MANAGEMENT
Goals of Treatment
Goals in Pain Management

- Involve the patient in the decision-making process
- Agree on realistic treatment goals *before* starting a treatment plan

---

Treating Underlying Causes of Joint Pain

• Many different conditions present with joint pain
  – Understanding clinical, laboratory and radiological features of these diseases can lead to early diagnosis and appropriate therapy

• Prompt recognition of underlying disease and institution of proper therapy can lead to improved prognosis

Ankylosing Spondylitis: Primary Goal

- Maximize long term health-related quality of life through:
  - Control symptoms and inflammation
  - Prevent progressive structural damage
  - Preserve/normalize function and social participation

Obstacles to Desirable Outcomes in Ankylosing Spondylitis

- No cure or medical intervention to prevent or retard ankylosing spondylitis progression
- Inconspicuous progressive structural damage may occur during clinically unrecognised “pre-spondylitic” phase
- Diagnosis often established only once structural damage is obvious
- Delay in diagnosis is significantly greater among women than men and ankylosing spondylitis is typically underdiagnosed in women
- Modified New York diagnostic criteria readily applicable to patients showing radiological evidence of ankylosing spondylitis
  - Of limited use in the absence of defined radiological signs.
- Many methods for assessment of ankylosing spondylitis have been suggested but no method has been accepted universally
- No guidelines for the use of assessment measures have been established
Rheumatoid Arthritis Therapy: Primary Goal

- Maximize long-term health-related quality of life through:
  - Control of symptoms
  - Prevention of structural damage
  - Normalization of function
  - Social participation
Rheumatoid Arthritis Therapy
Goals and Expectations

- Symptom control, including pain management\(^1\)
- Improvement in function and health-related quality of life\(^1\)
- Slow disease progression\(^2\)

*Improvement in patient function is a very important treatment goal for rheumatoid arthritis*

Treat to Target Algorithm for Rheumatoid Arthritis

- **Active rheumatoid arthritis**
  - Use a composite measure of disease activity every 1–3 months

- **Remission**
  - Adapt therapy if state is lost

- **Sustained remission**
  - Assess disease activity every 3–6 months

- **Low disease activity**
  - Adapt therapy according to disease activity

- **Sustained low disease activity**
  - Adapt therapy if state is lost

**Main target**

**Alternative target**

Pharmacological and Non-Pharmacological Therapies for Rheumatoid Arthritis Management

- DMARDs (biologic and non-biologic)
- NSAIDS
- Glucocorticoids
- Exercise
- Hydrotherapy
- Occupational therapy
- NSAIDS
- Glucocorticoids
- DMARDs (biologic and non-biologic)

DMARD = disease-modifying anti-rheumatic drug; NSAID = non-steroidal anti-inflammatory drug

Benefits of Treating Signs and Symptoms of Osteoarthritis

- Pain relief
- Improvement in range of motion
- Improved ability to participate in activities of daily living

Helping osteoarthritis patients maintain or regain some degree of *functionality* is an important benefit of treatment.

Goals of Osteoarthritis Treatment

- Slow disease progression, where possible
- Reduce pain
- Maintain or improve function
Osteoarthritis Therapy
Goals and Expectations

• Management of symptoms, including pain management
• Improvement in function and health-related quality of life

*Improvement in patient function* is a very important treatment goal for osteoarthritis

# Integrated Approach to Osteoarthritis Management

<table>
<thead>
<tr>
<th>Non-pharmacologic</th>
<th>Pharmacologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patient education</td>
<td>• Acetaminophen</td>
</tr>
<tr>
<td>• Phone contact (promote self-care)</td>
<td>• Oral NSAIDs</td>
</tr>
<tr>
<td>• Referral to physical therapist</td>
<td>• Topical NSAIDs and capsaicin</td>
</tr>
<tr>
<td>• Aerobic, strengthening, and/or water-based exercise</td>
<td>• Corticosteroid injections</td>
</tr>
<tr>
<td>• Weight reduction</td>
<td>• Hyaluronate injections</td>
</tr>
<tr>
<td>• Walking aids, knee braces</td>
<td>• Glucosamine, chondroitin sulphate and/or diacerein</td>
</tr>
<tr>
<td>• Proper footwear, insoles</td>
<td>• Weak opioids and narcotic analgesics for refractory pain*</td>
</tr>
<tr>
<td>• Thermal modalities</td>
<td></td>
</tr>
<tr>
<td>• Transcutaneous electrical nerve stimulation</td>
<td></td>
</tr>
<tr>
<td>• Acupuncture</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Surgical</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Total joint replacement</td>
<td>• Lavage/debridement in knee osteoarthritis†</td>
</tr>
<tr>
<td>• Unicompartmental knee replacement</td>
<td>• Joint fusion after failure of joint replacement</td>
</tr>
<tr>
<td>• Osteotomy and other joint preserving surgical procedures</td>
<td></td>
</tr>
</tbody>
</table>

*Pain resistant to ordinary treatment; †Controversial

NSAID = non-steroidal anti-inflammatory drug
Pharmacological and Non-Pharmacological Therapies for Osteoarthritis Management

*If effusion is present, aspirate and inject intra-articularly with corticosteroids
Coxib = COX-2-selective inhibitor; nsNSAID = non-selective non-steroidal anti-inflammatory drug
Combining Pharmacological and Non-pharmacological Therapies Is Most Effective in Managing Osteoarthritis

Non-pharmacological Treatment
Scientific Evidence on Complementary and Alternative Medicine for Arthritis Pain

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Promising evidence of potential benefit</th>
<th>Limited, mixed, or no evidence to support use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acupuncture</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Glucosamine/chondroitin</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Gamma-linolenic acid</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Herbal remedies</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Balneotherapy (mineral baths)</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Tai chi</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>
ASAS/EULAR Guidelines for the Non-pharmacological Management of Ankylosing Spondylitis

- Cornerstones are patient education and regular exercise
- Home exercises are effective but physical therapy exercises are more effective
- Patient associations and self-help groups may be useful
EULAR Recommendations for the Non-Pharmacological Management of Calcium Pyrophosphate Deposition

• For acute calcium pyrophosphate crystal arthritis, optimal and safe treatment includes:
  – Ice or cool packs
  – Temporary rest
  – Joint aspiration

• In combination with intra-articular injection of long-acting glucocorticosteroids, these approaches may be sufficient for many patients
EULAR Guidelines for the Non-Pharmacological Management of Rheumatoid Arthritis

- Dynamic exercises
- Occupational therapy
- Hydrotherapy
Non-pharmacological Treatment of Osteoarthritis

Core treatment:
- Weight reduction
- Exercise
- Education

Other modalities to potentially consider:
- Acupuncture
- Assisted devices (e.g., splints, insoles)
- Heat and cold therapy
- Transcutaneous electrical nerve stimulation

IASP Guidelines for the Non-pharmacological Management of Osteoarthritis

• Physical therapy
  – Strengthening and aerobic conditioning exercises reduce pain and improve function
    • Transcutaneous electrical nerve stimulation reduces pain
    • Cryotherapy improves function
    • Low level laser therapy reduces pain and improves function
    • Psychological management (cognitive behavioral therapy) reduces pain

IASP = International Association for the Study of Pain
OARSI: Non-pharmacological Treatment for Knee Osteoarthritis

Knee-Only Osteoarthritis with or without Comorbidities
Walking cane

All Patients
Land- and water-based exercise
Strength training
Weight management
Self-management and education
Biomechanical interventions

Multi-joint Osteoarthritis with Comorbidities*
Balneotherapy

OA = osteoarthritis; OARSI = Osteoarthritis Research Society International
*Comorbidities include diabetes, hypertension, cardiovascular disease, renal failure, gastrointestinal bleeding, depression and physical impairment limiting activity (including obesity)
EULAR Guidelines for the Non-pharmacological Management of Osteoarthritis

- Treatment should be individualized/tailored to the needs of each patient
- Recommendations include:
  - Physical exercise
  - Strengthening, aerobic, and range of motion exercises
  - Weight loss if patient is overweight
  - Use of appropriate and comfortable footwear
  - Use of walking aids, assistive technology, and adaptations at home or work
ACR Guidelines for the Non-pharmacological Management of Osteoarthritis

ACR conditionally recommends the following:

• Evaluate the ability to perform activities of daily living
• Instruct in joint protection techniques
• Provide assistive devices, as needed, to help patients
• Perform activities of daily living
• Instruct in use of thermal modalities
• Provide splints for patients with trapeziometacarpal joint osteoarthritis

ACR = American College of Rheumatology
AAOS: Non-pharmacological Management of Knee Osteoarthritis

Strong Recommendations

- Self-management programs
- Strengthening, low-impact aerobic exercise
- Neuromuscular education
- Physical activity

Moderate Recommendation

- Weight loss for patients with BMI ≥25 kg/m²

AAOS = American Academy of Orthopaedic Surgeons; BMI = body mass index
Non-pharmacological Interventions for Osteoarthritis

• Exercise and education are the interventions mostly commonly and strongly recommended by clinical practice guidelines

• Other commonly recommended modalities include:
  – Weight control
  – Walking aids, as indicated
  – Thermal modalities

Pharmacological Treatment
Mechanism-Based Treatment of Inflammatory Pain

Pain Treatment Options
- Acetaminophen
- nsNSAIDs/coxibs
- Opioids
- Local anesthetics/channel blockers
- Intra-articular corticosteroid/hyaluronate injections

What are NSAIDs (nsNSAIDs/coxibs)?

**NSAID = Non-Steroidal Anti-Inflammatory Drug**

- Analgesic effect via inhibition of prostaglandin production
- Broad class incorporating many different medications:

**Examples of nsNSAIDs:**
- Diclofenac
- Ibuprofen
- Naproxen

**Examples of Coxibs:**
- Celecoxib
- Etoricoxib
- Parecoxib

*coxib = COX-2-specific inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug*

How do nsNSAIDs/coxibs work?

Coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug
nsNSAID = non-specific non-steroidal anti-inflammatory drug

COX-2 Is Expressed in the CNS

• Prostaglandins in the CNS are important in central sensitization and hyperalgesia

• Peripheral inflammation leads to central induction of COX-2
  - Occurs even with complete sensory nerve block
  - Humoral signal (IL-6?) may play a role in signal transduction across blood-brain barrier
  - IL-1beta plays an important role centrally
  - Elevation of prostaglandins in CSF lead to hyperalgesia
  - Inhibition of IL-1beta synthesis or receptors reduce CSF levels of COX-2, prostaglandin and hyperalgesia
  - Inhibition of COX-2 centrally has similar effects

CNS = central nervous system; CSF = cerebrospinal fluid; IL = interleukin
COX-2 Results in Sensitization to Pain

• Peripheral Sensitization
  – COX-2 is expressed following tissue injury
  – Prostaglandins produced increase nociceptor sensitivity to pain

• Central Sensitization
  – Peripheral inflammation leads to induction of COX-2 in CNS
  – Occurs even with complete sensory nerve block, possibly due to a humoral signal
  – Prostaglandins produced by COX-2 in CNS cause further sensitization to pain

• Result: hyperalgesia and allodynia

CNS = central nervous system
COX-2 Is Involved in Central Sensitization

• Central induction of COX-2 result in increased prostaglandin production
• PGE2 stimulation of EP receptors in the dorsal horn will:
  – Activate PKC, phosphorylating and further enhancing NMDA channel opening
  – Directly activate certain dorsal horn neurons by opening EP2 receptor linked ion channels
  – Reduced inhibitory transmission of glycinergic inter-neurons
  – Increased depolarization and excitability of dorsal horn neurons

NMDA = N-methyl-D-aspartate; PGE2 = prostaglandin E2; PKC = protein kinase C
COX-2 Inhibition Minimizes Sensitization

• Signal for COX-2 induction likely to persist with peripheral inflammation

• To minimize sensitization, COX-2 should be inhibited centrally and in the periphery
  – As early as possible
  – Continued until peripheral inflammation resolved

• Ideal COX-2 inhibitor should be able to act in periphery as well as centrally
  – Should readily cross blood-brain barrier

Adverse Effects of nsNSAIDs/Coxibs

All NSAIDs:
- Gastroenteropathy
  - Gastritis, bleeding, ulceration, perforation
- Cardiovascular thrombotic events
- Renovascular effects
  - Decreased renal blood flow
  - Fluid retention/edema
  - Hypertension
- Hypersensitivity

Cox-1-mediated NSAIDs (nsNSAIDs):
- Decreased platelet aggregation

Coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Composite includes non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death compared with placebo; chart based on network meta-analysis involving 30 trials and over 100,000 patients.

Coxib = COX-2 inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Risk Factors for Gastrointestinal Complications Associated with nsNSAIDs/Coxibs

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio/Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of GI bleeding/perforation</td>
<td>13.5</td>
</tr>
<tr>
<td>Concomitant use of anticoagulants</td>
<td>6.4</td>
</tr>
<tr>
<td>History of peptic ulcer</td>
<td>6.1</td>
</tr>
<tr>
<td>Age ≥60 years</td>
<td>5.5</td>
</tr>
<tr>
<td>Single or multiple use of NSAID</td>
<td>4.7</td>
</tr>
<tr>
<td>Helicobacter pylori infection</td>
<td>4.3</td>
</tr>
<tr>
<td>Use of low-dose ASA within 30 days</td>
<td>4.1</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>2.4</td>
</tr>
<tr>
<td>Concomitant use of glucocorticoids</td>
<td>2.2</td>
</tr>
<tr>
<td>Smoking</td>
<td>2.0</td>
</tr>
</tbody>
</table>

ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor; GI = gastrointestinal; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug; SSRI = selective serotonin reuptake inhibitor

Gastrointestinal Effects of nsNSAIDs/Coxibs Beyond the Upper Gastrointestinal Tract

• There is strong evidence to suggest that potentially clinically relevant adverse gastrointestinal events are not limited to the upper gastrointestinal tract

• Studies suggest NSAIDs increase the risk for lower* gastrointestinal clinical events

*Lower gastrointestinal means distal to the ligament of Treitz or fourth segment of the duodenum
Coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug
Gastrointestinal Events Associated with NSAID Use in Real-Life Practice

Overall Symptomatic uncomplicated Complicated

<table>
<thead>
<tr>
<th></th>
<th>Total population</th>
<th>Patients with concomitant PPI</th>
<th>Patients without concomitant PPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>19</td>
<td>24</td>
<td>15</td>
</tr>
<tr>
<td>Symptomatic uncomplicated</td>
<td>18.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complicated</td>
<td></td>
<td></td>
<td>0.7</td>
</tr>
</tbody>
</table>

NSAID = non-steroidal anti-inflammatory drug; PPI = proton pump inhibitor

Guidelines for nsNSAIDs/Coxibs Use Based on Gastrointestinal Risk and ASA Use

<table>
<thead>
<tr>
<th></th>
<th>Gastrointestinal risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not elevated</td>
</tr>
<tr>
<td>Not on ASA</td>
<td>nsNSAID alone</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>On ASA</td>
<td>Coxib + PPI</td>
</tr>
<tr>
<td></td>
<td>nsNSAID + PPI</td>
</tr>
</tbody>
</table>

ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor; nsNSAID = non-selective non-steroidal anti-inflammatory drug; PPI = proton pump inhibitor

How Opioids Affect Pain

Modify perception, modulate transmission and affect transduction by:

- Altering limbic system activity; modify sensory and affective pain aspects
- Activating descending pathways that modulate transmission in spinal cord
- Affecting transduction of pain stimuli to nerve impulses

## Opioids and Pain Management

<table>
<thead>
<tr>
<th>Opioid Receptor</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mu</strong></td>
<td>Supraspinal analgesia, respiratory depression, sedation, miosis, euphoria, cardiovascular effects, pruritis, nausea/vomiting, decreased gastrointestinal motility, dependence, tolerance</td>
</tr>
<tr>
<td><strong>Delta</strong></td>
<td>Analgesia, euphoria, dysphoria, psychotomimetic effects</td>
</tr>
<tr>
<td><strong>Kappa</strong></td>
<td>Spinal analgesia, dysphoria, psychotomimetic effects, miosis, respiratory depression, sedation</td>
</tr>
</tbody>
</table>

Opioids Modulate Control of “ON” and “OFF” Cells

- Opioid stimulation of mu-receptors on “ON” cells
  - Reduced “ON” cell activity
  - Reduced facilitation of pain transmission at dorsal horn
  - Less pain

- Opioid stimulation of mu-receptors on GABA-ergic interneurons innervating “OFF” cells
  - Reduced GABA-ergic interneuron activity
  - Reduced inhibition of “OFF” cells
  - Increased “OFF” cell inhibition of pain transmission at dorsal horn
  - Less pain

GABA = γ-aminobutyric acid

Opioids Can Induce Hyperalgesia

• Primary hyperalgesia
  – Sensitization of primary neurons → decrease threshold to noxious stimuli within site of injury
  – May include response to innocuous stimuli
  – Increase pain from suprathreshold stimuli
  – Spontaneous pain

• Secondary hyperalgesia
  – Sensitization of primary neurons in surrounding uninjured areas
  – May involve peripheral and central sensitization

Opioids Can Induce Allodynia

- Pain evoked by innocuous stimuli
- Central sensitization → pain produced by Aβ fibers
- Possibly mediated by spinal NMDA receptors

NMDA = N-methyl-D-aspartate

# Adverse Effects of Opioids

<table>
<thead>
<tr>
<th>System</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>Nausea, vomiting, constipation</td>
</tr>
<tr>
<td>CNS</td>
<td>Cognitive impairment, sedation, lightheadedness, dizziness</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Orthostatic hypotension, fainting</td>
</tr>
<tr>
<td>Other</td>
<td>Urticaria, miosis, sweating, urinary retention</td>
</tr>
</tbody>
</table>

*CNS = central nervous system*

### Pain in Rheumatic Disease

**Consensus Panel Recommendations**

**Fixed Low-Dose Combination Therapy**
- Strong or weak opioid + acetaminophen
- NSAID + acetaminophen

**Monotherapy**
- NSAIDs – selective and non-selective COX-2 inhibitors
- Acetaminophen (paracetamol)
- Weak opioids (e.g., tramadol)
- Opioids – use with caution
- TCAs (e.g., amitriptyline, dosulepin, imipramine)
- Anticonvulsants (e.g., gabapentin, pregabalin)
- SNRIs (e.g., duloxetine, milnacipran)
- Corticosteroids – not recommended for long-term use
- Topical agents (e.g., lidocaine, diclofenac, capsaicin, salicylate)
  - Especially in combination with systemic agents

---

NSAID = non-steroidal anti-inflammatory drug; SNRI = serotonin norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Canadian Consensus on Prescribing NSAIDs

Patient requires NSAID

Low gastrointestinal risk

High cardiovascular risk (on ASA)

Avoid NSAID if possible

Primary concern = very high cardiovascular risk: naproxen + PPI

Low cardiovascular risk

Cannot avoid NSAID

Primary concern = very high gastrointestinal risk: coxib + PPI

nsNSAID

Low gastrointestinal risk

Low cardiovascular risk

Naproxen + PPI†

Primary concern = very high gastrointestinal risk: nsNSAID + PPI *

Low cardiovascular risk

High cardiovascular risk (on ASA)

coxib alone or nsNSAID + PPI*

ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific NSAID; PPI = proton pump inhibitor


*In high-risk patients, a coxib and an nsNSAID + PPI show similar reductions of rebleeding rates, but these reductions may be incomplete

†Most patients on ASA + naproxen would need an added PPI, but naproxen alone may be appropriate for some patients at very low gastrointestinal risk
nsNSAIDs/coxibs are recommended as first-line therapy

Acetaminophen and opioid (like) drugs might be considered for residual pain

Corticosteroid injections

Anti-TNF therapy
EULAR Recommendations for the Pharmacological Management of Calcium Pyrophosphate Deposition

For acute calcium pyrophosphate crystal arthritis:

- **First-line:**
  - Intra-articular injections of long-acting glucocorticosteroids

- **Second-line:**
  - Oral nsNSAID or coxib
  - Low-dose oral colchicine
  - Short tapering course
    - Oral or parenteral glucocorticosteroids
    - Adrenocorticotropic hormone

For chronic calcium pyrophosphate inflammatory crystal arthritis:

- **In order of preference:**
  - Oral nsNSAID/coxib and/or colchicine 0.5–1.0 mg/day
  - Low-dose corticosteroid
  - Methotrexate
  - Hydroxychloroquine

# Rheumatoid Arthritis Treatment Options

<table>
<thead>
<tr>
<th>Treatment Options</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>nsNSAIDs/coxibs</strong></td>
<td>Symptomatic treatment to reduce joint swelling and pain</td>
</tr>
</tbody>
</table>
| **DMARDs (biologic, non-biologic)** | Reduce/prevent joint damage, preserve joint integrity and function  
  - Methotrexate, leflunomide, hydroxychloroquine, minocycline, sulfasalazine  
  - Etanercept, infliximab, adalimumab (TNF inhibitors)  
  - Rituximab (anti-CD20)  
  - Abatacept (cytotoxic T-lymphocyte antigen 4 immunoglobulin)  
  - Tocilizumab (anti-interleukin 6 receptor) |
| **Glucocorticoids**           |  
  - Short-term use during flare-ups (oral or intramuscular)  
  - Local treatment for individual active joints (intra-articular) |
| **Surgery**                   | Carpal tunnel release, synovectomy, resection of metatarsal heads, total joint arthroplasty, joint fusion |
| **Supportive strategies**     |  
  - Patient education, cognitive-behavioral interventions  
  - Rehabilitation interventions |

Coxib = COX-2-specific inhibitor; DMARD = disease-modifying antirheumatic drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug; TNF = tumor necrosis factor

EULAR Guidelines for the Pharmacological Management of Rheumatoid Arthritis

- Patients at risk of developing persistent and/or erosive arthritis should be started with DMARDs as early as possible
  - Includes patients who do not yet fulfil diagnostic criteria
  - Methotrexate is considered the anchor drug and should be used first in patients at risk of developing persistent disease
- Consider nsNSAIDs/coxibs after evaluation of gastrointestinal, renal and cardiovascular status
- Systemic glucocorticoids should be considered as a mainly temporary adjunct to the DMARD strategy
- Consider intra-articular glucocorticoid injections for the relief of local symptoms of inflammation

Coxib = COX-2-specific inhibitor; DMARD = disease-modifying antirheumatic drug; EULAR = European League Against Rheumatism; nsNSAID = non-specific non-steroidal anti-inflammatory drug
# Selected Osteoarthritis Management Guidelines

<table>
<thead>
<tr>
<th>Organization</th>
<th>Year</th>
<th>Joints</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESCEO(^1)</td>
<td>2014</td>
<td>X</td>
</tr>
<tr>
<td>OARSI(^2)</td>
<td>2014</td>
<td>X</td>
</tr>
<tr>
<td>NICE(^3)</td>
<td>2014</td>
<td>X</td>
</tr>
<tr>
<td>AAOS(^4)</td>
<td>2013</td>
<td>X</td>
</tr>
<tr>
<td>South Africa(^5)</td>
<td>2013</td>
<td>X</td>
</tr>
<tr>
<td>ACR(^6)</td>
<td>2012</td>
<td>X</td>
</tr>
<tr>
<td>Chinese Orthopaedic Association(^7)</td>
<td>2010</td>
<td>X</td>
</tr>
<tr>
<td>Croatian Society for Rheumatology(^8)</td>
<td>2010</td>
<td>X</td>
</tr>
<tr>
<td>EULAR(^9)</td>
<td>2010</td>
<td>X</td>
</tr>
<tr>
<td>Mexico(^10)</td>
<td>2008</td>
<td>X</td>
</tr>
<tr>
<td>EULAR(^11)</td>
<td>2007</td>
<td>X</td>
</tr>
<tr>
<td>EULAR(^12)</td>
<td>2005</td>
<td>X</td>
</tr>
</tbody>
</table>

ACR = American College of Rheumatology; AAOS = American Academy of Orthopaedic Surgeons; NICE = National Institute of Clinical Excellence; ESCEO = European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis; EULAR = European League Against Rheumatism; OARSI = Osteoarthritis Research Society International.

Management of Osteoarthritis Flowchart

**CORE TREATMENT**
- Exercise
- Weight reduction
- Education

**CONSIDER**
- Acetaminophen ± topical NSAID gel
- Assisted devices (splints, insoles)
- Heat and cold therapy
- TENS/acupuncture
- Intra-articular steroid injection

**ASSESS GASTROINTESTINAL AND CARDIOVASCULAR RISK**
- Suggested cardiovascular threshold <20% 10-year risk without absolute contraindications
- Hepatic and renal profile
- No ASA use

**NSAID CONTRAINDICATION**
- Opioids (weak opioids, such as tramadol, preferred to strong opioids)

**ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug; PPI = proton pump inhibitor; TENS = transcutaneous electrical nerve stimulation**

ESCEO Algorithm for the Management of Osteoarthritis

**CORE TREATMENT**
- Exercise
- Weight reduction
- Education

**IF STILL OR SEVERELY SYMPTOMATIC:**
- Acetaminophen on a regular basis
  **OR**
- Glucosamine and/or chondroitin ± acetaminophen

**CORE TREATMENT**
- Intermittent or continuous nsNSAIDs or coxibs

**IF NEEDED:**
- Refer to physical therapist for knee braces/insoles
  **IF SYMPTOMATIC CAN ADD AT ANY TIME:**
  - Walking aids
  - Thermal agents
  - Manual therapy
  - Patellar taping
  - Acupuncture
  - TENS

**NORMAL GI RISK**
- nsNSAID with PPI
- Coxib (consider PPI)

**INCREASED GI RISK**
- Coxib with PPI

**INCREASED CV RISK**
- Prefer naproxen

**INCREASED RENAL RISK**
- Avoid nsNSAIDs/coxibs

Coxib = COX-2-specific inhibitor; ESCEO = European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis; nsNSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug; PPI = proton pump inhibitor; TENS = transcutaneous electrical nerve stimulation

Adapted from: Bruyère O et al. Semin Arthritis Rheum 2014; pii:S0049-0172(14)00108-5
ESCEO Algorithm for the Management of Osteoarthritis (cont’d)

IF STILL SYMPTOMATIC:
- Intra-articular hyaluronate or corticosteroids

LAST PHARMACOLOGICAL ATTEMPTS:
- Short-term weak opioids
- Duloxetine

END-STAGE DISEASE MANAGEMENT AND SURGERY (IF SEVERELY SYMPTOMATIC AND POOR QUALITY OF LIFE):
- Total joint (or unicompartmental knee) replacement
- Opioid analgesics

Combination of non-pharmacological and pharmacological treatment modalities is strongly recommended

Coxib = COX-2-specific inhibitor; ESCEO = European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis; nsNSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug; PPI = proton pump inhibitor; TENS = transcutaneous electrical nerve stimulation

Adapted from: Bruyère O et al. Semin Arthritis Rheum 2014; pii:S0049-0172(14)00108-5
IASP Guidelines for the Pharmacological Management of Osteoarthritis

Systemic Treatments

- Opioid agonists (e.g., tramadol)
- Acetaminophen
- nsNSAIDs/coxibs
- IL-1 inhibitors

Local Treatments

- Intra-articular corticosteroids or hyaluronic acid injection

Coxib = COX-2-specific inhibitor; IASP = International Association for the Study of Pain; IL = interleukin; nsNSAID = non-specific non-steroidal anti-inflammatory drug

International Association for the Study of Pain. Osteoarthritis-Related Pain.
OARSI: Pharmacological Treatment for Knee Osteoarthritis

<table>
<thead>
<tr>
<th>Knee-Only Osteoarthritis without Comorbidities</th>
<th>Multi-joint Osteoarthritis without Comorbidities*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>Acetaminophen</td>
</tr>
<tr>
<td>Capsaicin</td>
<td>Duloxetine</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>Oral nsNSAIDs and coxibs</td>
</tr>
<tr>
<td>Oral nsNSAIDs and coxibs</td>
<td>Topical nsNSAIDs</td>
</tr>
<tr>
<td>Topical nsNSAIDs</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Knee-Only Osteoarthritis with Comorbidities</th>
<th>Multi-joint Osteoarthritis with Comorbidities*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical nsNSAIDs</td>
<td>Duloxetine</td>
</tr>
<tr>
<td></td>
<td>Oral coxibs</td>
</tr>
</tbody>
</table>

| All Patients                                  |                                                  |
| Intra-articular corticosteroids               |                                                  |

coxib = COX-2-specific inhibitor; nsNSAID = non-selective non-steroidal anti-inflammatory drug; OA = osteoarthritis; OARSI = Osteoarthritis Research Society International

*Comorbidities include diabetes, hypertension, cardiovascular disease, renal failure, gastrointestinal bleeding, depression and physical impairment limiting activity (including obesity)

ACR Guidelines for the Pharmacological Management of Hand Osteoarthritis

ACR conditionally recommends using ≥1 of the following:

- Topical capsaicin
- Topical NSAIDs, including trolamine salicylate
- Oral NSAIDs, including coxibs
- Tramadol

ACR conditionally recommends health professionals should NOT use the following:

- Intra-articular therapies
- Opioid analgesics

ACR = American College of Rheumatology; coxib = COX-2-selective inhibitor; NSAID = non-steroidal anti-inflammatory drug
ACR Guidelines for the Pharmacological Management of Hip Osteoarthritis

ACR conditionally recommends using ≥1 of the following:

• Acetaminophen
• Oral NSAIDs
• Tramadol
• Intra-articular corticosteroid injections

ACR conditionally recommends health professionals should NOT use the following:

• Chondroitin sulfate
• Glucosamine

ACR = American College of Rheumatology; NSAID = non-steroidal anti-inflammatory drug
ACR Guidelines for the Pharmacological Management of Knee Osteoarthritis

ACR conditionally recommends using ≥1 of the following:
• Acetaminophen
• Oral NSAIDs
• Topical NSAIDs
• Tramadol
• Intra-articular corticosteroid injections

ACR conditionally recommends health professionals should NOT use the following:
• Chondroitin sulfate
• Glucosamine
• Topical capsaicin

ACR = American College of Rheumatology; NSAID = non-steroidal anti-inflammatory drug
### EULAR Guidelines for the Pharmacological Management of Osteoarthritis

<table>
<thead>
<tr>
<th>Pharmacotherapy</th>
<th>Hand</th>
<th>Hip</th>
<th>Knee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen ≤4 g/day</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Oral NSAIDs at lowest effective dose and shortest duration</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Intra-articular injection of corticosteroid</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Opioid analgesics</td>
<td>✗</td>
<td>✗</td>
<td>✔</td>
</tr>
<tr>
<td>SYSADOAs</td>
<td>✗</td>
<td>✗</td>
<td>✔</td>
</tr>
</tbody>
</table>

**EULAR** = European League Against Rheumatism; NSAID = non-steroidal anti-inflammatory drug; SYSADOA = symptomatic slow acting drugs for osteoarthritis

AAOS: Pharmacological Management of Knee Osteoarthritis

**Recommended**
- Coxibs
- Oral nsNSAIDs
- Topical nsNSAIDs
- Tramadol

**Not recommended**
- Chondroitin
- Glucosamine
- Growth factor injections
- Hyaluronic acid

**Insufficient evidence**
- Acetaminophen
- Intra-articular corticosteroids
- Opioids
- Pain patches

AAOS = American Academy of Orthopaedic Surgeons; coxib = COX-2-selective inhibitor; nsNSAID = non-selective non-steroidal anti-inflammatory drug
Measuring Treatment Response in Ankylosing Spondylitis: ASAS

**ASAS20**

- Improvement of ≥20% and absolute improvement of ≥10 units on a 0 to 100 scale in 3 or more of the following domains:
  - Patient global assessment (VAS global assessment)
  - Pain assessment (average of VAS total and nocturnal pain scores)
  - Function (BASFI score)
  - Inflammation (average of BASDAI’s last 2 VAS concerning morning stiffness intensity and duration)
- Absence of deterioration in the potential remaining domain
  - Deterioration defined as ≥20% worsening

**ASAS = Assessment in Ankylosing Spondylitis ; AS = ankylosing spondylitis; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functional Index; VAS = Visual Analog Scale**

ACR Criteria for Assessing Treatment Response in Rheumatoid Arthritis

20% improvement in tender and swollen joints

20% improvement in ≥3 of the following:
- Physician global assessments
- Patient global assessments
- Pain
- Disability
- Acute-phase reactant

ACR = American College of Rheumatology
## Quality Measures that Focus on Rheumatoid Arthritis: PQRI

<table>
<thead>
<tr>
<th>Number</th>
<th>Measure title</th>
<th>Description</th>
<th>Measure developer</th>
<th>Patient-level measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>106</td>
<td>DMARD Therapy</td>
<td>% of patients (≥18 years) prescribed, dispensed, or administered ≥1 ambulatory prescription for a DMARD</td>
<td>NCQA</td>
<td>Yes</td>
</tr>
<tr>
<td>176</td>
<td>TB Screening</td>
<td>% of patients with documentation of TB screening performed and results interpreted within 6 months prior to receiving a first course of therapy using a biologic DMARD</td>
<td>AMA-PCP/NCQA</td>
<td>Yes</td>
</tr>
<tr>
<td>177</td>
<td>Periodic Assessment of Disease Activity</td>
<td>% of patients with an assessment and classification of disease activity within 12 months</td>
<td>AMA-PCP/NCQA</td>
<td>Yes</td>
</tr>
<tr>
<td>178</td>
<td>Functional Status Assessment</td>
<td>% of patients for whom a functional status assessment was performed at least once within 12 months</td>
<td>AMA-PCP/NCQA</td>
<td>Yes</td>
</tr>
<tr>
<td>179</td>
<td>Assessment and Classification of Disease Prognosis</td>
<td>% of patients who have an assessment and classification of disease prognosis at least once within 12 months</td>
<td>AMA-PCP/NCQA</td>
<td>Yes</td>
</tr>
<tr>
<td>180</td>
<td>Glucocorticoid Management</td>
<td>% of patients assessed for glucocorticoid use and, for those on prolonged doses of prednisone ≥10 mg daily (or equivalent) with improvement or no change in disease activity, documentation of glucocorticoid management plan within 12 months</td>
<td>AMA-PCP/NCQA</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Reporting options for all are claims-based, registry, and managed group

AMA-PCPI = American Medical Association-sponsored Physician Consortium on Performance Improvement; DMARD = disease-modifying anti-rheumatic drug; NCQA = National Commission for Quality Assurance; PQRSI= Physician Quality Reporting Initiative; TB = tuberculosis

Quality Measures that Focus on Rheumatoid Arthritis: MDS

- MDS 3.0 is a revised nursing home tool for patient assessment and management
- Includes osteoarthritis in the diagnosis “Arthritis” under “Musculoskeletal” header of Active Disease Diagnosis section
- An updated pain section includes items about pain treatment regimens based on chart review and a direct-interview pain assessment

MDS = Minimum Data Set


## Assessing Treatment Response in Osteoarthritis: WOMAC™

<table>
<thead>
<tr>
<th>Pain subscale</th>
<th>Physical function subscale</th>
<th>Stiffness subscale</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Walking on a flat surface</td>
<td>1. Descending stairs</td>
<td>1. Morning stiffness</td>
</tr>
<tr>
<td>2. Going up/down stairs</td>
<td>2. Ascending stairs</td>
<td>2. Stiffness after sitting/lying/resting</td>
</tr>
<tr>
<td>3. While sleeping</td>
<td>3. Getting out of a chair</td>
<td></td>
</tr>
<tr>
<td>4. Sitting/lying down</td>
<td>4. Standing upright</td>
<td></td>
</tr>
<tr>
<td>5. Standing upright</td>
<td>5. Bending</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6. Walking on a flat surface</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7. Getting in/out of car</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8. Shopping</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9. Putting on socks/stockings</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10. Getting out of bed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11. Taking off socks/stockings</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12. Lying in bed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>13. Getting in/out of bath</td>
<td></td>
</tr>
<tr>
<td></td>
<td>14. Sitting</td>
<td></td>
</tr>
<tr>
<td></td>
<td>15. Getting on/off toilet</td>
<td></td>
</tr>
<tr>
<td></td>
<td>16. Heavy domestic duties</td>
<td></td>
</tr>
<tr>
<td></td>
<td>17. Light domestic duties</td>
<td></td>
</tr>
</tbody>
</table>

WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index
### Quality Measures that Focus on Osteoarthritis: PQRS

<table>
<thead>
<tr>
<th>Item</th>
<th>Number 109</th>
<th>Number 142</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Measure title</strong></td>
<td>Function and Pain Assessment</td>
<td>Assessment for Use of Anti-Inflammatory or Analgesic OTC Medications</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Percentage of patients visits (≥21 years) with a diagnosis of osteoarthritis with assessment for function and pain</td>
<td>Percentage of patients visits (≥21 years) with a diagnosis of osteoarthritis with assessment for use of anti-inflammatory or analgesic over-the-counter medications</td>
</tr>
<tr>
<td><strong>Measure developer</strong></td>
<td>AMA-PCPI</td>
<td>AMA-PCPI</td>
</tr>
<tr>
<td><strong>Reporting options</strong></td>
<td>Claims-based Registry</td>
<td>Claims-based Registry</td>
</tr>
<tr>
<td><strong>Patient-level measure</strong></td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

**AMA-PCPI** = American Medical Association-sponsored Physician Consortium on Performance Improvement;  
**PQRS** = Physician Quality Reporting System  
Quality Measures that Focus on Osteoarthritis: MDS

- MDS 3.0 is a revised nursing home tool for patient assessment and management
- Includes osteoarthritis in the diagnosis “Arthritis” under “Musculoskeletal” header of Active Disease Diagnosis section
- An updated pain section includes items about pain treatment regimens based on chart review and a direct-interview pain assessment

MDS = Minimum Data Set
# When to Refer Patients with Osteoarthritis

*Referral criteria should take into account the extent to which the condition is causing pain, disability, sleeplessness, loss of independence, inability to undertake normal activities, reduced functional capacity or psychiatric illness. N/A = not applicable.*


<table>
<thead>
<tr>
<th>Urgency</th>
<th>Hip osteoarthritis</th>
<th>Knee osteoarthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate</td>
<td>Evidence of infection in the joint</td>
<td>Evidence of infection in the joint</td>
</tr>
<tr>
<td>Urgent</td>
<td>Symptoms rapidly deteriorate and are causing severe disability</td>
<td>Evidence of acute inflammation (e.g., hemarthrosis, gout, pseudo-gout)</td>
</tr>
<tr>
<td>Soon</td>
<td>N/A</td>
<td>Joint continues to “give way” (i.e., fails to provide proper support) despite therapy</td>
</tr>
<tr>
<td></td>
<td>Symptoms rapidly deteriorate and are causing severe disability</td>
<td>Symptoms rapidly deteriorate and are causing severe disability</td>
</tr>
<tr>
<td>Routine appointment</td>
<td>Symptoms impair the quality of life*</td>
<td>Symptoms impair the quality of life*</td>
</tr>
</tbody>
</table>
Adherence
Osteoarthritis and Non-adherence to Select Analgesics

Discontinuation with 1 year, %

- Acetaminophen: 98%
- Weak opioid: 97%
- Strong opioid: 96%
- Tramadol: 93%
- nsNSAID: 87%

**nsNSAID** = non-specific non-steroidal anti-inflammatory drug

Strategies to Improve Adherence

- **S**implify regimen
- **I**mpart knowledge
- **M**odify patient beliefs and human behavior
- **P**rovide communication and trust
- **L**eave the bias
- **E**valuate adherence

Simplifying Medication Regimen

• If possible, adjust regimen to minimize:
  – Number of pills taken
  – Number of doses per day
  – Special requirements (e.g., bedtime dosing, avoiding taking medication with food, etc.)

• Recommend all medications be taken at the same time of day (if possible)
• Link taking medication to daily activities, such as brushing teeth or eating
• Encourage use of adherence aids such as medication organizers and alarms
Imparting Knowledge

• Provide clear, concise instructions (written and verbal) for each prescription
• Be sure to provide information at a level the patient can understand
• Involve family members if possible
• Provide handouts and/or reliable websites for patients to access information on their condition
• Provide concrete advice on how to cope with medication costs

## Modifying Patient Beliefs and Behaviors: Motivational Interviewing Technique

**Techniques**

- Express empathy
- Develop discrepancy
- Roll with resistance
- Support self efficacy

**Examples**

- “It’s normal to worry about medication side effects”
- “You obviously care about your health; how do you think not taking your pills is affecting it?”
- “I understand that you have a lot of other things besides taking pills to worry about”
- “It sounds like you have made impressive efforts to work your new medication into your daily routine”

---

Providing Communication and Trust: Communication Tips

• Be an active listener
  – Focus on the patient
  – Nod and smile to show you understand

• Make eye contact

• Be aware of your own body language
  – Face the patient
  – Keep arms uncrossed
  – Remove hands from pockets

• Recognize and interpret non-verbal cues

McDonough RP, Bennett MS. Am J Pharm Educ 2006; 70(3):58;
Srnka QM, Ryan MR. Am Pharm 1993; NS33(9):43-6.
Leaving the Bias

Learn more about how low health literacy can affect patient outcomes

Acknowledge biases

Specifically ask about attitudes, beliefs and cultural norms with regards to medication

Tailor communication to patient’s beliefs and level of understanding

Evaluating Adherence: 4-Step Strategy for Detecting Non-adherence

1. Ask an open-ended question about taking medicine

2. Normalize and universalize non-adherence to reverse the judgmental environment

3. Make the role of accurate information about adherence in medical decision-making explicit

4. Don’t ask about “forgetting” or “missed” doses until the first 3 steps have set the stage

Summary
Management of Chronic Joint Pain: Summary

• It is important to assess and treat underlying causes of joint pain to help guide choice of therapy and improve prognosis.

• Non-pharmacological strategies should be incorporated into the management plan for patients suffering from chronic joint pain when possible:
  – Exercise, weight loss and education should form the core treatment of osteoarthritis.
  – Education and exercise may also be beneficial in patients with rheumatoid arthritis and ankylosing spondylitis.

• Pharmacological management of chronic joint pain may include acetaminophen, nsNSAIDs/coxibs and/or opioids.

Coxib = COX-2-selective inhibitor; nsNSAID = non-selective non-steroidal anti-inflammatory drug.