).^{67, 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).^{68, level I}

ii. 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 NSAIDs and COX-2 inhibitors (rate ratio=1.22, 95% CI 0.78 to 1.93).^{69, level I}

The numbers of CV thromboembolic events are low in both celecoxib and diclofenac or naproxen groups at 12 weeks.^{59, level I} Long-term etoricoxib use (20 months) is also associated with comparable CV events with that of diclofenac.^{70, level I}

iii. 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.⁷¹ 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 cyclo-oxygenase-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 traditional NSAIDs with proton pump inhibitor (PPI) for primary ulcer prevention. **(Grade A)**
 - In patients with previous GI complications, combination of COX-2 inhibitors and PPI should be offered for GI protection. **(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 to those with renal, cardiac or hepatic impairment, hypertension and in the elderly.
- Those who are allergic to one NSAID may also be allergic to others.

d. 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 16learanc is a 16learance GAG which is usually found attached to proteins as part of a proteoglycan. Glucosamine or chondroitin 16learanc 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 the efficacy.

i. 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.^{72, level I; 73, level I; 74, level I}

Glucosamine hydrochloride or its combination with chondroitin sulfate is not efficacious as a structure or symptom modifier.^{72 - 73, level I; 75 - 76, level I}

Glucosamine 1500 mg per day is statistically more efficacious in pain reduction when compared to placebo.^{73 - 74, level I} Pain relieving effect of glucosamine sulfate can be seen by three months after its initiation.^{77, level I}

In terms of safety profile, glucosamine is well-tolerated and safe.^{72, level I; 73, level I; 74, level I; 75, level I} However, the effect of glucosamine on glucose metabolism needs further research.^{78, level I}

Recommendation 10

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

ii. Chondroitin

The evidence on efficacy of chondroitin sulfate in hip and knee OA for pain relief and its structure modifying effect is inconsistent.^{72 - 73, level I; 75 - 76, level I; 79, 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.^{80, level I} However, its efficacy as a structural modifier is still under debatable.^{81, level I; 82, level I; 83, level I}

In terms of safety profile, chondroitin sulfate is well-tolerated and safe.^{80, 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.

e. 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 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)].^{84, 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.^{84, level I}

In general, diacerein has an acceptable safety profile; it is safe and well tolerated.^{84, level I; 85, level I; 86, level I; 87, level I} However, the incidence of adverse events is higher compared to placebo ($p<0.01$), although most are mild to moderate.^{88, level I} Common adverse events are diarrhea, abdominal pain, nausea and vomiting.

Recommendation 11

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

7.2. Intra-articular Treatment

a. Corticosteroids

In a Cochrane systematic review of single/double blinded of 12 randomised controlled trials (n=653), the efficacy and safety of various preparation of intra-articular (IA) corticosteroids in the treatment of knee OA was evaluated.^{89, level I}

IA corticosteroids offered short-term pain relief at one week post-injection in patients with knee OA (WMD in VAS= -21.9mm, 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.^{89, 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.^{89, level I}

Recommendation 12

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

Oral corticosteroids have no role in the treatment of osteoarthritis.

b. 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.^{90, level I; 91, 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 pharmacoeconomics 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.³⁸

Viscosupplementation is generally well-tolerated and with no significant difference in safety profile between it and placebo.^{91, level I} The risk of overall adverse events is insignificant.^{90, level I}

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

7.3. 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 ($p < 0.0002$)^{92, 2005, level I} and at week 4 to 12 [SMD= -0.33, 95% CI -0.48 to -0.18]^{93, 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].^{93, level I}

Besides reducing pain and stiffness, physical function is also significantly improved with topical NSAIDs.^{92, level I; 93, level I; 94, 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.^{95, 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 (rubefaciants).³⁸

Recommendation 13

- Topical non-steroidal anti-inflammatory drugs may be offered in the treatment of osteoarthritis. **(Grade A)**

8. ALTERNATIVE TREATMENTS

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.

a. 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:^{96, 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.

b. 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:^{97, 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=0.45, 95% CI 0.21 to 0.70).^{98, level I}

c. Ginger

In a small RCT of short duration, ginger 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.^{99, level I}

Recommendation 14

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

9. 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

9.1 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.^{100 – 101, 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.

9.2 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 cut 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 carry 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.

9.3 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.^{102, level x} 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, 93% of TKR was due to degenerative OA.^{103, 2004, 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.^{102, level x}

b. Total Hip Replacement (THR)

The indication for THR is similar to TKR. However, with the advancement in implant design, metallurgy and surgical technique, THR is also advocated for the younger patient with severe hip OA.

9.4 Partial Joint Replacement

The advantages of partial knee replacement over total knee replacement are less blood loss intra-operatively 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 10-year implant survivorship of UKR is about 85%.^{104 level x; 105}

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.

9.5 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 a 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 of the knee except in selected conditions*. **(Grade A)**
- Joint Replacement should be offered to patients with severe osteoarthritis. **(Grade A)**

*Refer to 9.1

9.6 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.¹⁰⁶

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.^{107, 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.^{108, level III} However, there is no further improvement after 6 months.^{108, level III; 109, 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.

10. REFERRAL

10.1 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- and long-term morbidity. Rheumatology opinion should be sought for evaluation of arthritis with unclear diagnosis.

10.2 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.

11. 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 preparation to prevent OA. An important aspect of primary prevention is to identify those individuals at risk.

12. 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.

12.1 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

12.2 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**:-

$$\begin{array}{l} \text{Percentage of patients} \\ \text{with symptomatic OA} \\ \text{and at risk of GI} \\ \text{complications} \\ \text{prescribed with} \\ \text{NSAIDs alone} \end{array} = \frac{\begin{array}{l} \text{No. of patients with symptomatic OA and at risk of} \\ \text{GI complications prescribed with NSAIDs alone} \end{array}}{\begin{array}{l} \text{No. of patients with OA and at risk of GI} \\ \text{complications} \end{array}} \times 100\%$$

REFERENCES

1. Vos T, Flaxman AD., Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010.[Erratum appears in Lancet. 2013 Feb 23;381(9867):628 Note: AlMazroa, Mohammad A [added]; Memish, Ziad A [added]]. Lancet. 2012 Dec 15;380(9859):2163-96.
2. National Institutes of Health, World Health Organization. Global Health and Aging, NIH, Techn. Rep, NIH Publication no. 11-77372011 Contract No.: NIH Publication no. 11-7737.
3. Pereira D, Peleteiro B, Araujo J, et al. The effect of osteoarthritis definition on prevalence and incidence estimates: a systematic review. *Osteoarthritis Cartilage*. 2011 Nov;19(11):1270-85.
4. Haugen IK, Englund M, Aliabadi P, et al. Prevalence, incidence and progression of hand osteoarthritis in the general population: the Framingham Osteoarthritis Study. *Ann Rheum Dis*. 2011 Sep;70(9):1581-6.
5. Murphy L, Schwartz TA, Helmick CG, et al. Lifetime risk of symptomatic knee osteoarthritis. *Arthritis Rheum*. 2008 Sep 15;59(9):1207-13.
6. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. *Arthritis Rheum*. 2008 Jan;58(1):26-35.
7. Veerapen K, Wigley RD, Valkenburg H. Musculoskeletal pain in Malaysia: a COPCORD survey. *J Rheumatol*. 2007 Jan;34(1):207-13.
8. Blagojevic M, Jink, C, Jeffery A, et al. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2010 Jan;18(1):24-33.
9. Spector TD, Cicuttini F, Baker J, et al. Genetic influences on osteoarthritis in women: a twin study. *BMJ*. 1996 Apr 13;312(7036):940-3.
10. Tanamas S, Hanna, FS, Cicuttini FM, et al. Does knee malalignment increase the risk of development and progression of knee osteoarthritis? A systematic review. *Arthritis Rheum*. 2009 Apr 15;61(4):459-67.
11. Ministry of Health Malaysia. Management of Osteoarthritis. Kuala Lumpur: MoH; 2002.
12. Altman R, Alarcon G, Appelrouth D, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. *Arthritis Rheum*. 1990 Nov;33(11):1601-10.
13. Altman R, Alarcon G, Appelrouth D, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. *Arthritis Rheum*. 1991 May;34(5):505-14.
14. Altman R, Asch E, Bloch D, et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum*. 1986 Aug;29(8):1039-49.
15. Zhang W, Doherty M, Peat G, et al. EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis. *Ann Rheum Dis*. 2010 Mar;69(3):483-9.
16. Moller B, Bonel H, Rotzetter M, et al. Measuring finger joint cartilage by ultrasound as a promising alternative to conventional radiograph imaging. *Arthritis Rheum*. 2009 Apr 15;61(4):435-41.
17. Keen HI, Wakefield RJ, Grainger AJ, et al. An ultrasonographic study of osteoarthritis of the hand: synovitis and its relationship to structural pathology and symptoms. *Arthritis Rheum*. 2008 Dec 15;59(12):1756-63.
18. D'Agostino MA, Conaghan P, Le Bars M, et al. EULAR report on the use of ultrasonography in painful knee osteoarthritis. Part 1: prevalence of inflammation in osteoarthritis. *Ann Rheum Dis*. 2005 Dec;64(12):1703-9.
19. Conaghan P, D'Agostino MA, Ravaud P, et al. EULAR report on the use of ultrasonography in painful knee osteoarthritis. Part 2: exploring decision rules for clinical utility. *Ann Rheum Dis*. 2005 Dec;64(12):1710-4.
20. Kao M-J, Wu M-P, Tsai M-W, et al. The effectiveness of a self-management program on quality of life for knee osteoarthritis (OA) patients. *Arch Gerontol Geriatr*. 2012 Mar-Apr;54(2):317-24.
21. Coleman S, Briffa NK, Carroll G, et al. A randomised controlled trial of a self-management education program for osteoarthritis of the knee delivered by health care professionals. *Arthritis Res Ther*. 2012;14(1):R21.
22. Hansson EE, Jonsson-Lundgren M, Ronnheden AM, et al. Effect of an education programme for patients with osteoarthritis in primary care--a randomized controlled trial. *BMC Musculoskeletal Disord*. 2010;11:244.
23. Ravaud P, Flipo RM, Boutron I, et al. ARTIST (osteoarthritis intervention standardized) study of standardised consultation versus usual care for patients with osteoarthritis of the knee in primary care in France: pragmatic randomised controlled trial. *BMJ*. 2009;338:b421.

24. Pendleton A, Arden N, Dougados M, et al. EULAR recommendations for the management of knee osteoarthritis: report of a task force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Ann Rheum Dis.* 2000 Dec;59(12):936-44.
25. Egger GJ, Binns AF, Rössner SR. *Lifestyle Medicine.* Sydney: McGraw-Hill; 2007.
26. Bliddal H, Leeds AR, Stigsgaard L, et al. Weight loss as treatment for knee osteoarthritis symptoms in obese patients: 1-year results from a randomised controlled trial. *Ann Rheum Dis.* 2011 Oct;70(10):1798-803.
27. Christensen R, Bartels EM, Astrup A, et al. Effect of weight reduction in obese patients diagnosed with knee osteoarthritis: a systematic review and meta-analysis. *Ann Rheum Dis.* 2007 Apr;66(4):433-9.
28. Messier SP, Loeser RF, Miller GD, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. *Arthritis Rheum.* 2004 May;50(5):1501-10.
29. Messier SP, Gutekunst DJ, Davis C, et al. Weight loss reduces knee-joint loads in overweight and obese older adults with knee osteoarthritis. *Arthritis Rheum.* 2005 Jul;52(7):2026-32.
30. Fernandes L, Hagen KB, Bijlsma JW, et al. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. *Ann Rheum Dis.* 2013 Jul;72(7):1125-35.
31. Fransen M, McConnell S Exercise for osteoarthritis of the knee. *Cochrane Database of Systematic Reviews* 2008, Issue 4 Art No: CD004376.
32. Fransen M, McConnell S, Hernandez-Molina G, et al. . Exercise for osteoarthritis of the hip. *Cochrane Database of Systematic Reviews* 2009, Issue 3 Art No: CD007912.
33. Bartels EM, Lund H, Hagen KB, et al Aquatic exercise for the treatment of knee and hip osteoarthritis. *Cochrane Database of Systematic Reviews* 2007, Issue 4 Art No: CD005523.
34. Rutjes AWS, Nüesch E, Sterchi R, et al Transcutaneous electrostimulation for osteoarthritis of the knee. *Cochrane Database of Systematic Reviews* 2009, Issue 4 Art No: CD002823.
35. Hochberg MC, Altman RD, April KT, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res.* 2012 Apr;64(4):465-74.
36. Brosseau L, Yonge KA, Welch V, et al. Thermotherapy for treatment of osteoarthritis. *Cochrane Database of Systematic Reviews* 2003, Issue 4 Art No: CD004522.
37. Rutjes AWS, Nüesch E, Sterchi R, et al Therapeutic ultrasound for osteoarthritis of the knee or hip. *Cochrane Database of Systematic Reviews* 2010, Issue 1 Art No: CD003132.
38. National Collaborating Centre for Chronic Conditions. Osteoarthritis: national clinical guideline for care and management in adults. London Royal College of Physicians; 2008.
39. Stamm TA, Machold KP, Smolen JS, et al. Joint protection and home hand exercises improve hand function in patients with hand osteoarthritis: a randomized controlled trial. *Arthritis Rheum.* 2002 Feb;47(1):44-9.
40. Boustedt C, Nordenskiöld U, Lundgren Nilsson A. Effects of a hand-joint protection programme with an addition of splinting and exercise: one year follow-up. *Clin Rheumatol.* 2009 Jul;28(7):793-9.
41. Shakoor MA, Taslim MA, Hossain MS. Effects of activity modification on the patients with osteoarthritis of the knee. *Bangladesh Med Res Counc Bull.* 2007 Aug;33(2):55-9.
42. Gay MC, Philippot P, Luminet O. Differential effectiveness of psychological interventions for reducing osteoarthritis pain: a comparison of Erikson [correction of Erickson] hypnosis and Jacobson relaxation. *Eur J Pain.* 2002;6(1):1-16.
43. McCaffrey R, Freeman E. Effect of music on chronic osteoarthritis pain in older people. *J Adv Nurs.* 2003 Dec;44(5):517-24.
44. Baird CL, Sands LP. Effect of guided imagery with relaxation on health-related quality of life in older women with osteoarthritis. *Res Nurs Health.* 2006 Oct;29(5):442-51.
45. Barrios JA, Crenshaw JR, Royer TD, et al. Walking shoes and laterally wedged orthoses in the clinical management of medial tibiofemoral osteoarthritis: a one-year prospective controlled trial. *Knee.* 2009 Mar;16(2):136-42.
46. Hunter DJ, Harvey W, Gross KD, et al. A randomized trial of patellofemoral bracing for treatment of patellofemoral osteoarthritis. *Osteoarthritis Cartilage.* 2011 Jul;19(7):792-800.
47. Brouwer RW, van Raaij TM, Verhaar JAN, et al. Brace treatment for osteoarthritis of the knee: a prospective randomized multi-centre trial. *Osteoarthritis Cartilage.* 2006 Aug;14(8):777-83.
48. Towheed T, Maxwell L, Judd M, et al. Acetaminophen for osteoarthritis. *Cochrane Database of Systematic Reviews* 2006, Issue 1 Art No: CD004257.

49. Lee C, Straus WL, Balshaw R, et al. A comparison of the efficacy and safety of nonsteroidal antiinflammatory agents versus acetaminophen in the treatment of osteoarthritis: a meta-analysis. *Arthritis Rheum* 2004 Oct 15;51(5):746-54.
50. Altman RD, Zinsenheim JR, Temple AR, et al. Three-month efficacy and safety of acetaminophen extended-release for osteoarthritis pain of the hip or knee: a randomized, double-blind, placebo-controlled study. *Osteoarthritis Cartilage*. 2007 Apr;15(4):454-61.
51. Doherty M, Hawkey C, Goulder M, et al. A randomised controlled trial of ibuprofen, paracetamol or a combination tablet of ibuprofen/paracetamol in community-derived people with knee pain. *Ann Rheum Dis*. 2011 Sep;70(9):1534-41.
52. Temple AR, Benson GD, Zinsenheim JR, et al. Multicenter, randomized, double-blind, active-controlled, parallel-group trial of the long-term (6-12 months) safety of acetaminophen in adult patients with osteoarthritis. *Clin Ther*. 2006 Feb;28(2):222-35.
53. Cepeda MS, Camargo F, Zea C, et al. Tramadol for osteoarthritis: a systematic review and metaanalysis. *J Rheumatol*. 2007 Mar;34(3):543-55.
54. Thorne C, Beaulieu AD, Callaghan DJ, et al. A randomized, double-blind, crossover comparison of the efficacy and safety of oral controlled-release tramadol and placebo in patients with painful osteoarthritis. *Pain Res Manag*. 2008 Mar-Apr;13(2):93-102.
55. Beaulieu AD, Peloso PM, Haraoui B, et al. Once-daily, controlled-release tramadol and sustained-release diclofenac relieve chronic pain due to osteoarthritis: a randomized controlled trial. *Pain Res Manag*. 2008 Mar-Apr;13(2):103-10.
56. Rosenthal NR, Silverfield JC, Wu SC, et al. Tramadol/acetaminophen combination tablets for the treatment of pain associated with osteoarthritis flare in an elderly patient population. *J Am Geriatr Soc*. 2004 Mar;52(3):374-80.
57. Silverfield JC, Kamin M, Wu SC, et al. Tramadol/acetaminophen combination tablets for the treatment of osteoarthritis flare pain: a multicenter, outpatient, randomized, double-blind, placebo-controlled, parallel-group, add-on study. *Clin Ther*. 2002 Feb;24(2):282-97.
58. Bjordal JM, Ljunggren AE, Klovning A, et al. Non-steroidal anti-inflammatory drugs, including cyclo-oxygenase-2 inhibitors, in osteoarthritic knee pain: meta-analysis of randomised placebo controlled trials. *BMJ*. 2004 Dec 4;329(7478):1317.
59. Singh G, Fort JG, Goldstein JL, et al. Celecoxib versus naproxen and diclofenac in osteoarthritis patients: SUCCESS-I Study.[Erratum appears in *Am J Med*. 2006 Sep;119(9):801]. *Am J Med*. 2006 Mar;119(3):255-66.
60. Bingham CO 3rd, Smugar SS, Wang H, et al. Early response to COX-2 inhibitors as a predictor of overall response in osteoarthritis: pooled results from two identical trials comparing etoricoxib, celecoxib and placebo. *Rheumatology (Oxford)*. 2009 Sep;48(9):1122-7.
61. Castellsague J, Riera-Guardia N, Calingaert B, et al. Individual NSAIDs and upper gastrointestinal complications: a systematic review and meta-analysis of observational studies (the SOS project). *Drug Saf*. 2012 Dec 1;35(12):1127-46.
62. Laine L, Curtis SP, Cryer B, et al. Assessment of upper gastrointestinal safety of etoricoxib and diclofenac in patients with osteoarthritis and rheumatoid arthritis in the Multinational Etoricoxib and Diclofenac Arthritis Long-term (MEDAL) programme: a randomised comparison. *Lancet*. 2007 Feb 10;369(9560):465-73.
63. Hunt RH, Harper S, Callegari P, et al. Complementary studies of the gastrointestinal safety of the cyclo-oxygenase-2-selective inhibitor etoricoxib. *Aliment Pharmacol Ther*. 2003 Jan;17(2):201-10.
64. Hunt RH, Harper S, Watson DJ, et al. The gastrointestinal safety of the COX-2 selective inhibitor etoricoxib assessed by both endoscopy and analysis of upper gastrointestinal events. *Am J Gastroenterol*. 2003 Aug;98(8):1725-33.
65. Rostom A, Dube C, Wells GA, et al. Prevention of NSAID-induced gastroduodenal ulcers. *Cochrane Database of Systematic Reviews* 2002, Issue 4 Art No: CD002296.
66. Sugano K, Kontani T, Katsuo S, et al. Lansoprazole for secondary prevention of gastric or duodenal ulcers associated with long-term non-steroidal anti-inflammatory drug (NSAID) therapy: results of a prospective, multicenter, double-blind, randomized, double-dummy, active-controlled trial. *J Gastroenterol*. 2012 May;47(5):540-52.
67. Sugano K, Matsumoto Y, Itabashi T, et al. Lansoprazole for secondary prevention of gastric or duodenal ulcers associated with long-term low-dose aspirin therapy: results of a prospective, multicenter, double-blind, randomized, double-dummy, active-controlled trial. *J Gastroenterol*. 2011 Jun;46(6):724-35.
68. Chan FKL, Lanas A, Scheiman J, et al. Celecoxib versus omeprazole and diclofenac in patients with osteoarthritis and rheumatoid arthritis (CONDOR): a randomised trial.[Erratum appears in *Lancet*. 2011 Jul 16;378(9787):228]. *Lancet*. 2010 Jul 17;376(9736):173-9.

69. Trelle S, Reichenbach S, Wandel S, et al. Cardiovascular safety of non-steroidal anti-inflammatory drugs: network meta-analysis. *BMJ*. 2011;342:c7086.
70. Combe B, Swergold G, McLay J, et al. Cardiovascular safety and gastrointestinal tolerability of etoricoxib vs diclofenac in a randomized controlled clinical trial (The MEDAL study). *Rheumatology (Oxford)*. 2009 Apr;48(4):425-32.
71. Ministry of Health Malaysia. Management of Chronic Kidney Disease. Putrajaya: MoH; June 2011.
72. Wandel S, Juni P, Tendal B, et al. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis. *BMJ*. 2010;341:c4675.
73. Black C, Clar C, Henderson R, et al. The clinical effectiveness of glucosamine and chondroitin supplements in slowing or arresting progression of osteoarthritis of the knee: a systematic review and economic evaluation. *Health Technol Assess*. 2009 Nov Nov;13(52):1-148.
74. Towheed T, Maxwell L, Anastassiades TP, et al. Glucosamine therapy for treating osteoarthritis. *Cochrane Database of Systematic Reviews* 2005, Issue 2 Art No: CD002946.
75. Sawitzke AD, Shi H, Finco MF, et al. Clinical efficacy and safety of glucosamine, chondroitin sulphate, their combination, celecoxib or placebo taken to treat osteoarthritis of the knee: 2-year results from GAIT. *Ann Rheum Dis*. 2010 Aug;69(8):1459-64.
76. Sawitzke AD, Shi H, Finco MF, et al. The effect of glucosamine and/or chondroitin sulfate on the progression of knee osteoarthritis: a report from the glucosamine/chondroitin arthritis intervention trial. *Arthritis Rheum*. 2008 Oct;58(10):3183-91.
77. Pavelka K, Gatterova J, Olejarova M, et al. Glucosamine sulfate use and delay of progression of knee osteoarthritis: a 3-year, randomized, placebo-controlled, double-blind study. *Arch Intern Med*. 2002 Oct 14;162(18):2113-23.
78. Dostrovsky NR, Towheed TE, Hudson RW, et al. The effect of glucosamine on glucose metabolism in humans: a systematic review of the literature. *Osteoarthritis Cartilage*. 2011 Apr;19(4):375-80.
79. Kahan A, Uebelhart D, De Vathaire F, et al. Long-term effects of chondroitins 4 and 6 sulfate on knee osteoarthritis: the study on osteoarthritis progression prevention, a two-year, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum*. 2009 Feb;60(2):524-33.
80. Gabay C, Medinger-Sadowski C, Gascon D, et al. Symptomatic effects of chondroitin 4 and chondroitin 6 sulfate on hand osteoarthritis: a randomized, double-blind, placebo-controlled clinical trial at a single center. *Arthritis Rheum*. 2011 Nov;63(11):3383-91.
81. Rovetta G, Monteforte P, Molfetta G, et al. A two-year study of chondroitin sulfate in erosive osteoarthritis of the hands: behavior of erosions, osteophytes, pain and hand dysfunction. *Drugs Exp Clin Res*. 2004;30(1):11-6.
82. Rovetta G, Monteforte P, Molfetta G, et al. Chondroitin sulfate in erosive osteoarthritis of the hands. *Int J Tissue React*. 2002;24(1):29-32.
83. Verbruggen G, Goemaere S, Veys EM. Systems to assess the progression of finger joint osteoarthritis and the effects of disease modifying osteoarthritis drugs. *Clin Rheumatol*. 2002 Jun;21(3):231-43.
84. Rintelen B, Neumann K, Leeb BF. A meta-analysis of controlled clinical studies with diacerein in the treatment of osteoarthritis.[Erratum appears in *Arch Intern Med*. 2007 Mar 12;167(5):444]. *Arc Intern Med*. 2006 Sep 25;166(17):1899-906.
85. Pavelka K, Trc T, Karpas K, et al. The efficacy and safety of diacerein in the treatment of painful osteoarthritis of the knee: a randomized, multicenter, double-blind, placebo-controlled study with primary end points at two months after the end of a three-month treatment period. *Arthritis Rheum*. 2007 Dec;56(12):4055-64.
86. Louthrenoo W, Nilganuwong S, Aksaranugraha S, et al. The efficacy, safety and carry-over effect of diacerein in the treatment of painful knee osteoarthritis: a randomised, double-blind, NSAID-controlled study. *Osteoarthritis Cartilage*. 2007 Jun;15(6):605-14.
87. Dougados M, Nguyen M, Berdah L, et al. Evaluation of the structure-modifying effects of diacerein in hip osteoarthritis: ECHODIAH, a three-year, placebo-controlled trial. Evaluation of the Chondromodulating Effect of Diacerein in OA of the Hip. *Arthritis Rheum*. 2001 Nov;44(11):2539-47.
88. Brahmachari B, Chatterjee S, Ghosh A. Efficacy and safety of diacerein in early knee osteoarthritis: a randomized placebo-controlled trial. *Clin Rheumatol*. 2009 Oct;28(10):1193-8.
89. Bellamy N, Campbell J, Welch V, et al. Intraarticular corticosteroid for treatment of osteoarthritis of the knee. *Cochrane Database of Systematic Reviews* 2006, Issue 2 Art No: CD005328.
90. Rutjes AWS, Juni P, da Costa BR, et al. Viscosupplementation for osteoarthritis of the knee: a systematic review and meta-analysis. *Ann Intern Med*. 2012 Aug 7;157(3):180-91.

91. Bellamy N CJ, Welch V, et al. Viscosupplementation for the treatment of osteoarthritis of the knee. *Cochrane Database of Systematic Reviews* 2006, Issue 2 Art No: CD005321.
92. Niethard FU, Gold MS, Solomon GS, et al. Efficacy of topical diclofenac diethylamine gel in osteoarthritis of the knee. *J Rheumatol.* 2005 Dec;32(12):2384-92.
93. Towheed TE. Pennsaid therapy for osteoarthritis of the knee: a systematic review and metaanalysis of randomized controlled trials. *J Rheumatol.* 2006 Mar;33(3):567-73.
94. Trnavsky K, Fischer M, Vogtle-Junkert U, et al. Efficacy and safety of 5% ibuprofen cream treatment in knee osteoarthritis. Results of a randomized, double-blind, placebo-controlled study. *J Rheumatol.* 2004 Mar;31(3):565-72.
95. Makris UE, Kohler MJ, Fraenkel L. Adverse effects of topical nonsteroidal antiinflammatory drugs in older adults with osteoarthritis: a systematic literature review. *J Rheumatol.* 2010 Jun;37(6):1236-43.
96. Manheimer E, Cheng K, Linde K, et al. Acupuncture for peripheral joint osteoarthritis. . *Cochrane Database of Systematic Reviews* 2010, Issue 1 Art No: CD001977.
97. Little CV, Parsons T, Logan S. . Herbal therapy for treating osteoarthritis. *Cochrane Database of Systematic Reviews* 2000, Issue 4 Art No: CD002947.
98. Christensen R, Bartels EM, Astrup A, et al. Symptomatic efficacy of avocado-soybean unsaponifiables (ASU) in osteoarthritis (OA) patients: a meta-analysis of randomized controlled trials. *Osteoarthritis Cartilage.* 2008 Apr;16(4):399-408.
99. Bliddal H, Rosetzky A, Schlichting P, et al. A randomized, placebo-controlled, cross-over study of ginger extracts and ibuprofen in osteoarthritis. *Osteoarthritis Cartilage.* 2000 Jan;8(1):9-12.
100. Moseley B. Arthroscopic surgery did not provide additional benefit to physical and medical therapy for osteoarthritis of the knee. *J Bone Joint Surg Am.* [Comment]. 2009 May;91(5):1281.
101. Kirkley A, Birmingham TB, Litchfield RB, et al. A randomized trial of arthroscopic surgery for osteoarthritis of the knee.[Erratum appears in *N Engl J Med.* 2009 Nov 12;361(20):2004]. *N Engl J Med.* 2008 Sep 11;359(11):1097-107.
102. Health Quality Ontario. Total knee replacement: an evidence-based analysis. *Ontario Health Technol Assess Ser.* 2005;5(9):1-51.
103. Canadian Institute for Health Information. Canadian Joint Replacement Registry 2004 Annual Report CIHI.
104. Spahn G, Hofmann GO, von Engelhardt LV, et al. The impact of a high tibial valgus osteotomy and unicondylar medial arthroplasty on the treatment for knee osteoarthritis: a meta-analysis. *Knee Surg Sports Traumatol Arthrosc.* 2013 Jan;21(1):96-112.
105. Ministry of Health Singapore. Osteoarthritis of the Knees. Singapore: MoH; 2007.
106. Health Technology Assessment Section (MaHTAS) MDD, Ministry of Health Malaysia. Autologous Peripheral Blood Stem Cells for Articular Cartilage Repair. Serial No. 006/2013.2013.
107. Vasiliadis HS, Wasiak J. Autologous chondrocyte implantation for full thickness articular cartilage defects of the knee. *Cochrane Database of Systematic Reviews* 2010, Issue 10 Art No: CD003323.
108. Spakova T, Rosocha J, Lacko M, et al. Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. *Am J Phys Med Rehabil.* 2012 May;91(5):411-7.
109. Kon E, Buda R, Filardo G, et al. Platelet-rich plasma: intra-articular knee injections produced favorable results on degenerative cartilage lesions. *Knee Surg Sports Traumatol Arthrosc.* 2010 Apr;18(4):472-9.

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

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

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

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

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

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

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

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

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?

**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	Dysthymia, cyclothymia, fibromyalgia
	Ethnic, cultural, coping skills

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 knees down firmly against the bed. Hold for five seconds, then return to the original position and relax.

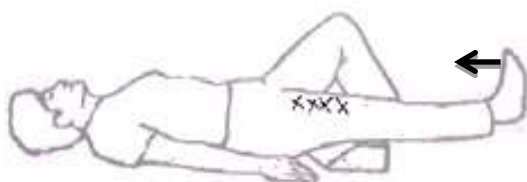


Figure C

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.

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.

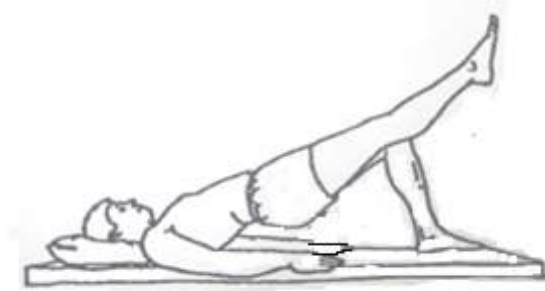


Figure B

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

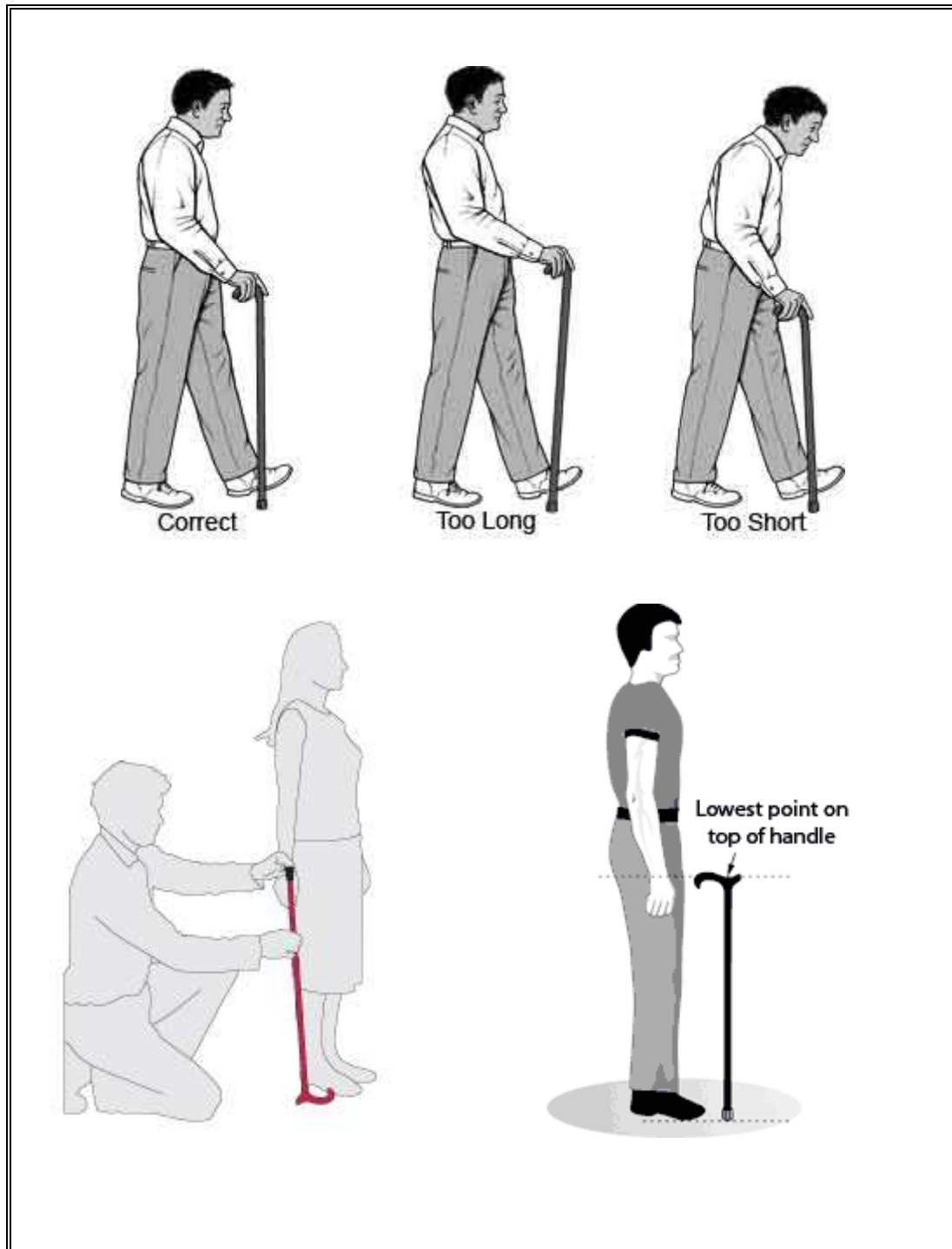
Lie on your back with knees bent. Squeeze your buttocks together and lift your bottom off the floor. Hold for five seconds, then return to the original position and relax.



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.

APPROPRIATE MEASUREMENT FOR WALKING STICK



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 minimize 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 Counc Bull. 2007 Aug;33(2):55-9

SUGGESTED MEDICATION DOSAGES AND SIDE EFFECTS

Drug Class	Drug	Recommended Dosages	Side effects	Caution and Contraindications	Comments
Simple analgesic	Paracetamol	0.5 – 1gm, 6 – 8-hourly Max: 4gm/day	Rare	Hepatic impairment, alcohol dependence	Preferred drug particularly in elderly patients Liver damage following overdose
Non-selective NSAIDs	Ibuprofen	400 – 800 mg, 6 – 8-hourly Max: 3200 mg/day	Peptic ulcer GI bleed	Gastroduodenal ulcer Asthma	Current data suggest that increased CV risk may be an effect of the NSAID/coxib class Physicians and patients should weigh the benefits and risks of NSAID/coxib therapy
	Mefenemic Acid	250 – 500 mg, 6 – 8-hourly Max: 1500 mg/day	Platelet dysfunction Renal impairment	Bleeding disorder Renal dysfunction	
	Diclofenac sodium	50 – 150 mg daily, 8 – 12 hourly Max: 150 mg/day	Hypertension Allergic reaction in susceptible individuals	Ischaemic heart disease Cerebrovascular disease	
	Meloxicam	7.5 – 15 mg daily Max: 15 mg/day	Increase in CVS events	Inflammatory bowel disease	
	Naproxen	250 – 500 mg, 12-hourly Max: 1500 mg/day			
	Naproxen sodium	275- 550 mg, 12 hourly Max: 1650mg/day			
Selective COX -2 inhibitors	Piroxicam	10 – 20 mg daily, in single or divided doses Max: 20 mg/day			
	Celecoxib	200 mg daily Max: 200 mg/day	Renal impairment Allergic reaction in susceptible individuals Increase in CVS events	Ischaemic heart disease Cerebrovascular disease Contraindicated in hypersensitivity to 37learance37des	Associated with a lower risk of serious upper gastrointestinal side effects Current data suggest that increased CV risk may be an effect of the NSAID/coxib class

Drug Class	Drug	Recommended Dosages	Side effects	Caution and Contraindications	Comments
	Etoricoxib	60 mg daily Max: 90 mg/day	Hypertension Renal impairment Increase in CVS events	Uncontrolled hypertension Ischaemic heart disease Cerebrovascular disease	Physicians and patients should weigh the benefits and risks of NSAID/coxib therapy
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 mg daily	Interaction with TCA, SSRI and SNRI
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 3 divided doses Max 1500 mg/day	Nausea Dyspepsia Heartburn Vomiting Constipation Diarrhoea Headache	Hypersensitivity to glucosamine or any of its components Use with caution for patients with an allergy to shellfish and shellfish products Asthmatic patients may be at risk for an asthma exacerbation when taking the combination of glucosamine and chondroitin	

Drug	Recommended Dosages	Side effects	Caution and Contraindications	Comments
Chondroitin sulfate	200 – 400 mg, 8 – 12 hourly Max 1200 mg	Dyspepsia Nausea Vomiting	Asthmatic patients may be at risk for an asthma exacerbation when taking chondroitin Contraindicated in patients with prostate cancer or are at high risk for developing prostate cancer Caution in diabetics as chondroitin affects glucose level	
Diacerein	50 mg 12-hourly	Diarrhoea Epigastric pain Nausea Vomiting Intense yellow colouring of urine Skin reactions	Hypersensitivity to anthraquinone derivatives Inflammatory organic bowel disease (ulcerative colitis, Crohn's disease) Intestinal obstruction or partial obstruction, Severe liver failure Rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption due to presence of lactose.	Creatinine clearance (ml/min) <30 Dosage Recommendation 25 mg daily Antacid use may decrease diacerein absorption, so it is advised to take antacids within an interval of two hours
Avocado soybean unsaponifiables	300 mg daily	Diarrhea 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	Infrequent lipid-scented regurgitations which may be avoided by taking the capsule during a meal.

Sources:

- i. Sunthornsaj N, Fun LW, Evangelista LF et. Al (Ed). MIMS.com. 117th Edition 2009. Hong Kong: CMPMedica; 2009
- ii. Thomson Reuters. Micromedex® 1.0 (Healthcare Series). Greenwood Village Thomson Reuters; 2009
- iii. [National Drug Formulary 2008, Pharmaceutical Services Division, Ministry of Health Malaysia](#)
- iv. [Summary of Product Characteristics, PIASCLEDINE®300. Expanscience™ Laboratoires.](#)

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
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
MD	mean difference
mg	milligram
mL	milliliter
mm	millimeter
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
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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