# NATIONAL CLINICAL GUIDELINES

THE MANAGEMENT OF OSTEARTHRITIS IN ADULTS

# Ministry of Public Health

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# **Abbreviations**

The abbreviations used in this guideline are as follows:

ACI Autologous Chondrocyte Implantation

AMIC Autologous Matrix Induced Chondrogenesis

ANA Antinuclear Antibodies

Anti-CCP Anticyclic Citrullinated Peptide

**BMI** Body mass index

**CBC** Complete Blood Count

COX-2 Cyclo-Oxygenase 2

**CRFA** Cooled radiofrequency ablation

**CRP** C-Reactive Protein

**ESR** Erythrocyte Sedimentation Rate

**ESWT** Extra-corporeal shockwave therapy

MCM Methylsulfonylmethane

MDT Multidisciplinary Team

**MWM** Mobilisation with movement

NSAID Non-Steroidal Anti-Inflammatory Drug

**OA** Osteoarthritis

**ROM** Range of Motion Test

**TENS** Transcutaneous Electrical Nerve Stimulation

**U&E** Urea and Electrolytes Test

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# 1 Information about this Guideline

#### 1.1 Objective and Purpose of the Guideline

The purpose of this guideline is to define the appropriate prevention, diagnosis, and management of osteoarthritis in adults aged 40 years old and above. The objective is to guide the appropriate prevention, investigation, treatment, and referral of patients presenting to provider organisations in Qatar. It is intended that the guideline will be used primarily by healthcare professionals in Primary and Specialist Care settings, especially orthopaedic surgeons, rheumatologists, physiotherapists and sport medicine specialists.

#### 1.2 Scope of the Guideline

This guideline covers the following aspects of care:

- Investigation of patients with suspected osteoarthritis.
- Primary Care Management, including education and lifestyle advice, physiotherapy, Dietary supplements, and pharmacological treatments.
- Criteria for referral to Specialist Care.
- Specialist management, including opioid analgesia, Intra-articular joint injections, and surgical management.

# 1.3 Editorial Approach

This guideline document has been developed and issued by the Ministry of Public Health of Qatar (MOPH), through a process which aligns with international best practice in guideline development and localisation. The guideline will be reviewed on a regular basis and updated to incorporate comments and feedback from stakeholders across Qatar.

The editorial methodology, used to develop this guideline, has involved the following critical steps:

- Extensive literature search for well-reputed, published evidence relating to the topic.
- Critical appraisal of the literature.
- Development of a draft summary guideline.
- Review of the summary guideline with a Guideline Development Group, comprised of practising healthcare professionals, subject matter experts and patient representatives, from across Qatar.
- Independent review of the guideline by the National Clinical Guidelines & Pathways Committee, appointed by the MOPH, from amongst stakeholder organisations across Qatar.

Whilst the MOPH has sponsored the development of the guideline, the MOPH has not influenced the specific recommendations made within it.

#### 1.4 Sources of Evidence

The professional literature published in the English language has been systematically queried using specially developed, customised, and tested search strings. Search strategies are developed to allow efficient yet comprehensive analysis of relevant publications for a given topic and to maximise retrieval of articles with certain desired characteristics pertinent to a guideline.

For each guideline, all retrieved publications have been individually reviewed by a clinical editor and assessed in terms of quality, utility, and relevance. Preference is given to publications that:

- 1. Are designed with rigorous scientific methodology.
- 2. Are published in higher-quality journals (i.e. journals that are read and cited most often within their field).
- 3. Address an aspect of specific importance to the guideline in question.

Further information about the literature search and appraisal process is included in the appendix.

# 1.5 Evidence Grading and Recommendations

Recommendations made within this guideline are supported by evidence from the medical literature and where possible the most authoritative sources have been used in the development of this guideline. In order to provide insight into the evidence basis for each recommendation, the following evidence hierarchy has been used to grade the level of authoritativeness of the evidence used, where recommendations have been made within this guideline.

Where the recommendations of international guidelines have been adopted, the evidence grading is assigned to the underlying evidence used by the international guideline. Where more than one source has been cited, the evidence grading relates to the highest level of evidence cited:

# Level 1 (L1):

- o Meta-analyses.
- o Randomised controlled trials with meta-analysis.
- o Randomised controlled trials.
- o Systematic reviews.

# Level 2 (L2):

- o Observational studies, examples include:
  - Cohort studies with statistical adjustment for potential confounders.
  - Cohort studies without adjustment.
  - Case series with historical or literature controls.
  - Uncontrolled case series.
- o Statements in published articles or textbooks.

#### Level 3 (L3):

- Expert opinion.
- Unpublished data, examples include:
  - Large database analyses.
  - Written protocols or outcomes reports from large practices.

In order to give additional insight into the reasoning underlying certain recommendations and the strength of recommendation, the following recommendation grading has been used, where recommendations are made:

- Recommendation Grade A (RGA): Evidence demonstrates at least moderate certainty of at least moderate net benefit.
- Recommendation Grade B (RGB): Evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended.
- Recommendation Grade C (RGC): Evidence demonstrates potential harm that outweighs benefit; additional research is recommended.
- Recommendation of the GDG (R-GDG): Recommended best practice based on the clinical experience of the Guideline Development Group members.

# 1.6 Guideline Development Group Members

The following table lists members of the Guideline Development Group (GDG) nominated by their respective organisations and the Clinical Governance Group. The GDG members have reviewed and provided feedback on the draft guideline relating to the topic. Each member has completed a declaration of conflicts of interest, which has been reviewed and retained by the MOPH.

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# 1.7 National Clinical Guidelines & Pathways Committee Members

The following table lists members of the National Clinical Guidelines & Pathways Committee (NCGPC), appointed by the MOPH. The NCGPC members have reviewed and provided their feedback and approval of the guideline document. Each member has completed a declaration of conflicts of interest, which has been reviewed and retained by the MOPH.

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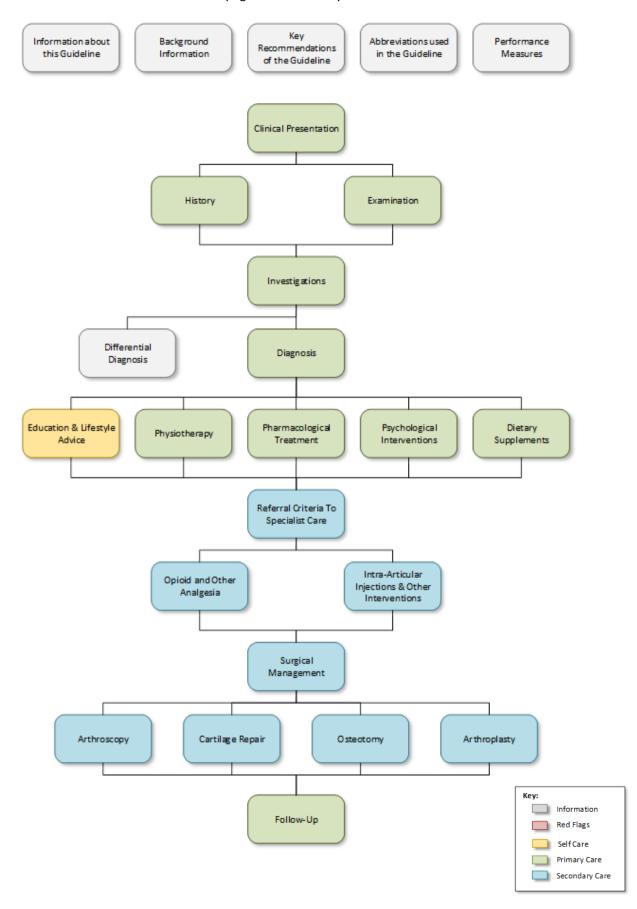
# 1.8 Responsibilities of Healthcare Professionals

This guideline has been issued by the MOPH to define how care should be provided in Qatar. It is based upon a comprehensive assessment of the evidence as well as its applicability to the national context of Qatar. Healthcare professionals are expected to take this guidance into account when exercising their clinical judgement in the care of patients presenting to them.

The guidance does not override individual professional responsibility to take decisions which are appropriate to the circumstances of the patient concerned. Such decisions should be made in consultation with the patient, their guardians, or carers and should consider the individual risks and benefits of any intervention that is contemplated in the patient's care.

# 2 Osteoarthritis Pathway

Click on a box below to see the relevant page of the Pathway.



# 3 Key Recommendations of the Guideline

The key recommendations of this guideline are:

#### **Clinical Presentation** (Section 5):

- The key symptoms of osteoarthritis (OA) include<sup>1,15</sup>:
  - o Joint pain (sudden or slowly developing).
  - Stiffness of the joint.
  - o Reduced function of the joint.
- OA symptoms typically worsen with activity or prolonged inactivity and improve with rest<sup>1–3</sup>.

# **Investigations** (Section 8):

- Blood tests are be expected to be normal in patients with OA, but patients with other types of rheumatological conditions (e.g. inflammatory arthritis), would have abnormal results<sup>1,3,19</sup>.
- The following investigations should be considered and performed when necessary:
  - Blood tests<sup>1,3,16,17,19</sup> [L1, RGA]:
    - Complete blood count (CBC).
    - Urea and electrolytes.
  - o Bilateral radiographs of joints should be taken. These should be standing radiographs when examining weight-bearing joints e.g. hip and knee <sup>1,3,16,17</sup> [**L1, RGB**].
- Radiographic findings do not correlate well with the severity of disease and may not be present at early stages<sup>1,19</sup>.

#### **Diagnosis** (Section 9):

- OA can be diagnosed without investigations, if the patient<sup>1,3,15</sup>:
  - o Is 45 years of age or older.
  - o Has pain that gets worse with activity and improves with rest.
  - Has ≤30 minutes of morning stiffness.
  - Has bony joint enlargement.
  - Has limited range of motion.
- Atypical features and a history of trauma may indicate alternative or additional diagnoses<sup>15</sup>.
- Knee pain is not always caused by OA. It can be referred from the lumbar spine or the hip joint 1,16.
- Some patients with OA may be asymptomatic<sup>21,22</sup>.

# **Primary Care Management** (Section 10):

- The primary care team should develop an OA management plan which focuses on improvement of function as well as on minimisation of pain and prevention of further functional loss<sup>1,3</sup> [L2, RGA].
- All treatment decisions should take into account patient's health beliefs and preferences, as well as their overall medical status<sup>4</sup> [L1, RGA].

# **Education and Lifestyle Advice** (Section 10.1):

- Consider behavioural interventions and lifestyle changes that are appropriate for the individual, including<sup>3,4,16,17,19</sup> [L1, RGA]:
  - Weight loss:
    - Interventions aimed at weight loss should be the core treatment for patients with a BMI of >25 kg/m².
    - Weight loss is strongly recommended for patients with OA of the knees and hips.
  - Optimisation of fitness.
  - Mood improvement.

- Reducing stress:
- Sleep hygiene:
- Ensuring optimal footwear with shock-absorbing properties for patients with lower limb OA.
- o Ensuring optimal seat height at desks (i.e. knee flexion is not less than 90°)<sup>24</sup>.

# **Exercise and Physiotherapy** (Section 10.2):

- Performing a wide range of exercises rather than focusing on a single type is recommended<sup>4,25</sup> [L1, RGA].
- Intensity of the activities should be adjusted for patient's abilities<sup>4,15,24</sup> [L1, RGA].
- If joints are very painful, stiff, strenuous exercises should be avoided<sup>24</sup> [**L2**, **RGC**].
- Physical therapy is not recommended for patients with later stages of hip OA as it provides little
  or no benefit<sup>26</sup> [L1, RGB].

#### Aids and Devices (Section 10.3):

- The following aids may be considered in patients with malalignment of joints<sup>1,3,4,15,16,19,25</sup> [L1, RGA]:
  - Knee braces or sleeves.
  - o Joint supports.
  - o Orthotic insoles.
  - Hand orthoses are strongly recommended for patients with OA of the first carpometacarpal joint.

#### **Pharmacological Treatment in Primary Care** (Section 10.4):

- Non-steroidal anti-inflammatory drugs (NSAIDs) are recommended as the first-line medication for pain relief in patients with OA<sup>1</sup>.
- The lowest effective dose of NSAIDs for the shortest possible period of time is highly encouraged<sup>1,15,16,19</sup> [L1, RGA]:
  - o **Topical NSAIDs** are preferred over oral NSAIDs<sup>15,33</sup> [L1, RGA]:
    - Recommended in patients with knee or hand osteoarthritis.
  - Oral NSAIDs/cyclo-oxygenase 2 (COX-2) inhibitors should be considered if topical NSAIDs are ineffective or provide insufficient pain relief<sup>15</sup> [L1, RGA]:
    - Oral NSAIDs/COX-2 inhibitors should be prescribed on an as required basis, rather than as a regular medication<sup>1</sup> [L2, RGA].
    - Before prescribing NSAIDs, associated modifiable and non-modifiable risk factors for adverse effects, should be considered [R-GDG].
  - Acetaminophen may be considered for short-term and episodic use<sup>4,19,34,35</sup> [L1, RGB].
  - Opioid analgesics have poor evidence in chronic pain from osteoarthritis and should be reserved for patients who do not achieve enough pain relief with acetaminophen and NSAIDs/COX-2 inhibitors<sup>15,19</sup>.
  - Such patients should be managed by a healthcare specialist in Specialist Care (see Section 12.1).

# **Psychological Interventions** (*Section 10.5*):

- Psychological interventions are associated with positive effects on pain, self-efficacy, fatigue, and coping in patient with OA<sup>41</sup> [L1, RGB].
- Interventions such as antidepressants, cognitive behavioural therapy (CBT) or stress management training, may be considered in patients with chronic pain<sup>4,42</sup> [L1, RGA].

#### **Referral Criteria to Specialist Care** (Section 11):

- Patients who require the following should be referred for specialist care:
  - o Pain management with opioid analgesics (see Section 12.1).
  - o Intra-articular injections and other interventions (see Section 12.2).
  - o Joint surgery (see *Sections 11.1 and 12.3*).
- Decisions about surgery should be based on discussions between the patient, referring clinicians and surgeons<sup>15</sup> [**L1**].
- The patient's age, sex, smoking, BMI, comorbidities as well as location and severity of OA should be reviewed prior to surgery but should not be barriers to referral<sup>3,15</sup>.

#### **Specialist Management** (Section 12):

- A multidisciplinary team (MDT) may be required to manage patients with OA. The MDT should include<sup>16</sup>:
  - o Physiotherapist.
  - o Dietitian.
  - Rheumatologist.
  - o Pain specialist.
  - o Internist.
  - Orthopaedic surgeon.
  - Sport and Exercise Medicine Physician (for athletes with OA).

# **Opioid and Other Analgesics in Specialist Care** (Section 12.1):

- If NSAIDs/COX-2 inhibitors and acetaminophen do not provide sufficient pain relief, opioid and other analgesics may be considered<sup>15,19</sup> [L1, RGA].
- The lowest effective dose for the shortest possible period of time is highly encouraged<sup>4</sup> [L1, RGA].
- Opioids are not recommended for periods longer than 1-3 months due to their side effects and long-term addiction potential<sup>19,40</sup> [L2, RGC].

#### Intra-Articular Injections and Other Interventions in Specialist Care (Section 12.2):

- Intraarticular injections of glucocorticoids can be considered for the relief of moderate to severe pain in people with OA<sup>1,4,15–17</sup> [L1, RGA].
  - The injections into hip joints should be made under fluoroscopic or ultrasound guidance to ensure accurate drug delivery into the joint<sup>4</sup> [L1, RGA].
  - Ultrasound guidance is not mandatory for injections into knee and hand joints<sup>4</sup> [L1, RGB].
     Use of ultrasound guidance is however preferable [R-GDG].
- Genicular branch block and genicular branch radiofrequency denervation for knee OA in patients not suitable for total knee replacement, may be considered<sup>49,50</sup>. However, these interventions should only be offered Specialist Care setting [**R-GDG**].

# **Surgical Management** (Section 12.3):

Surgical options for OA include<sup>3,51</sup>:

- Arthroscopy (see Section 12.3.1):
  - Arthroscopy is not recommended as routine treatment of knee OA<sup>15</sup> as its role is controversial<sup>3,51,53</sup>.
  - Arthroscopy may, however, be considered in some cases, e.g. in patients with knee OA and a superimposed structural lesion (e.g. meniscal tear)<sup>51,53</sup> [L2, RGB].

- Cartilage Repair (see Section 12.3.2):
  - Cartilage repair techniques should be considered in younger patients with cartilage lesions of limited size<sup>53</sup> [L2. RGA]:
    - The repair is indicated for patients with focal cartilage defects.
    - The repair is not indicated, if the defect is to extended cartilage.
  - Cartilage repair is not recommended in patients with<sup>53</sup> [**L2, RGB**]:
    - Axial malalignment.
    - Ligamentous instability.
    - Patella maltracking.
- Osteotomy (see Section 12.3.3):
  - Osteotomy may be considered<sup>51,53</sup> [**L2**]:
    - In younger patients with predominantly unicompartmental OA (e.g. knee OA with varus or valgus alignment).
    - In patients who undergo cartilage repair procedures and require normalisation of the biomechanical environment as an adjunct treatment.
  - Before osteotomy, the condition of the unaffected compartment(s) should be checked and its/their health confirmed<sup>53</sup> [L2].
- Partial and Total Arthroplasties (see Section 12.3.4):
  - Arthroplasty should be reserved as the last-choice treatment option<sup>51,53</sup> [L2]:
    - It should only be considered in patients:
      - With progressive knee instability or end-stage OA; and
      - For whom other treatments have failed or are contraindicated.
    - It should be avoided in patients younger than 60 years but can be performed in patients over the age of 50 years who have advanced debilitating OA [R-GDG].
  - Partial (unicompartmental) arthroplasty may be considered if only one compartment is affected by OA<sup>53</sup> [L2, RGA].
  - Total arthroplasty may be considered if more than one compartment of the joint is affected <sup>51,53</sup> [L2; RGA].
- Personalised rehabilitation exercise program should be offered to patients after surgery<sup>16,52</sup> [L2, RGA]
- After discharge from the hospital, patients should be encouraged to continue the rehabilitation exercise program at home<sup>52</sup> [L2, RGA].

# 4 Background Information

#### 4.1 Definition

Osteoarthritis (OA) is a degenerative joint disease, which leads to bone damage through a degenerative cascade of progressive cartilage loss<sup>1,2</sup>.

**Primary (idiopathic) OA** is diagnosed in the absence of a predisposing trauma or disease<sup>1,3</sup>. It is associated with risk factors listed in *Section 4.4*.

Secondary (posttraumatic) OA is characterised by pre-existing joint abnormality including 1,3:

- Trauma or injury.
- Congenital joint disorders.
- Inflammatory or infectious arthritis.
- Avascular necrosis.
- Paget's disease.
- Osteopetrosis.
- Osteochondritis dissecans.
- Metabolic disorders (e.g. hemochromatosis, Wilson's disease).
- Hemoglobinopathy.
- Ehlers-Danlos syndrome.
- Marfan syndrome.
- Crystal deposition.
- Acromegaly.

# 4.2 Prevalence

OA is the most common form of arthritis<sup>2,4,5</sup>. The most frequently affected appendicular joints are knees, hips, lower spine, and hands<sup>4,5</sup>.

The prevalence of OA is poorly documented in the Middle East region, including Qatar. In 2011-2012, the prevalence of OA was reported to be 70% among women of Qatari nationality and 30% among women of other nationalities residing in Qatar<sup>5</sup>. Of women with OA 87.5% were obese<sup>5</sup>. The WHO estimates that worldwide, 9.6% of men and 18.0% of women aged over 60 years have symptomatic osteoarthritis<sup>6</sup>.

Among active athletes 18-36 years old, which comprise one of risk groups (see *Section 4.4*), the prevalence of radiographically detected knee OA was 8.5%<sup>7</sup>.

# 4.3 Aetiology

OA is a disease characterised by pathology of the entire joint which leads to bone damage<sup>1,4</sup>. Pathological changes include<sup>4,8</sup>:

- Progressive loss and destruction of articular cartilage.
- Thickening of subchondral bone.
- Osteophyte formation.
- Inflammation of the synovium.
- Degeneration of ligaments and menisci of the knee.
- Hypertrophy of the joint capsule.

The earliest changes (surface fibrillation, irregularity, and focal erosions) occur in the articular cartilage<sup>4</sup>. With time, they expand and involve more of the joint surface. Bony erosions and thickenings can appear at later stages<sup>2,4</sup>. In end-stage OA, calcium phosphate and calcium pyrophosphate dihydrate crystals are present<sup>4</sup>.

#### 4.4 Risk Factors

Risk factors for developing OA include<sup>1,2,9-11</sup>:

- Older age.
- Gender:
  - Women are more likely to develop hand, foot, and knee OA<sup>12</sup>.
  - Men are more likely to develop shoulder and cervical spine OA<sup>13</sup>.
- Ethnicity.
- Obesity.
- Muscle weakness.
- Abnormal bone mineral density and mass.
- Abnormal loading of the joints.
- Poor diet (e.g. vitamin deficiency).
- Joint injury (e.g. fracture).
- Occupation (e.g. firefighting, construction work) and sports (e.g. professional sportsmen).

#### 4.5 Comorbidities

The following comorbid conditions are frequently associated with OA<sup>1,4,11,14</sup>:

- Radiculopathies.
- Hypertension.
- Cardiovascular diseases and stroke.
- Metabolic syndrome.
- Peptic ulcer.
- Mood disorders.
- Impaired coping skills.

# 4.6 Prognosis

OA cannot be cured. All treatments aim to reduce symptoms and either repair or replace damaged tissue<sup>1</sup>. Once the disease commences, OA is likely to progressively worsen over time. Currently, it is not possible to predict which patients will have rapid progressing OA and which patients will remain stable in the earlier stages of disease<sup>1</sup>.

Usually, rapid progression is seen in<sup>2</sup>:

- Older patients.
- Obese individuals.
- Patients with involvement of multiple joints.

The overall prognosis depends on the number of affected joints and the severity of the disease<sup>2</sup>. After joint replacement, the outcomes are generally good but the timing of surgery and fitness of the patient are key determinants of success<sup>1</sup>. Revision of prosthesis is usually required after 10-15 years<sup>2</sup>.

# 5 Clinical Presentation

The key symptoms of OA include<sup>1,15</sup>:

- Joint pain (sudden or slowly developing).
- Stiffness of the joint.
- Reduced function of the joint.

Other possible symptoms include<sup>1</sup>:

- Joint or bony swelling.
- Joint deformity.
- Muscle weakness.
- Balance problems.

OA symptoms typically worsen with activity or prolonged inactivity and improve with rest<sup>1-3</sup>.

In addition to OA symptoms, patients may experience additional symptoms as a result of pain and functional limitation. These include<sup>4</sup>:

- Mood disorders (e.g. depression, anxiety).
- Altered sleep.
- Chronic widespread pain.
- Impaired coping skills.

# 6 History

The following points in the history are important to elicit from the patient with suspected OA<sup>3,15,16</sup>:

- Information about their general health:
  - o Chronic health conditions.
  - Metabolic disorders.
  - o Obesity.
- History of injury or trauma to joints.
- Previous surgeries.
- Features of musculoskeletal pain:
  - Onset of symptoms.
  - Duration of pain and symptoms.
  - Specific location of pain.
  - Characteristics of the pain.
  - Alleviating and aggravating factors.
  - Radiation of pain.
  - Specific timing of symptoms.
  - Severity of symptoms.
  - The patient's functional activity.
- Psychological impact of the disease:
  - o Screening for mood disorders (depression and anxiety).
  - Other current stress in life.
- Social impacts of the disease:
  - Occupation and ability to perform their work.
  - Ability to complete activities of daily living.
  - Hobby and leisure activities.
  - o Family duties.
- Attitudes to exercise and sport activities.

- Influence of comorbidities:
  - o Sleep problems.
  - o Falls.
- Pain assessment:
  - Self-help strategies.
  - o Analgesics.
- Allergies to any medications.

# 7 Examination

If OA is suspected, a thorough examination should be performed<sup>1,3,16–20</sup> [L1, RGA]:

- Assessment of weight<sup>18</sup>:
  - Weight and height measurements.
  - o Calculation of the Body Mass Index (BMI).
  - Waist or neck circumference measurements (if BMI is not conclusive).
  - Blood pressure and pulse.
- Physical examination of the joints and surrounding tissues, including for signs of 1,3,17:
  - o Bony enlargement.
  - O Signs of inflammation (e.g. swelling, redness).
  - o Joint line tenderness.
  - o Erythema.
  - o Coarse crepitus.
  - Muscle atrophy.
  - o Effusions.
  - o Joint deformities (e.g. varus, valgus, Z-deformities).
  - Heberden's or Bouchard's nodes.
  - o Presence and location of any scars from previous surgical procedures or trauma.
- Range of motion<sup>3,16,17</sup>:
  - o Range of motion (ROM) examination (both active and passive).
  - Limitations of ROM.
  - o Abnormal motions.
  - o Loss of smooth mechanical movement.
  - Ligamentous instability.
- Strength and neurovascular assessments<sup>16,17</sup>.
- Comparison of leg length (relevant for hip OA)<sup>19</sup>.

# 8 Investigations

Blood tests are be expected to be normal in patients with OA, but patients with other types of rheumatological conditions (e.g. inflammatory arthritis), would have abnormal results<sup>1,3,19</sup>.

The following investigations should be considered and performed when necessary:

- Blood tests<sup>1,3,16,17,19</sup> [**L1, RGA**]:
  - o Complete blood count (CBC).
  - Urea and electrolytes.
- Bilateral radiographs of joints should be taken. These should be standing radiographs when examining weight-bearing joints e.g. hip and knee <sup>1,3,16,17</sup> [**L1, RGB**].
- Examine for:
  - o Dislocations.

- o Erosions.
- o Calcification.
- Marginal osteophytes.
- Joint space narrowing.
- Subchondral sclerosis.
- o Cysts.

Note: Radiographic findings do not correlate well with the severity of disease and may not be present at early stages<sup>1,19</sup>.

# 9 Diagnosis

OA can be diagnosed without investigations, if the patient<sup>1,3,15</sup>:

- Is 45 years of age or older.
- Has pain that gets worse with activity and improves with rest.
- Has ≤30 minutes of morning stiffness.
- Has bony joint enlargement.
- Has limited range of motion.

Radiography and laboratory tests are not always required for the diagnosis of OA and the condition can be diagnosed using clinical criteria only<sup>1,3,16,17</sup>.

# 9.1 Differential Diagnosis

The differential diagnosis of OA pain should include 1,15,17 [L1, RGA]:

- Rheumatoid arthritis.
- Psoriatic arthritis.
- Crystalline arthritis.
- Septic arthritis.
- Hemochromatosis.
- Bursitis.
- Avascular necrosis.
- Tendinitis.
- Radiculopathy.
- Malignancy.
- Other soft tissue abnormalities.

# Note:

- Atypical features and a history of trauma may indicate alternative or additional diagnoses<sup>15</sup>.
- Knee pain is not always caused by OA. It can be referred from the lumbar spine or the hip joint<sup>11,16</sup>.
- Some patients with OA may be asymptomatic<sup>21,22</sup>.

# 10 Primary Care Management

The primary care team should develop an OA management plan which focuses on improvement of function as well as on minimisation of pain and prevention of further functional loss<sup>1,3</sup> [L2, RGA]. The care plan should be discussed with the patient<sup>15</sup>.

All treatment decisions should take into account patient's health beliefs and preferences, as well as their overall medical status<sup>4</sup> [L1, RGA]. This guideline applies to patients with no specific contraindications to the recommended therapies.

#### 10.1 Education and Lifestyle Advice

All patients diagnosed with OA should be provided with verbal and written information about the condition and its management<sup>15</sup>. Consider behavioural interventions and lifestyle changes that are appropriate for the individual, including<sup>3,4,16,17,19</sup> [L1, RGA]:

- Weight loss:
  - o Interventions aimed at weight loss should be the core treatment for patients with a BMI of >25 kg/m².
  - Weight loss is strongly recommended for patients with OA of the knees and hips.
  - A loss of >-5% of the body weight can be associated with significant changes in the clinical and mechanical outcome.
  - A dose-response has been noted with regards to the amount of weight loss that is required to result in improvement of symptoms or function.
  - The efficacy of weight loss for OA symptom management is enhanced by the use of a concomitant exercise programme.
  - More information related to the management of excessive weight in adults can be found in the MOPH National Guidelines on Management of Obesity in Adults<sup>18</sup> and Bariatric Endoscopy and Surgery in Adults<sup>23</sup>.
- Optimisation of fitness:
  - Development of regular home exercise programs.
  - o Introduction of supervised exercises, including physiotherapy (see Section 10.2.1).
- Mood improvement:
  - o Positive thinking.
  - Regular physical exercise.
  - o Engaging in hobbies.
  - o Goal setting.
- Reducing stress:
  - o Elimination of stress-inducing factors.
  - o Problem-solving.
- Sleep hygiene:
  - Minimisation of naps during a daytime.
  - Avoidance of excessive light at night.
  - Development of a bedtime routine.
  - Creation of a pleasant sleep environment.
  - Avoidance of alcohol, nicotine, and other stimulants before sleep.
- Ensuring optimal footwear with shock-absorbing properties for patients with lower limb OA.
- Ensuring optimal seat height at desks (i.e. knee flexion is not less than 90°)<sup>24</sup>.

Thermotherapy (i.e., the application of local heat or cold) should be considered for pain relief as supplementation to primary treatments<sup>3,13</sup> [L1, RGA].

- Heat treatments enhance circulation and soothe stiff joints and tired muscles.
- Cold treatments slow circulation and reduce swelling and pain.

# 10.2 Exercise and Physiotherapy

No physiotherapy intervention is superior to the other<sup>25</sup>. It is likely that a combination of treatments is most effective<sup>4,25</sup> [**L1, RGA**].

#### 10.2.1 Physical Exercise

Performing a wide range of exercises rather than focusing on a single type is recommended<sup>4,25</sup> [L1, RGA]. Intensity of the activities should be adjusted for patient's abilities<sup>4,15,24</sup> [L1, RGA].

General requirements are<sup>24</sup>:

- More than 30 minutes of basic activity (e.g. walking) should be present every day.
- 3-5 sessions (20-60 min each) of aerobic exercise are recommended each week.
- 2-3 sessions (8-10 different exercises, each with 8-12 repetitions) of strength developing exercises are recommended each week.

Physiotherapy for patients with OA should focus on<sup>3,4,15–17,19</sup> [L1, RGA]:

- Low-impact aerobic exercises:
- Resistance training.
- Muscle strengthening exercises.
- Gentle yoga.
- Cycling on stationary bicycles.
- Aquatic exercises (e.g. swimming).
- Balance training.
- Tai chi.

If joints are very painful, stiff, strenuous exercises should be avoided<sup>24</sup> [**L2**, **RGC**]. Patients with the lower limb OA should also avoid<sup>3,19,24</sup> [**L2**, **RGC**]:

- Golf.
- Jogging.
- Ball sports.
- Contact sports.

Physical therapy is not recommended for patients with later stages of hip OA as it provides little or no benefit<sup>26</sup> [L1, RGB].

#### 10.2.2 Aids and Devices

The following aids may be considered in patients with malalignment of joints<sup>1,3,4,15,16,19,25</sup> [L1, RGA]:

- Knee braces or sleeves.
- Joint supports.
- Orthotic insoles.
- Hand orthoses are strongly recommended for patients with OA of the first carpometacarpal joint.

Consider assistive devices (e.g. cane, crutches, walking sticks or tap turners) as adjuncts to the main treatment<sup>3,15</sup> [L1, RGA].

Kinesiotaping (e.g. taping the patella) is not recommended for routine use but may be considered in some patients<sup>4,25</sup> [**L1**, **RGB**]. The patient's age and adequacy of skin care, should be assessed to minimise the risk of adverse effects of this treatment<sup>25</sup> [**L1**, **RGC**].

#### 10.2.3 Treatments Not Recommended in Osteoarthritis

The following treatments have insufficient evidence of benefit and are **not** recommended for routine use:

- Massage therapy<sup>4</sup> [L1, RGB].
- Manual therapy<sup>4,25</sup> [**L1, RGB**].
- Iontophoresis<sup>4</sup> [L1, RGB].
- Pulsed vibration therapy<sup>4</sup> [L1, RGB].
- Electrotherapy (i.e. transcutaneous electrical nerve stimulation (TENS))<sup>4,15,19</sup> [L1, RGC].
- Acupuncture<sup>4,15,19</sup> [**L1, RGB**].

# 10.3 Dietary Supplements

The following supplements may help with OA symptoms. They are not recommended for routine use but may be beneficial for some patients:

- Methylsulfonylmethane (MCM)<sup>27</sup> [L2, RGB].
- Curcuma longa (turmeric)<sup>27,28</sup> [**L2, RGB**].
- *Pinus pinaster* bark extract<sup>27</sup> [**L2, RGB**].
- Boswellia serrata extract<sup>27</sup>[**L2, RGB**].
- Vitamin K (ideally through green-vegetable consumption)<sup>29</sup> [L1, RGB].

The following dietary supplements are **not** recommended for treatment due to limited benefit in patients with OA:

- Marine omega-3 fatty acids (fish oil, krill oil, green-lipped mussel extracts)<sup>4,27</sup> [L1, RGB].
- Vitamin D<sup>4,29,30</sup> [L1, RGB].
- Vitamin E<sup>27,29</sup>[**L2, RGC**].
- Antioxidants<sup>29</sup>[**L1, RGB**].
- Glucosamine<sup>4,15-17,19,27,31</sup> [L1, RGB].
- Chondroitin sulphate<sup>4,15–17,19,27,31</sup> [L1, RGB].
- Combination therapy of glucosamine and chondroitin<sup>27,32</sup> [L1, RGB].
- Collagen derivatives (collagen hydrolysate, Undenatured collagen, willow bark extract)<sup>27</sup> [L2, RGB].
- Rose hip<sup>27</sup> [L2, RGB].
- Avocado/soybean extracts<sup>27</sup> [L2, RGB].
- Harpagophytum procumbens (devil's claw)<sup>28</sup> [L2, RGB].
- Zingiber officinale (ginger)<sup>28</sup> [L2, RGB].

# 10.4 Pharmacological Treatment

Non-steroidal anti-inflammatory drugs (NSAIDs) are recommended as the first-line medication for pain relief in patients with OA<sup>1</sup>. They remain the mainstay of pharmacological management of OA. The lowest effective dose of NSAIDs for the shortest possible period of time is highly encouraged<sup>1,15,16,19</sup> [L1, RGA]:

- **Topical NSAIDs** are preferred over oral NSAIDs<sup>15,33</sup> [L1, RGA]:
  - o Recommended in patients with knee or hand osteoarthritis.
  - Topical NSAIDs may be ineffective in patients with hip OA due to the depth of the joint<sup>4,19</sup>.
- Oral NSAIDs/cyclo-oxygenase 2 (COX-2) inhibitors should be considered if topical NSAIDs are ineffective or provide insufficient pain relief<sup>15</sup> [L1, RGA].
  - Consider the following medications<sup>34</sup>:

- Diclofenac<sup>3,35,36</sup>.
- Ibuprofen<sup>3,37</sup>.
- Naproxen<sup>3,38</sup>.
- Aspirin<sup>3,39</sup>.
- Etoricoxib<sup>19,40</sup>.
- Celecoxib<sup>40</sup>.
- The choice of medication should be based on<sup>3,15,16</sup> [**L2, RGA**]:
  - Patient preference and patient acceptability, regarding side effects and relative contraindications.
  - Individual patient risk factors and comorbidities.
- Oral NSAIDs/COX-2 inhibitors should be prescribed on an as required basis, rather than as a regular medication<sup>1</sup> [L2, RGA].
- The duration of treatment should be based on effectiveness, adverse effects, and past medical history<sup>16</sup>.
- Close monitoring is required<sup>1</sup> [L2].
- Before prescribing NSAIDs, associated modifiable and non-modifiable risk factors for adverse effects, should be considered [R-GDG]:
  - Patients should be properly educated regarding NSAIDs use.
  - H. pylori infection should be considered and treated before initiating NSAIDs [R-GDG].
  - Patients who need to be on long-term NSAIDs should be prescribed a
    gastroprotective agent, preferably a proton pump inhibitor<sup>15</sup> [L1, RGA]. These
    patients should be closely monitored for any adverse events.

**Acetaminophen** may be considered for short-term and episodic use<sup>4,19,34,35</sup> [L1, RGB]:

**Opioid analgesics** have poor evidence in chronic pain from osteoarthritis and should be reserved for patients who do not achieve enough pain relief with acetaminophen and NSAIDs/COX-2 inhibitors<sup>15,19</sup>. Such patients should be managed by a healthcare specialist in Specialist Care (see *Section 12.1*).

The following medicines are **not** recommended for treatment of OA symptoms:

- Rubefacients<sup>15,19</sup> [**L1**].
- Methotrexate<sup>4</sup> [L1, RGB].
- Oral glucocorticoids<sup>1</sup> [L2, RGB].
- Hydroxychloroquine<sup>4</sup> [L1, RGB].

# **10.5** Psychological Interventions

Psychological interventions are associated with positive effects on pain, self-efficacy, fatigue, and coping in patient with OA<sup>41</sup> [L1, RGB]. The effects on physical function, anxiety, depression, and psychological disability are positive but non-significant<sup>41</sup> [L1, RGB]. Interventions such as antidepressants, cognitive behavioural therapy (CBT) or stress management training, may be considered in patients with chronic pain<sup>4,42</sup> [L1, RGA].

# 11 Referral Criteria to Specialist Care

Patients who require the following should be referred for specialist care:

- Pain management with opioid analgesics (see Section 12.1).
- Intra-articular injections and other interventions (see Section 12.2).
- Joint surgery (see Sections 11.1 and 12.3).

#### 11.1 Referral for Surgery

The following patients should be considered for a joint surgery<sup>1,3,15,19</sup> [L1, RGA]:

- Patients who experience joint symptoms that substantially compromise quality of life.
- Patients who are refractory to conservative, non-surgical treatment.

Candidates for elective knee replacement should have:

- Moderate-to-severe persistent pain (as rated using the *Oxford Knee Score*) which is not adequately relieved by a course of non-surgical management lasting at least 6 months.
  - o For patients with an *Oxford Knee Score* of 0-19<sup>43,44</sup>:
    - Refer for an orthopaedic surgical opinion, if the patient meets local BMI criteria.
  - o For patients with an Oxford Knee Score of 20-29<sup>43,44</sup>:
    - Conservative measures should be continued for 3-6 months, with referral to orthopaedics, if there is no improvement after this time.
- AND Clinically significant functional limitation or stability of the knee joint, resulting in diminished quality of life.
- AND Radiographic evidence of advanced joint damage.

Decisions about surgery should be based on discussions between the patient, referring clinicians and surgeons<sup>15</sup> [**L1**]. The patient's age, sex, smoking, BMI, comorbidities as well as location and severity of OA should be reviewed prior to surgery but should not be barriers to referral<sup>3,15</sup>.

Prior to joint surgery, the patient should receive:

- Access to appropriate information (see Section 10.1).
- Treatment for overweight or obesity (if present) (see Section 10.1)
- Physiotherapy through physical activity and exercise (see Section 10.2).

All patients considered for a joint surgery should receive information about 15:

- Benefits and risk factors of surgery
- Potential consequences of not having surgery
- Recovery and rehabilitation after surgery
- Available care pathways.
- How having a prosthesis might affect them and change their life.

# 12 Specialist Management

A multidisciplinary team (MDT) may be required to manage patients with OA. The MDT should include<sup>16</sup>:

- Physiotherapist.
- Dietitian.
- Rheumatologist.
- Pain specialist.
- Internist.
- Orthopaedic surgeon.
- Sport and Exercise Medicine Physician (for athletes with OA).

# 12.1 Opioid and Other Analgesics

If NSAIDs/COX-2 inhibitors and acetaminophen do not provide sufficient pain relief, opioid and other analgesics may be considered<sup>15,19</sup> [**L1**, **RGA**]. These include the following medications<sup>4,40</sup>:

- Buprenorphine
- Codeine.
- Hydromorphone
- Oxycodone.
- Tapentadol.
- Tilidine.
- Tramadol.
- Fentanyl.
- Morphine.

The lowest effective dose for the shortest possible period of time is highly encouraged<sup>4</sup> [L1, RGA]. Opioids are not recommended for periods longer than 1-3 months due to their side effects and long-term addiction potential<sup>19,40</sup> [L2, RGC].

#### 12.2 Intra-Articular Injections and Other Interventions

Intraarticular injections of glucocorticoids and platelet rich plasma, can be considered for the relief of moderate to severe pain in people with OA<sup>1,4,15–17</sup> [L1, RGA].

- The injections into hip joints should be made under fluoroscopic or ultrasound guidance to ensure accurate drug delivery into the joint<sup>4</sup> [L1, RGA].
- Ultrasound guidance is not mandatory for injections into knee and hand joints<sup>4</sup> [L1, RGB]. Use of ultrasound guidance is however preferable [R-GDG].

The following intraarticular injections are currently not recommended for the management of OA<sup>45,46</sup>:

- Hyaluronic acid<sup>1,4,15,45</sup> [**L1, RGB**].
- Botulinum toxin<sup>4,45</sup> [**L1, RGB**].
- Tumour necrosis factor inhibitors<sup>4,45</sup> [L1, RGB].
- Interleukin-1 receptor antagonists<sup>4,45,47</sup> [L1, RGB].
- Growth factor therapy<sup>45,47,48</sup> [**L1, RGB**].
- Cell therapies (e.g. mesenchymal stem cells, platelet-rich plasma, adipose tissue injections)<sup>4,19,45,47</sup>
   [L1, RGB].

Genicular branch block and genicular branch radiofrequency denervation for knee OA in patients not suitable for total knee replacement, may be considered<sup>49,50</sup>. However, these interventions should only be offered Specialist Care setting [**R-GDG**].

# 12.3 Surgical Management

Surgical options for OA include<sup>3,51</sup>:

- Arthroscopy (see Section 12.3.1).
- Cartilage repair (see Section 12.3.2).
- Osteotomy (see Section 12.3.3).
- Partial and total arthroplasties (see Section 12.3.4).

Personalised rehabilitation exercise program should be offered to patients after surgery<sup>16,52</sup> [**L2, RGA**]. After discharge from the hospital, patients should be encouraged to continue the rehabilitation exercise program at home<sup>52</sup> [**L2, RGA**].

# 12.3.1 Arthroscopy

Arthroscopic procedures include debridement and lavage to remove any blood, fluid or loose pieces from the inner joint space<sup>3</sup>. Arthroscopy is not recommended as routine treatment of knee OA<sup>15</sup> as its role is controversial<sup>3,51,53</sup>.

Arthroscopy may, however, be considered in some cases, e.g. in patients with knee OA and a superimposed structural lesion (e.g. meniscal tear)<sup>51,53</sup> [**L2**, **RGB**]:

- The risk of complications is relatively small.
- Arthroscopy may provide only short-term benefit.
- Arthroscopy cannot alter the progression of OA.

# 12.3.2 Cartilage Repair

Cartilage repair techniques should be considered in younger patients with cartilage lesions of limited size<sup>53</sup> [**L2**, **RGA**]:

- The repair is indicated for patients with focal cartilage defects.
- The repair is not indicated, if the defect is to extended cartilage.

Cartilage repair techniques for knee OA Include<sup>51,53</sup>:

- Bone marrow stimulation:
  - Techniques include the following and can be performed arthroscopically:
    - Abrasion.
    - Drilling.
    - Microfracture.
- Replacement techniques:
  - o Techniques include:
    - Mosaicplasty.
    - Osteochondral allograft transplantation.
  - o Can be performed either arthroscopically (for small defects) or open (for large defects).
- Grafting and combined techniques such as:
  - o Periosteal flap transplantation.
  - Autologous chondrocyte implantation (ACI).

o Autologous matrix induced chondrogenesis (AMIC).

Cartilage repair is not recommended in patients with<sup>53</sup> [L2, RGB]:

- Axial malalignment.
- Ligamentous instability.
- Patella maltracking.

#### 12.3.3 Osteotomy

Osteotomy is performed to realign joints, unload the damaged compartment, slow down degenerative processes, and relieve pain (if present)<sup>51,53</sup>.

Osteotomy may be considered<sup>51,53</sup> [**L2**]:

- In younger patients with predominantly unicompartmental OA (e.g. knee OA with varus or valgus alignment).
- In patients who undergo cartilage repair procedures and require normalisation of the biomechanical environment as an adjunct treatment.

Before osteotomy, the condition of the unaffected compartment(s) should be checked and its/their health confirmed<sup>53</sup> [**L2**].

# 12.3.4 Arthroplasty

Arthroplasty should be reserved as the last-choice treatment option<sup>51,53</sup> [L2]:

- It should only be considered in patients:
  - With progressive knee instability or end-stage OA; and
  - o For whom other treatments have failed or are contraindicated.
- It should be avoided in patients younger than 60 years but can be performed in patients over the age of 50 years who have advanced debilitating OA [**R-GDG**].

Partial (unicompartmental) arthroplasty may be considered if only one compartment is affected by OA<sup>53</sup> [**L2**, **RGA**]:

- Before surgery, the condition of the unaffected compartment(s) should be assessed and its health confirmed<sup>53</sup> [**L2**].
- Patients with malalignment of the joint are not recommended for arthroplasty<sup>53</sup> [L2, RGC].

Total arthroplasty may be considered if more than one compartment of the joint is affected <sup>51,53</sup> [**L2; RGA**]. However, pain may persist in patients after total arthroplasty <sup>53</sup>.

# 13 Follow-Up

Regular reviews (at least annual) should be implemented for patients with<sup>2,15</sup> [L1]:

- Troublesome joint pain.
- Symptomatic osteoarthritis.
- More than one joint with symptoms.
- More than one comorbidity.
- Taking regular medication for their osteoarthritis.

Patients who undergo surgery should be reviewed more frequently, at 16 [L2]:

- 2 weeks after surgery.
- 6 weeks after surgery.
- 3 months after surgery.
- 1 year after surgery.

Patients may resume their low-impact sports activities when strength, mobility, and balance are regained [L2].

The following aspects should be monitored<sup>1,15</sup> [**L1**]:

- Current symptoms of OA.
- Progression of symptoms and the long-term course of OA.
- Impact of OA on patient's everyday activities and quality of life.
- Patient's weight and enrolment in exercise and weight reduction (if required).
- Comorbid conditions.
- Appropriateness, effectiveness, and tolerability of applied treatments.
- Patient's up-to-date knowledge of the condition.
- Psychological aspects (e.g. patient's concerns, preferences).
- Patient's ability to access services.

# 14 Secondary Prevention of Osteoarthritis

Prevention strategies are intended to prevent the onset of OA by reducing the risk factors (see *Section 4.4*) $^{54}$ . These include:

- Maintenance of healthy weight<sup>4</sup>:
  - Mediterranean diet is recommended for healthy weight management<sup>18,55</sup> [L1, RGA].
  - Referral to a dietitian for weight loss and to physical therapy may be necessary to regain joint function and muscle strength<sup>16,18</sup> [L1, RGA].
- Following a healthy diet enriched with sufficient nutrients and minerals:
  - Mediterranean diet may also provide some benefits in prevention of OA-related musculoskeletal inflammation<sup>56</sup> [L2, RGB].
  - No specific nutritional interventions are currently recommended for OA prevention<sup>57</sup> [L1, RGB].
  - No phytochemicals are currently recommended for OA prevention<sup>58</sup> [L1, RGB].
- Proper physical activity to avoid muscle weakness<sup>54</sup> [L2, RGA].
- Avoiding traumatic sports and events<sup>54</sup> [**L2, RGA**].
- Avoiding joint injuries and bone fractures<sup>4</sup> [L2, RGA].

# 15 Key Considerations for Patient Preferences

Patient preferences refer to patient perspectives, beliefs, expectations, and goals for health and life, and to the steps employed by individuals in assessing the potential benefits, harms, costs, and limitations of the management options in relation to one another. Patients may have preferences when it comes to defining their problems, identifying the range of management options and selecting or ranking the outcomes used to compare these options.

It is important for healthcare professionals to develop an understanding of the patient as an individual and the unique way in which each person experiences a condition and its impact on their life.

The following recommendations are therefore made for physicians and other healthcare professionals regarding general principles of patient care in Qatar. All clinicians and health care practitioners involved in patients' care in the State of Qatar should:

- **Respect Patients:** Treat patients with respect, kindness, dignity, courtesy and honesty. Ensure that the environment is conducive to discussion and that the patient's privacy is respected, particularly when discussing sensitive, personal issues. Ask the patient how they wish to be addressed and ensure that their choice is respected and used.
- Maintain Confidentiality: Respect the patient's right to confidentiality and avoid disclosing or sharing patients' information without their informed consent. In this context, students and anyone not directly involved in the delivery of care should first be introduced to the patient before starting consultations or meetings, and let the patient decide if they want them to stay.
- Clarify Third-Party Involvement: Clarify with the patient at the first point of contact whether and
  how they like their partner, family members or carers to be involved in key decisions about their
  care or management and review this regularly. If the patient agrees, share information with their
  partner, family members or carers.
- **Obtain Informed Consent:** Obtain and document informed consent from patients, in accordance with MOPH policy and guidance.
- Encourage Shared Decision Making: Ensure that patients are involved in decision making about
  their own care, or their dependent's care, and that factors that could impact the patient's
  participation in their own consultation and care including physical or learning disabilities, sight,
  speech or hearing impairments and problems with understanding, reading or speaking English are
  addressed.
- Disclose Medical Errors: Disclose errors when they occur and show empathy to patients.
- **Ensure Effective Communication:** Explore ways to improve communication including using pictures, symbols or involving an interpreter or family members. Avoid using medical jargon. Use words the patient will understand and confirm understanding by asking questions.
- **Ensure Continuity of Care:** Provide clear and timely sharing of patient information between healthcare professionals especially at the point of any transitions in care.

# **16** Performance Measures

A list of potential performance measures is given below in *Table 16.1*<sup>59</sup>.

Number	Numerator	Denominator
OA01	The number in the denominator with a record of having received written information about osteoarthritis and its management.	The number of adults diagnosed with osteoarthritis in the last 12 months.
OA02	The number in the denominator who are offered support to lose weight.	The number of adults diagnosed with osteoarthritis who are recorded to have a BMI >25.
OA03	The number in the denominator who were supported with non-surgical core treatments for at least 3 months.	The number of adults with osteoarthritis referred for consideration of joint surgery.

Table 16.1: Performance Measures.

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# **Appendix: Detailed Description of the Literature Search**

A systematic search for existing literature on osteoarthritis was performed in the period February 23<sup>rd</sup> – March 10<sup>th</sup>, 2020.

The search for clinical practice guidelines on oteoarthritis diagnosis and/or management was performed in the *PubMed* database and websites of relevant organisations and societies including the *Institute for Quality and Efficiency in Health Care (IQWiG), Arthritis Foundation, Osteoarthritis Foundation International (OAFI), American Psychological Association,* and other. The present guideline is primarily based on UK NICE and American College of Rheumatology/Arthritis Foundation guidelines and is supplemented with other relevant studies.

Peer-reviewed scientific publications were found in PubMed and via *Google Scholar* Internet search engine. Non-peer reviewed studies were identified in *bioRxiv*. Books were checked on PubMed. Information published on medical websites and drug prescribing information sheets were found via Google search engine.

The included publications were identified using the term "osteoarthritis" and specified with the following terms in combinations:

Aetiology, prevalence, management, comorbidities, depression, prognosis, examination, investigation, test, nutrition, diet, supplement, alternative/modern/novel medication, acupuncture, aspirin, naproxen, diclofenac, paracetamol, opioids, pain, exercise, physical activity, surgery, osteotomy, prevention, followup.

Figure A.1 on the next page demonstrates graphically the results of the search and application of exclusion criteria.

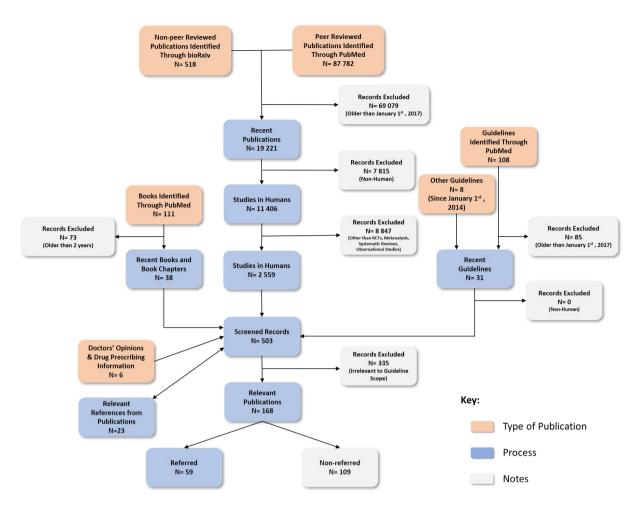


Fig A.1: Literature search results and application of exclusion criteria.

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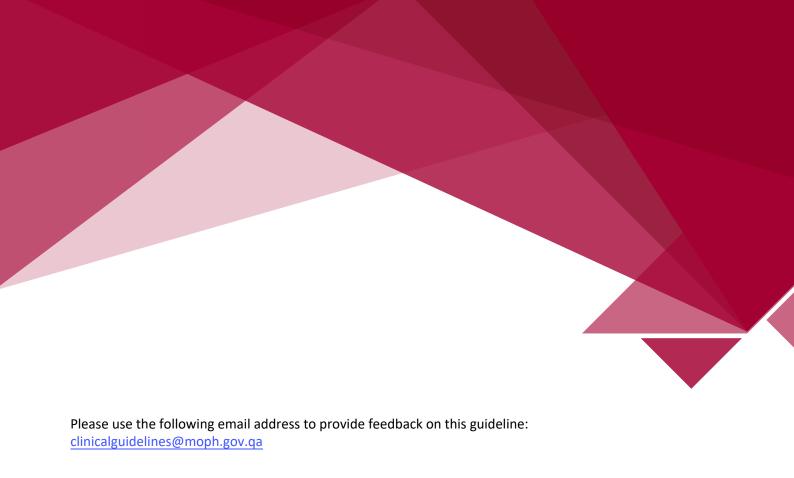
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