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# MANAGEMENT

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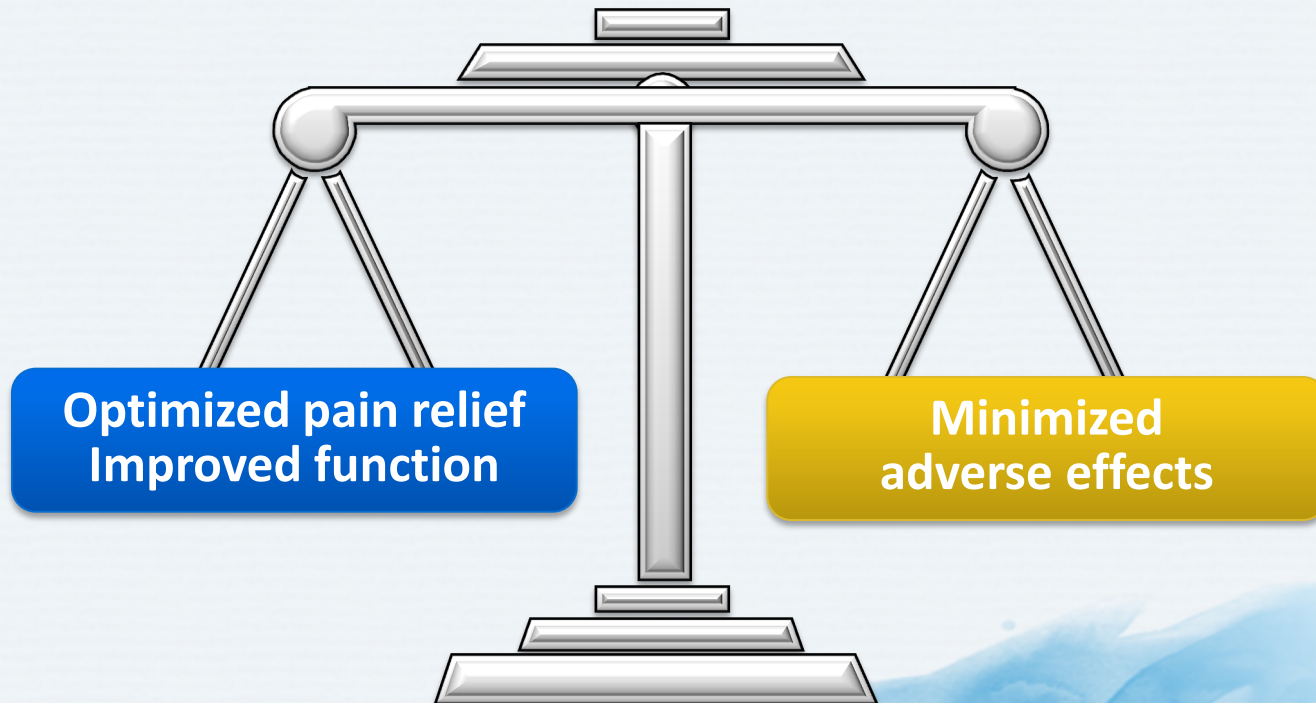
# Goals of Treatment



# Goals in Pain Management

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



# Treating Underlying Causes of Joint Pain

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- 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

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- 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

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- 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

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- 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

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- Symptom control, including pain management<sup>1</sup>
- Improvement in function and health-related quality of life<sup>1</sup>
- Slow disease progression<sup>2</sup>

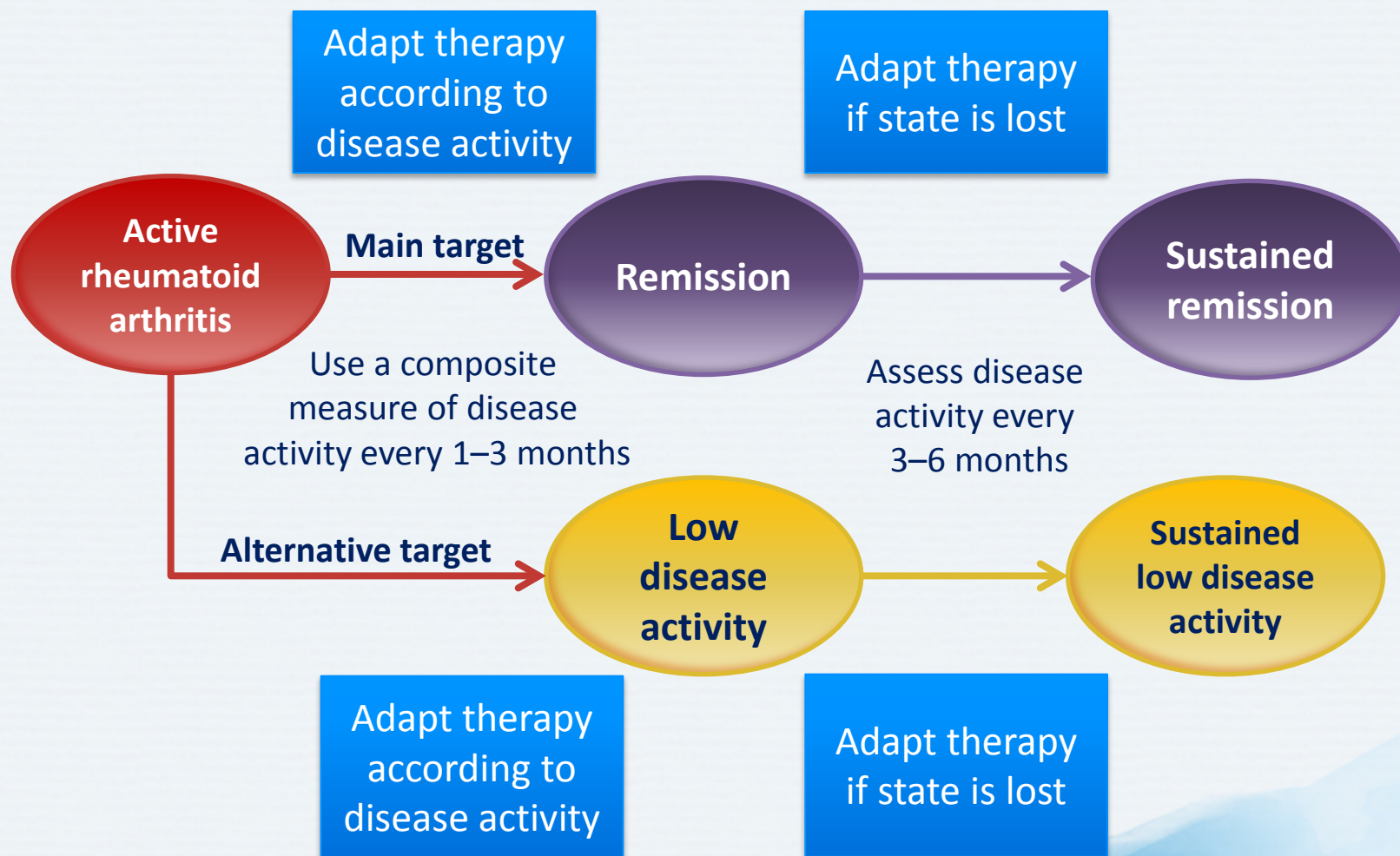
***Improvement in patient function* is a very important treatment goal for rheumatoid arthritis**

1. Genovese MC. In: Firestein GS *et al* (eds). *Kelley's Textbook of Rheumatology*. Vol 2, 8th ed. Saunders Elsevier; Philadelphia, PA: 2008;

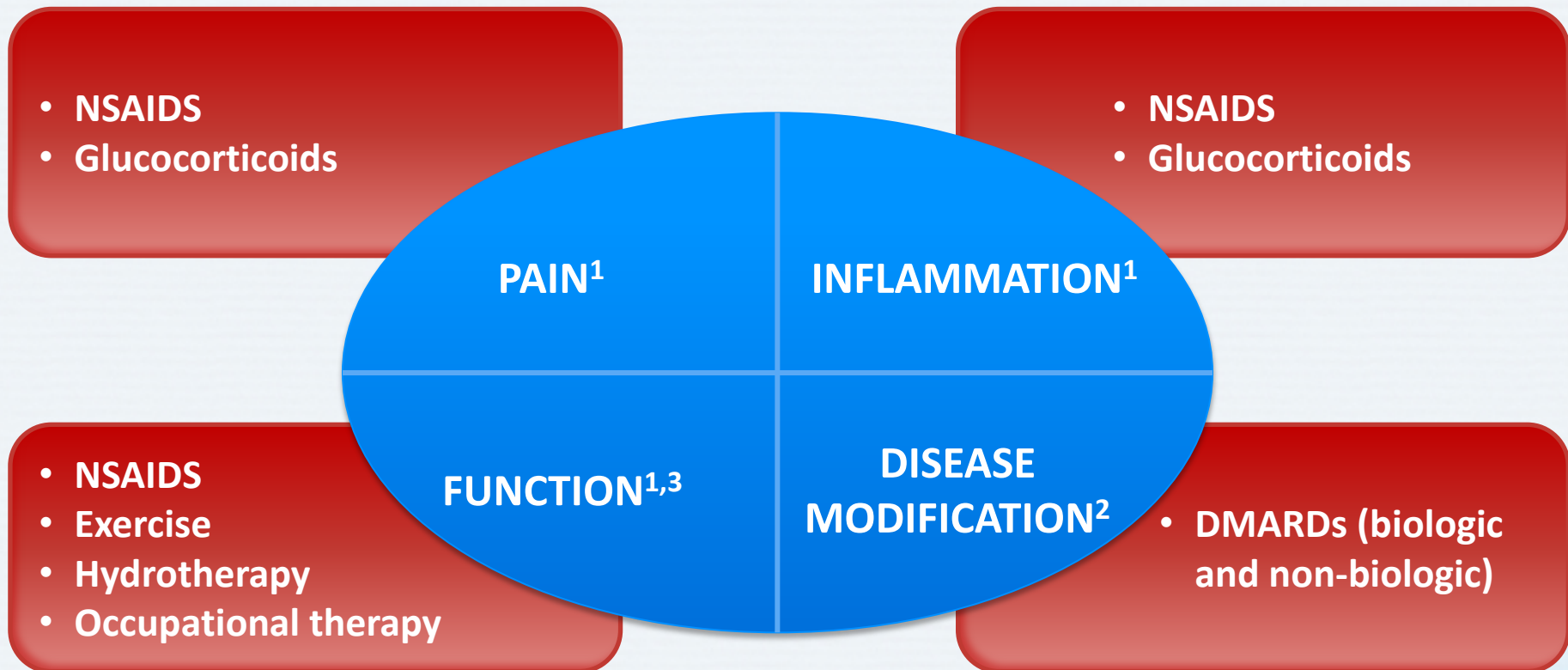
2. O'Dell JR. In: Goldman L, Ausiello D (eds). *Cecil Medicine*. 23rd ed. Saunders Elsevier; Philadelphia, PA: 2007.



# Treat to Target Algorithm for Rheumatoid Arthritis



# Pharmacological and Non-Pharmacological Therapies for Rheumatoid Arthritis Management



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

1. Combe B *et al. Ann Rheum Dis* 2007; 66(1):34-45; 2. Saag KG *et al. Arthritis Rheum* 2008; 59(6):762-84;

3. O'Dell JR. In: Goldman L, Ausiello D (eds). *Cecil Medicine*. 23rd ed. Saunders Elsevier; Philadelphia, PA: 2007.

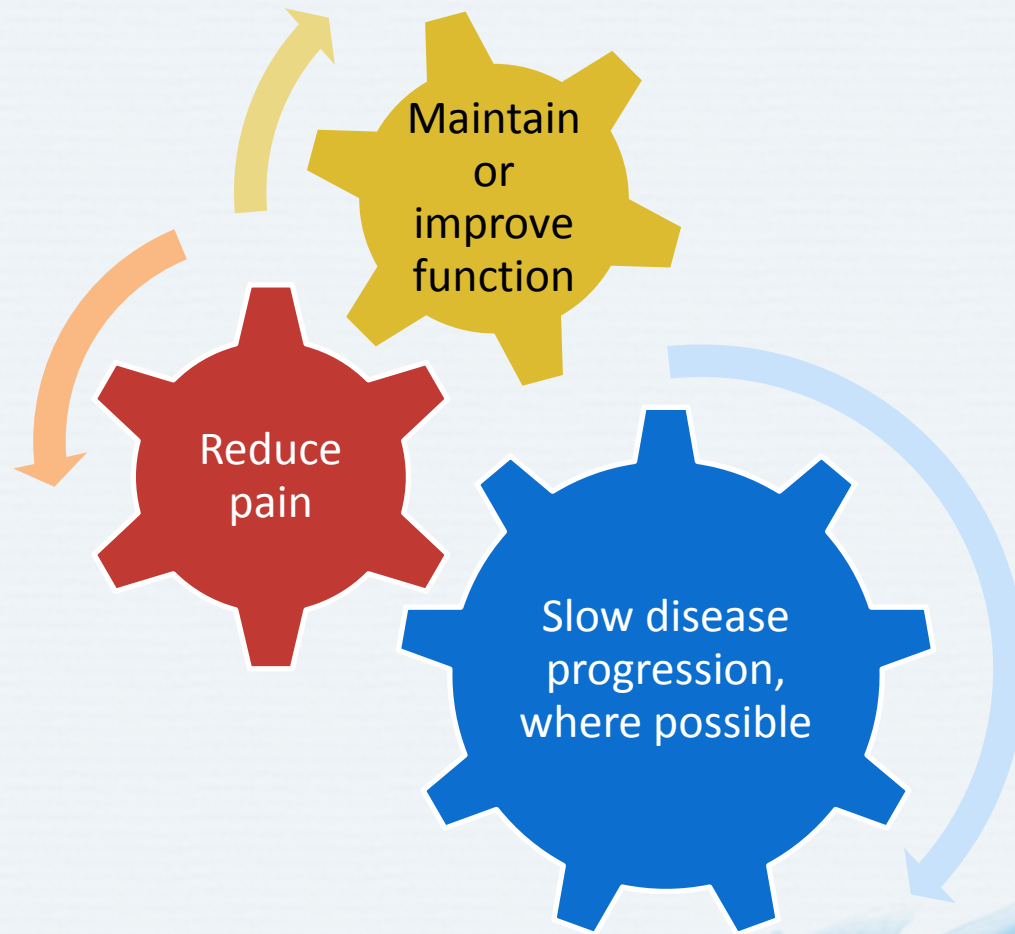
# Benefits of Treating Signs and Symptoms of Osteoarthritis

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- 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



# Osteoarthritis Therapy Goals and Expectations

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- 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

Non-pharmacologic	Pharmacologic
<ul style="list-style-type: none"> <li>• Patient education</li> <li>• Phone contact (promote self-care)</li> <li>• Referral to physical therapist</li> <li>• Aerobic, strengthening, and/or water-based exercise</li> <li>• Weight reduction</li> <li>• Walking aids, knee braces</li> <li>• Proper footwear, insoles</li> <li>• Thermal modalities</li> <li>• Transcutaneous electrical nerve stimulation</li> <li>• Acupuncture</li> </ul>	<ul style="list-style-type: none"> <li>• Acetaminophen</li> <li>• Oral NSAIDs</li> <li>• Topical NSAIDs and capsaicin</li> <li>• Corticosteroid injections</li> <li>• Hyaluronate injections</li> <li>• Glucosamine, chondroitin sulphate and/or diacerein</li> <li>• Weak opioids and narcotic analgesics for refractory pain*</li> </ul>
Surgical	
<ul style="list-style-type: none"> <li>• Total joint replacement</li> <li>• Unicompartamental knee replacement</li> <li>• Osteotomy and other joint preserving surgical procedures</li> </ul>	<ul style="list-style-type: none"> <li>• Lavage/debridement in knee osteoarthritis<sup>†</sup></li> <li>• Joint fusion after failure of joint replacement</li> </ul>

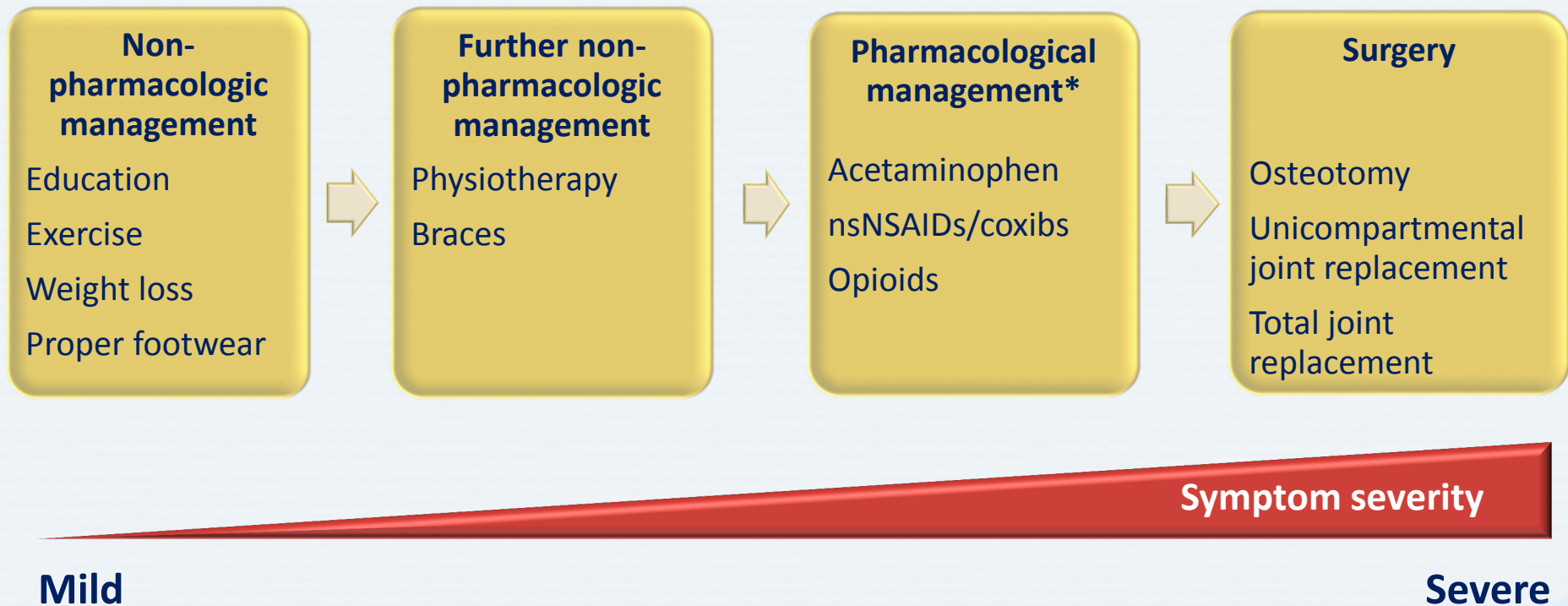
\*Pain resistant to ordinary treatment; <sup>†</sup>Controversial

NSAID = non-steroidal anti-inflammatory drug

Zhang W *et al. Osteoarth Cartil* 2008; 16(12):137-62.



# Pharmacological and Non-Pharmacological Therapies for Osteoarthritis Management



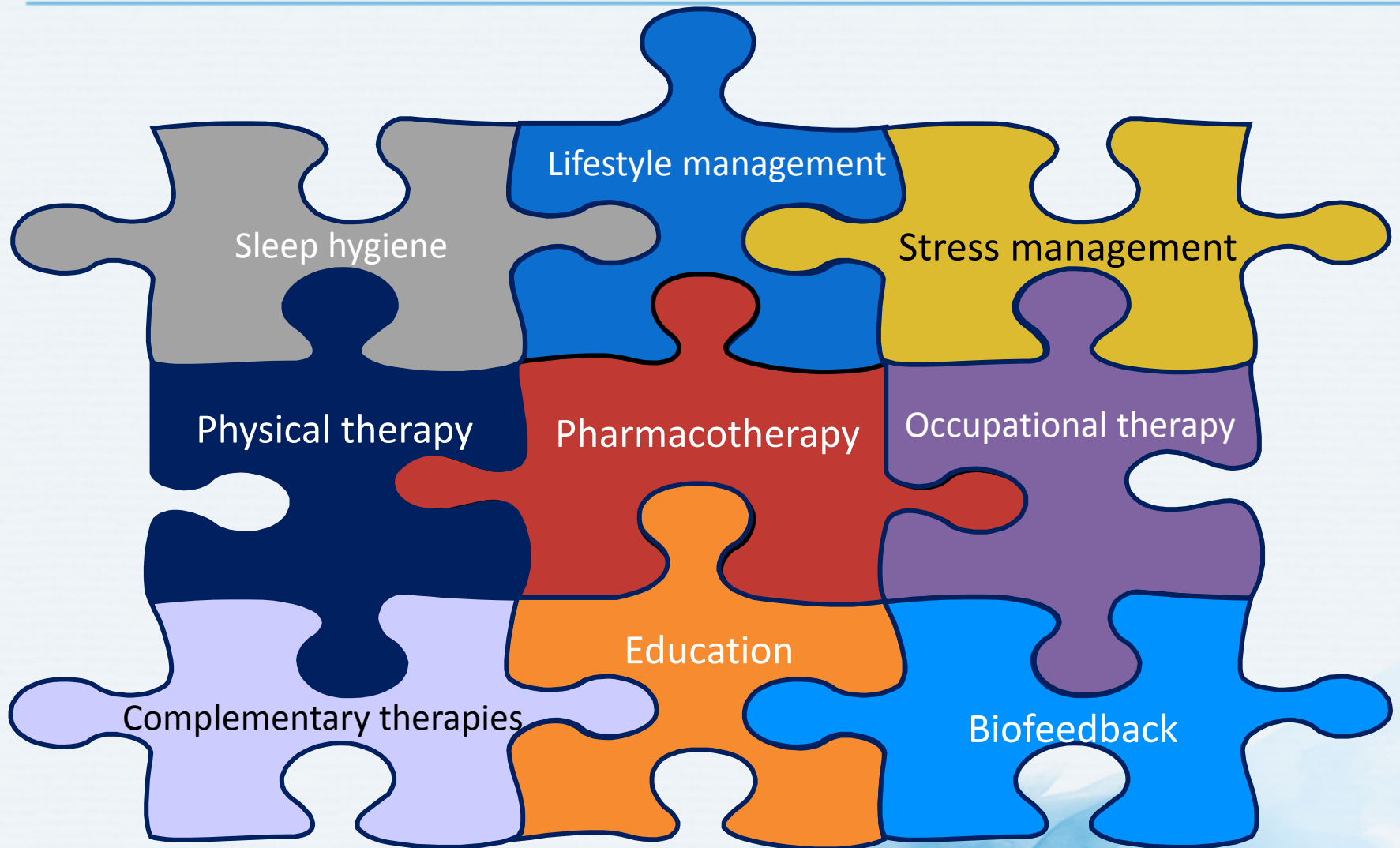
\*If effusion is present, aspirate and inject intra-articularly with corticosteroids

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

Hunter DJ *et al.* *BMJ* 2006; 332(7542):639-42; Richmond J *et al.* *J Am Acad Orthop Surg* 2009; 17(9):591-600; Zhang W *et al.* *Osteoarth Cartil* 2008; 16(12):137-62.



# Combining Pharmacological and Non-pharmacological Therapies Is Most Effective in Managing Osteoarthritis



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# Non-pharmacological Treatment

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# Scientific Evidence on Complementary and Alternative Medicine for Arthritis Pain

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Therapy	Promising evidence of potential benefit	Limited, mixed, or no evidence to support use
Acupuncture	✓	
Glucosamine/chondroitin		✓
Gamma-linolenic acid		✓
Herbal remedies		✓
Balneotherapy (mineral baths)		✓
Tai chi		✓

# ASAS/EULAR Guidelines for the Non-pharmacological Management of Ankylosing Spondylitis

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- 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

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- 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

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- 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

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- 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

# 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)

McAlindon TE *et al. Osteoarth Cartil* 2014; 22(3):363-88.

# EULAR Guidelines for the Non-pharmacological Management of Osteoarthritis

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- 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

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## **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

# 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  $\geq 25$  kg/m<sup>2</sup>

# Non-pharmacological Interventions for Osteoarthritis

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- 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

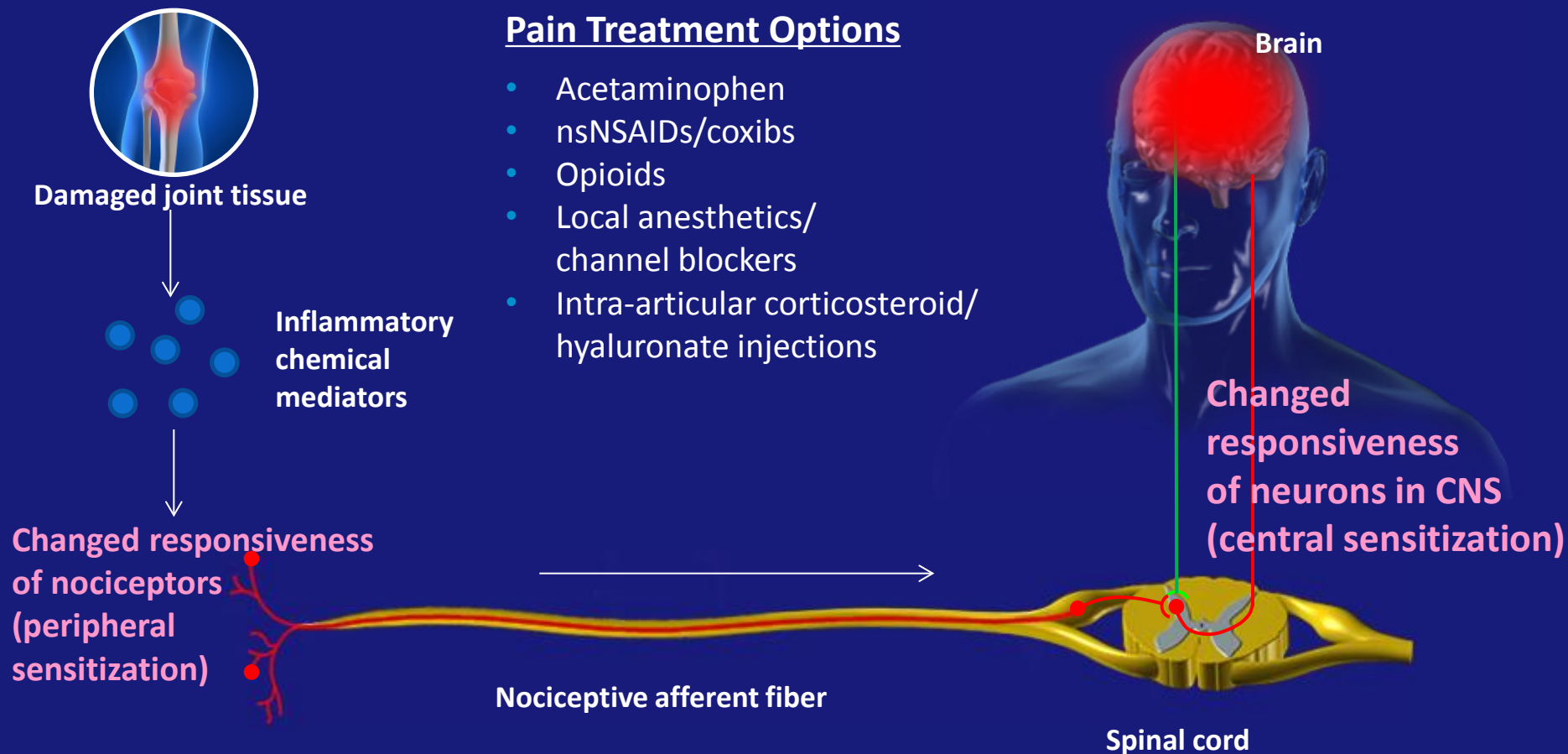
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# Pharmacological Treatment





# Mechanism-Based Treatment of Inflammatory Pain



CNS = central nervous system; coxib = COX-2 inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Hochberg MC et al. *Arthritis Care Res (Hoboken)* 2012; 64(4):465-74; Scholz J et al. *Nat Neurosci* 2002; 5(Suppl):1062-7.

# What are NSAIDs (nsNSAIDs/coxibs)?

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NSAID = **N**on-**S**teroidal **A**nti-**I**nflammatory **D**rug

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

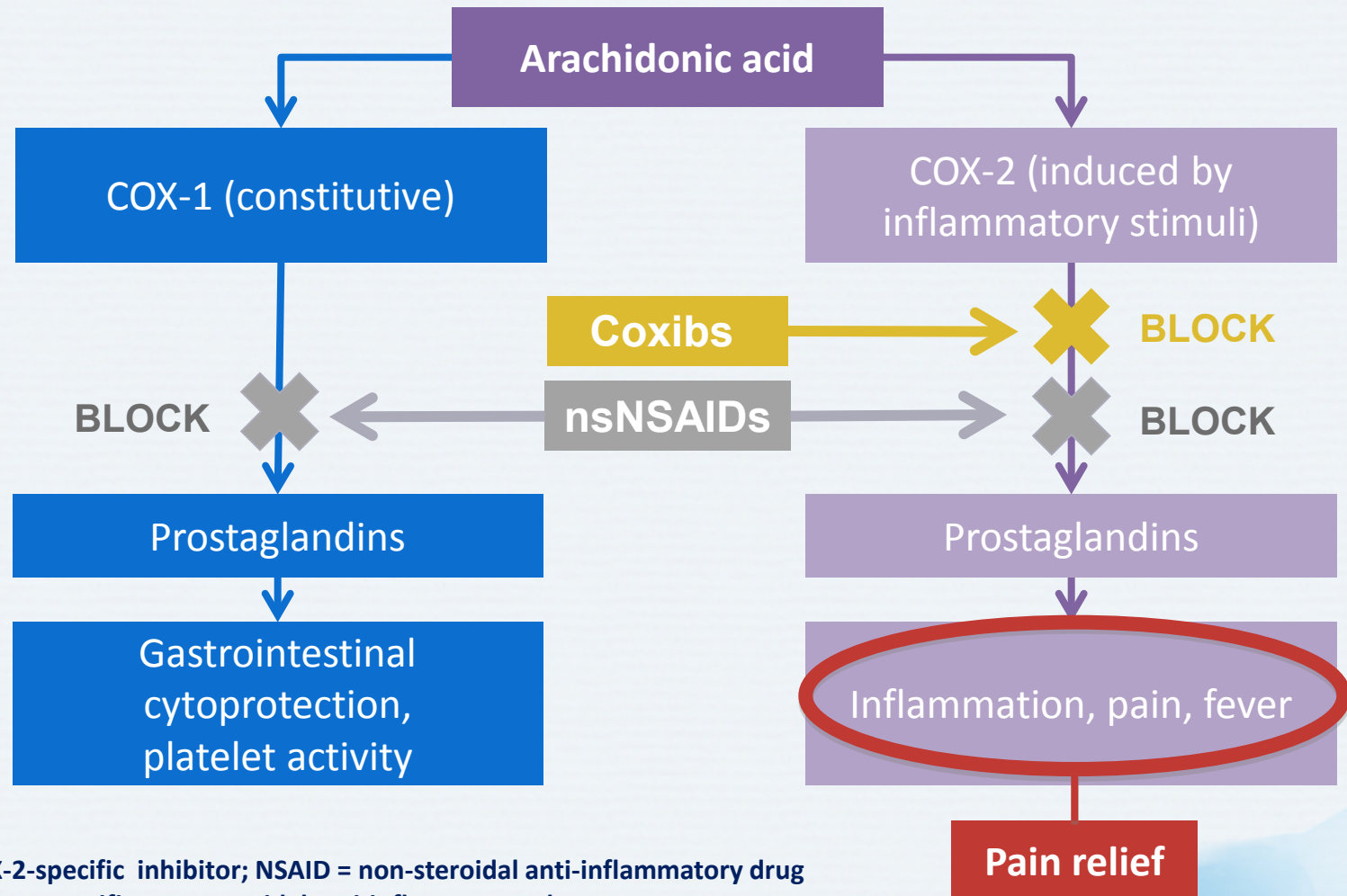
## *Examples of nsNSAIDs:*

- Diclofenac
- Ibuprofen
- Naproxen

## *Examples of Coxibs:*

- Celecoxib
- Etoricoxib
- Parecoxib

# How do nsNSAIDs/coxibs work?



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

Gastrosource. *Non-steroidal Anti-inflammatory Drug (NSAID)-Associated Upper Gastrointestinal Side-Effects*. Available at: <http://www.gastrosource.com/11674565?itemId=11674565>.

Accessed: December 4, 2010; Vane JR, Botting RM. *Inflamm Res* 1995;44(1):1-10.

# COX-2 Is Expressed in the CNS

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- Prostaglandins in the CNS are important in central sensitization and hyperalgesia<sup>1</sup>
- Peripheral inflammation leads to central induction of COX-2<sup>2</sup>
  - Occurs even with complete sensory nerve block<sup>3</sup>
  - Humoral signal (IL-6?) may play a role in signal transduction across blood-brain barrier<sup>3</sup>
  - IL-1beta plays an important role centrally<sup>3</sup>
  - Elevation of prostaglandins in CSF lead to hyperalgesia<sup>3</sup>
  - Inhibition of IL-1beta synthesis or receptors reduce CSF levels of COX-2, prostaglandin and hyperalgesia<sup>3</sup>
  - Inhibition of COX-2 centrally has similar effects<sup>3,4</sup>

**CNS = central nervous system; CSF = cerebrospinal fluid; IL = interleukin**

1. Taiwo YO, Levine JD. *Brain Res* 1986; 373(1-2):81-4; 2. Ghilardi JR *et al. J Neurosci* 2004; 24(11):2727-32;

3. Samad TA *et al. Nature* 2001; 410(6827):471-5; 4. Smith CJ *et al. Proc Natl Acad Sci US* 1998; 95(22):13313-8.

# COX-2 Results in Sensitization to Pain

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- 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**

Ahmadi S *et al. Nat Neurosci* 2002; 5(1):34-40; Baba H *et al. J Neurosci* 2001; 21(5):1750-6;

Samad TA *et al. Nature* 2001; 410(6827):471-5; Woolf CJ, Salter MW. *Science* 2000; 288(5472):1765-9.

# COX-2 Is Involved in Central Sensitization

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- 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**

Ahmadi S *et al. Nat Neurosci* 2002; 5(1):34-40; Baba H *et al. J Neurosci* 2001; 21(5):1750-6;

Samad TA *et al. Nature* 2001; 410(6827):471-5; Woolf CJ, Salter MW. *Science* 2000; 288(5472):1765-9.



# COX-2 Inhibition Minimizes Sensitization

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- 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

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## 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):

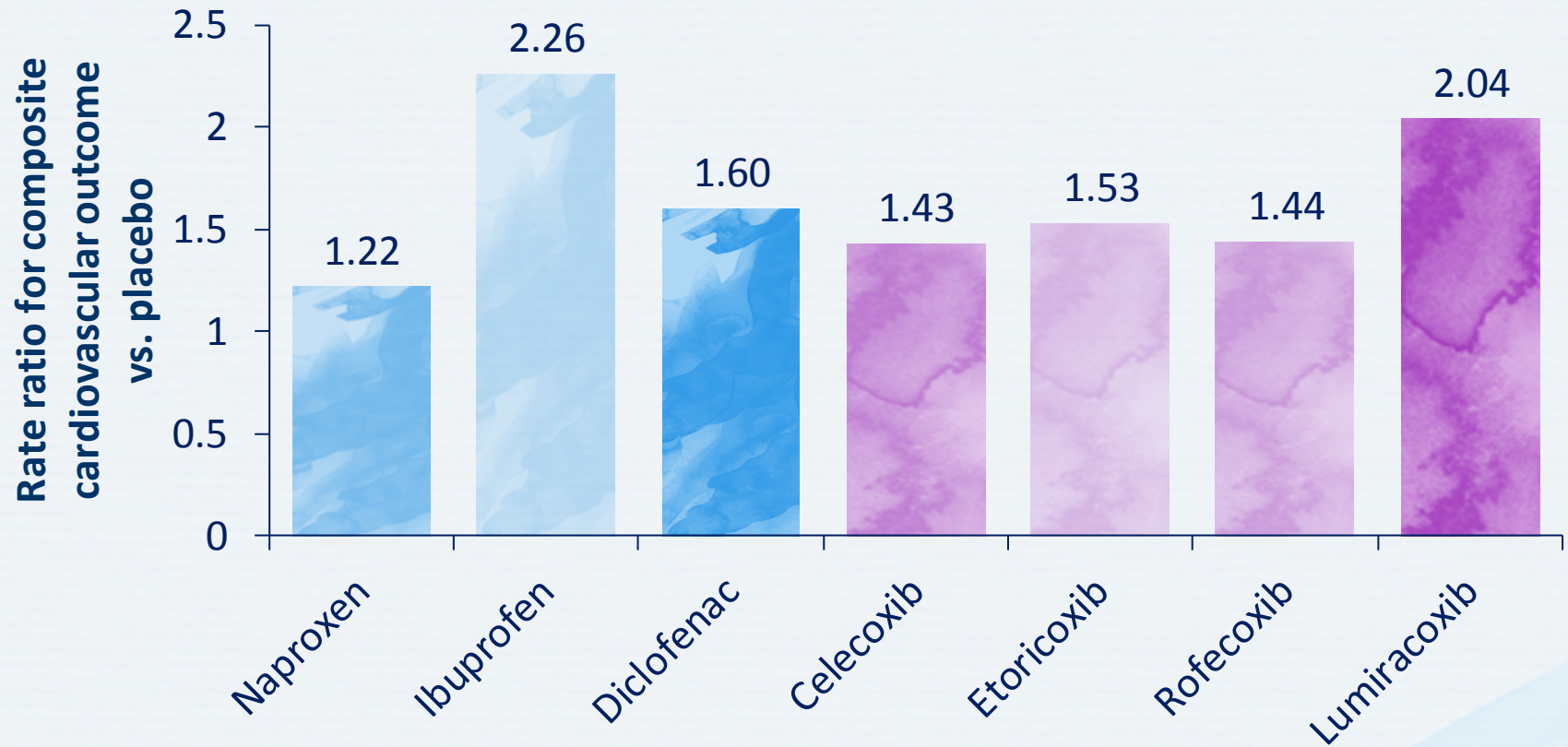
- Decreased platelet aggregation

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

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

Clemett D, Goa KL. *Drugs* 2000; 59(4):957-80; Grosser T *et al.* In: Brunton L *et al* (eds.). *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. (online version). McGraw-Hill; New York, NY: 2010.

# nsNSAIDs/Coxibs and Cardiovascular Risk

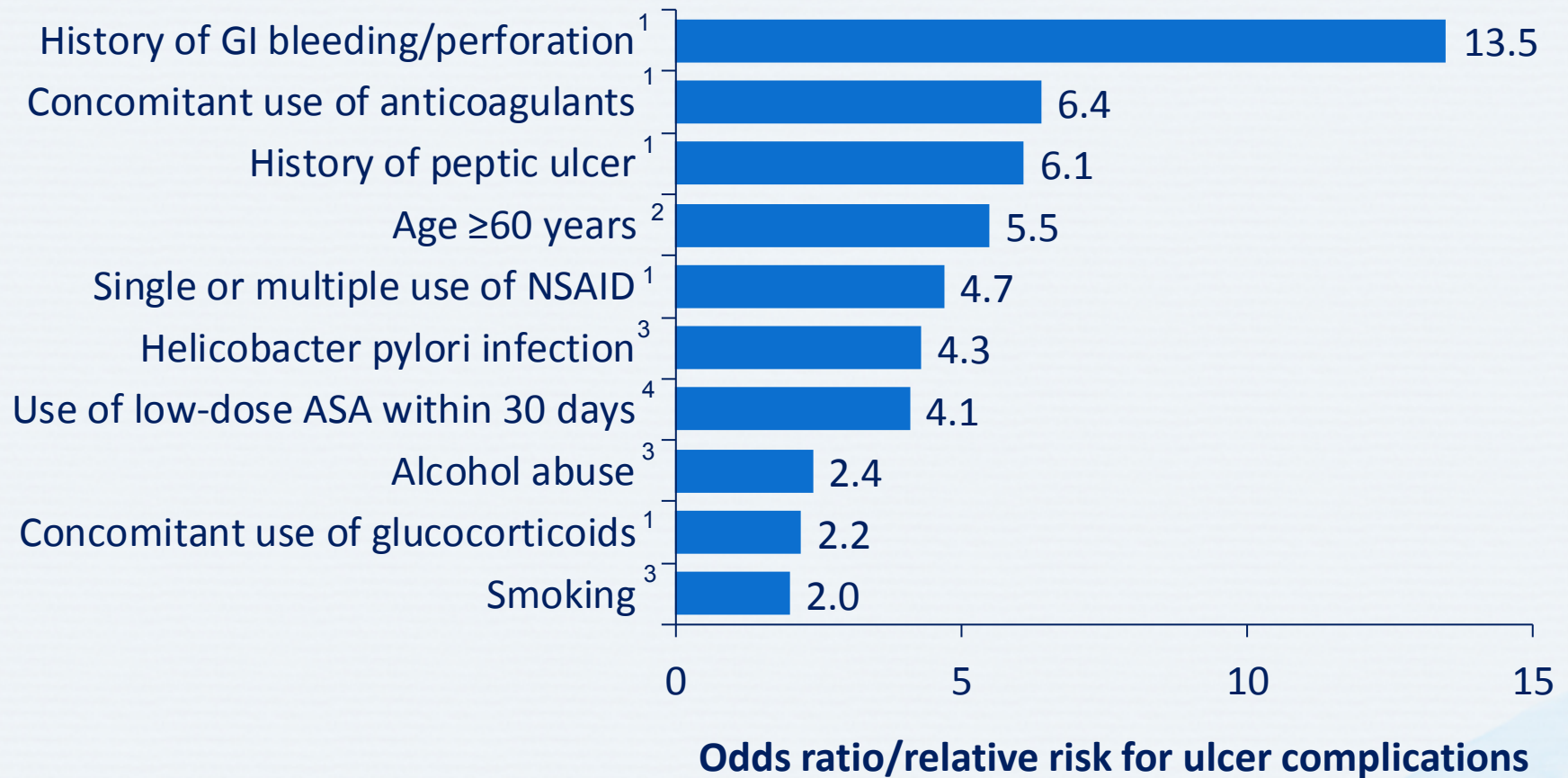


Composite includes non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death compared with placebo; chart based on network meta-analysis involving 30 trials and over 100,000 patients.

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

Trelle S *et al.* *BMJ* 2011; 342:c7086.

# Risk Factors for Gastrointestinal Complications Associated with nsNSAIDs/Coxibs



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

1. Garcia Rodriguez LA, Jick H. *Lancet* 1994; 343(8900):769-72; 2. Gabriel SE et al. *Ann Intern Med* 1991; 115(10):787-96;  
3. Bardou M, Barkun AN. *Joint Bone Spine* 2010; 77(1):6-12; 4. Garcia Rodríguez LA, Hernández-Díaz S. *Arthritis Res* 2001; 3(2):98-101.

# Gastrointestinal Effects of nsNSAIDs/Coxibs Beyond the Upper Gastrointestinal Tract

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- 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

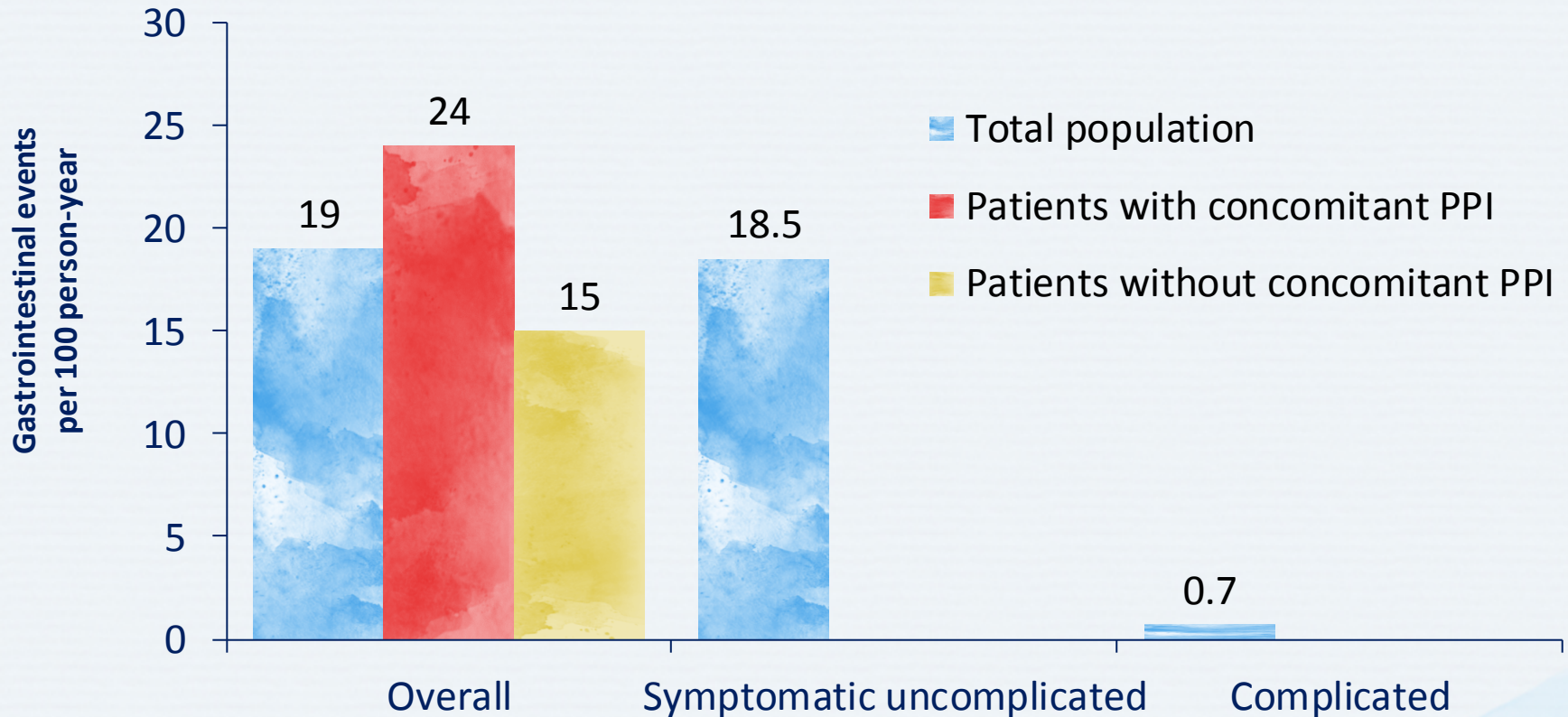
Coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug;

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

Allison MC *et al.* *N Engl J Med* 1992; 327(11):749-54; Chan FK *et al.* *N Engl J Med* 2002; 347(26):2104-10; Fujimori S *et al.* *Gastro Endoscopy* 2009; 69(7):1339-46; Laine L *et al.* *Gastroenterology* 2003; 124(2):288-92; Lanas A, Sopeña F. *Gastroenterol Clin N Am* 2009; 38(2):333-53.



# Gastrointestinal Events Associated with NSAID Use in Real-Life Practice



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

Lanas A et al. *Ann Rheum Dis* 2013; doi:10.1136/annrheumdis-2013-204155.

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

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	Gastrointestinal risk	
	Not elevated	Elevated
Not on ASA	nsNSAID alone	Coxib nsNSAID + PPI
On ASA	Coxib + PPI nsNSAID + PPI	Coxib + PPI nsNSAID + PPI

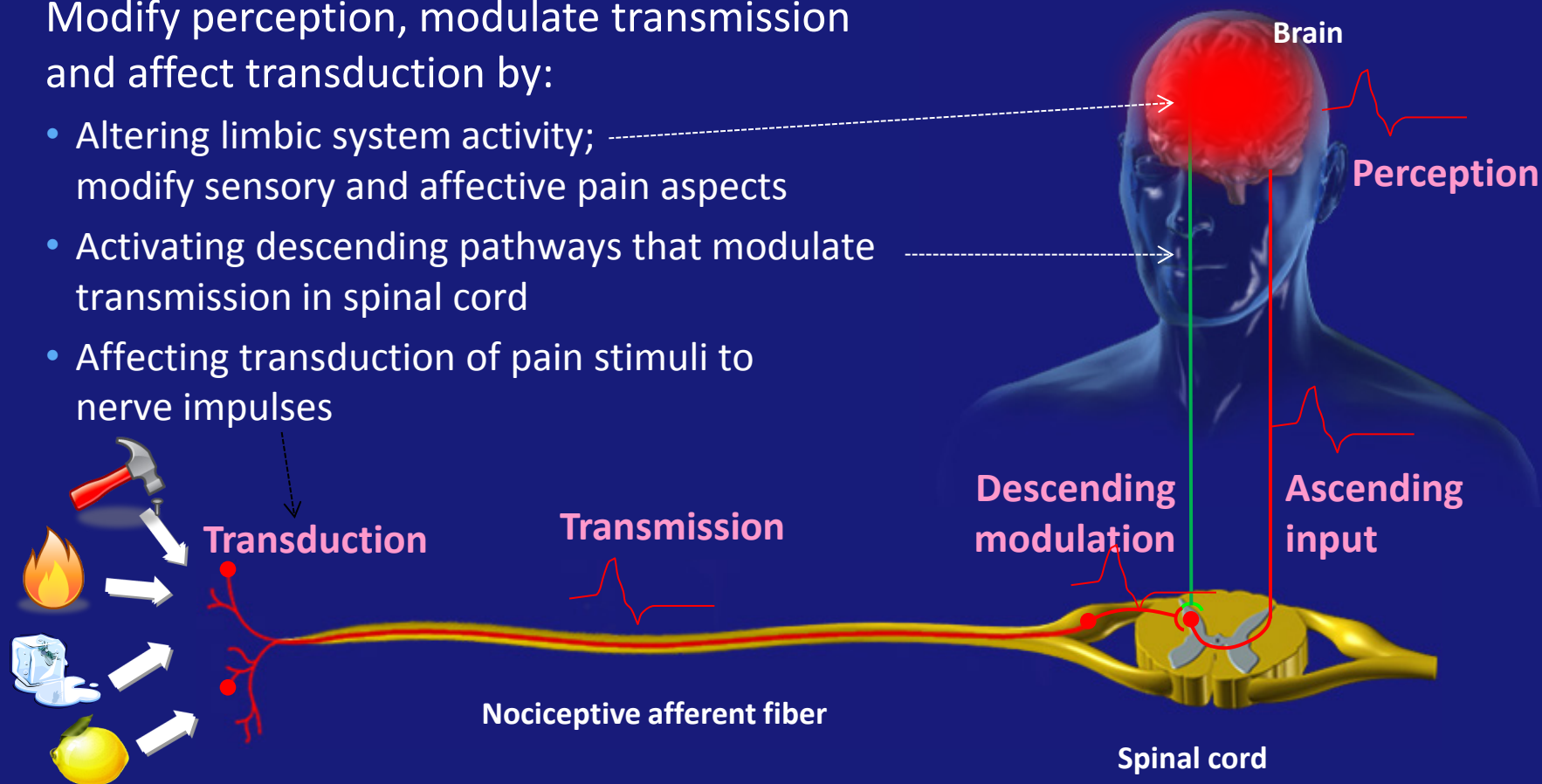
ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor;  
nsNSAID = non-selective non-steroidal anti-inflammatory drug; PPI = proton pump inhibitor

Tannenbaum H et al. *J Rheumatol* 2006; 33(1):140-57.

# 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



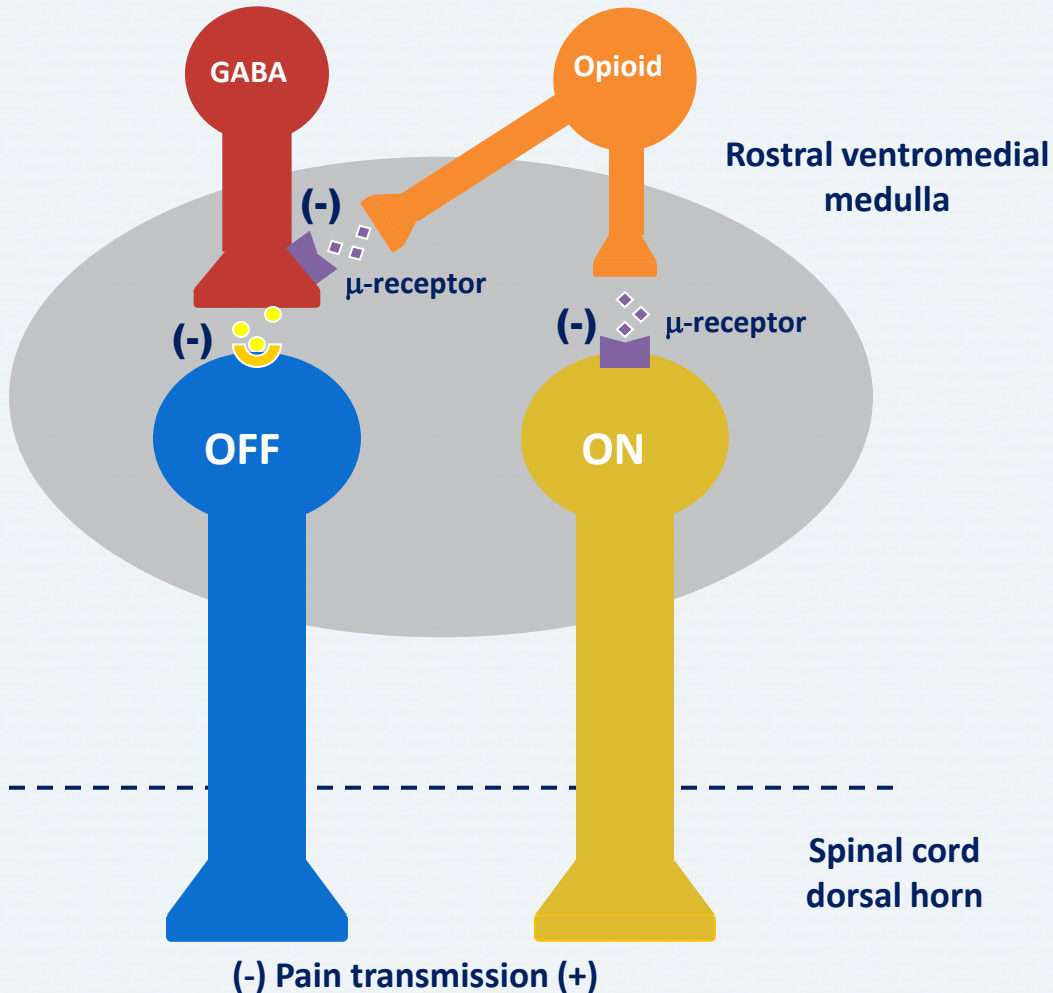


# Opioids and Pain Management

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Opioid Receptor	Response
<b>Mu</b>	Supraspinal analgesia, respiratory depression, sedation, miosis, euphoria, cardiovascular effects, pruritis, nausea/vomiting, decreased gastrointestinal motility, dependence, tolerance
<b>Delta</b>	Analgesia, euphoria, dysphoria, psychotomimetic effects
<b>Kappa</b>	Spinal analgesia, dysphoria, psychotomimetic effects, miosis, respiratory depression, sedation

# 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**

Fields HL *et al.* In: McMahon SB, Koltzenburg M (eds). *Wall and Melzack’s Textbook of Pain*. 5th ed. Elsevier; London, UK: 2006.

# Opioids Can Induce Hyperalgesia

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- 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

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- Pain evoked by innocuous stimuli
- Central sensitization → pain produced by A $\beta$  fibers
- Possibly mediated by spinal NMDA receptors

**NMDA = N-methyl-D-aspartate**

Dolan S, Nolan AM. *Neuroreport* 1999; 10(3):449-52; Raja SN *et al.* In: Wall PB, Melzack R (eds). *Textbook of Pain*. 4th ed. Churchill Livingstone; London, UK: 1999; Woolf CJ. *Drugs* 1994; 47(Suppl 5):1-9.

# Adverse Effects of Opioids

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System	Adverse effects
Gastrointestinal	Nausea, vomiting, constipation
CNS	Cognitive impairment, sedation, lightheadedness, dizziness
Respiratory	Respiratory depression
Cardiovascular	Orthostatic hypotension, fainting
Other	Urticaria, miosis, sweating, urinary retention

**CNS = central nervous system**

Moreland LW, St Clair EW. *Rheum Dis Clin North Am* 1999; 25(1):153-91; Yaksh TL, Wallace MS. In: Brunton L *et al* (eds). *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. (online version). McGraw-Hill; New York, NY: 2010.

# Pain in Rheumatic Disease

## Consensus Panel Recommendations

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### Fixed Low-Dose Combination Therapy

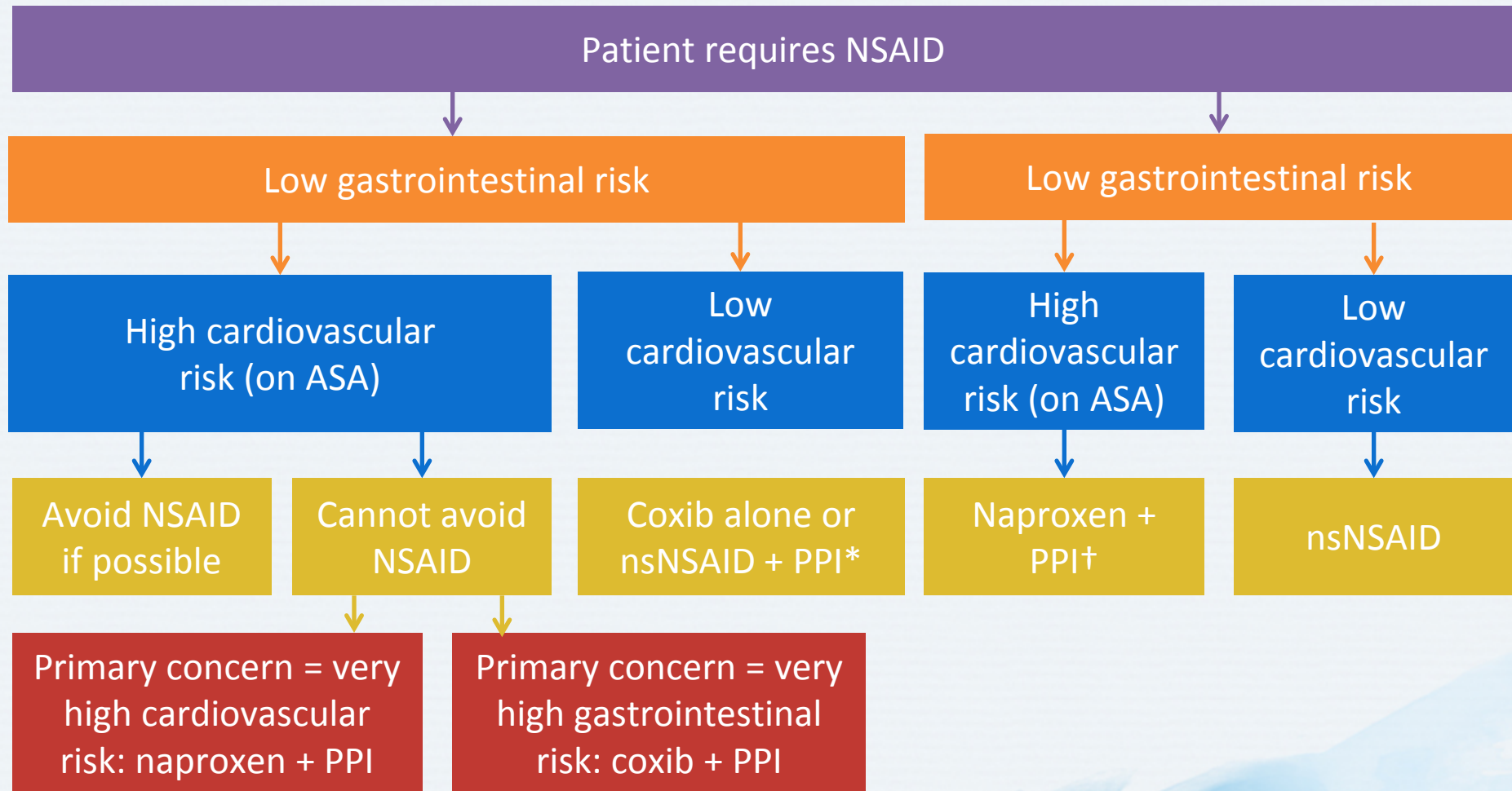
- Strong or weak opioid + acetaminophen
- NSAID + acetaminophen

### 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



# Canadian Consensus on Prescribing NSAIDs



\*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

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

Rostom A et al. *Aliment Pharmacol Ther* 2009; 29(5):481-96.



# ASAS/EULAR Guidelines for the Pharmacological Management of Ankylosing Spondylitis

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- 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
    - Adrenocorticotrophic 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

<b>nsNSAIDs/coxibs</b>	Symptomatic treatment to reduce joint swelling and pain
<b>DMARDs</b> (biologic, non-biologic)	<p>Reduce/prevent joint damage, preserve joint integrity and function</p> <ul style="list-style-type: none"> <li>• Methotrexate, leflunomide, hydroxychloroquine, minocycline, sulfasalazine</li> <li>• Etanercept, infliximab, adalimumab (TNF inhibitors)</li> <li>• Rituximab (anti-CD20)</li> <li>• Abatacept (cytotoxic T-lymphocyte antigen 4 immunoglobulin)</li> <li>• Tocilizumab (anti-interleukin 6 receptor)</li> </ul>
<b>Glucocorticoids</b>	<ul style="list-style-type: none"> <li>• Short-term use during flare-ups (oral or intramuscular)</li> <li>• Local treatment for individual active joints (intra-articular)</li> </ul>
<b>Surgery</b>	Carpal tunnel release, synovectomy, resection of metatarsal heads, total joint arthroplasty, joint fusion
<b>Supportive strategies</b>	<ul style="list-style-type: none"> <li>• Patient education, cognitive-behavioral interventions</li> <li>• Rehabilitation interventions</li> </ul>

**Coxib** = COX-2-specific inhibitor; **DMARD** = disease-modifying antirheumatic drug;

**nsNSAID** = non-specific non-steroidal anti-inflammatory drug; **TNF** = tumor necrosis factor

ACR Subcommittee on Rheumatoid Arthritis Guidelines. *Arthritis Rheum* 2002; 46(2):328-46; Saag KG et al. *Arthritis Rheum* 2008; 59(6):762-84; Smolen JS et al. *Lancet* 2007; 370(9602):1861-74.

# EULAR Guidelines for the Pharmacological Management of Rheumatoid Arthritis

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- 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

Combe B *et al. Ann Rheum Dis* 2007; 66(1):34-45.

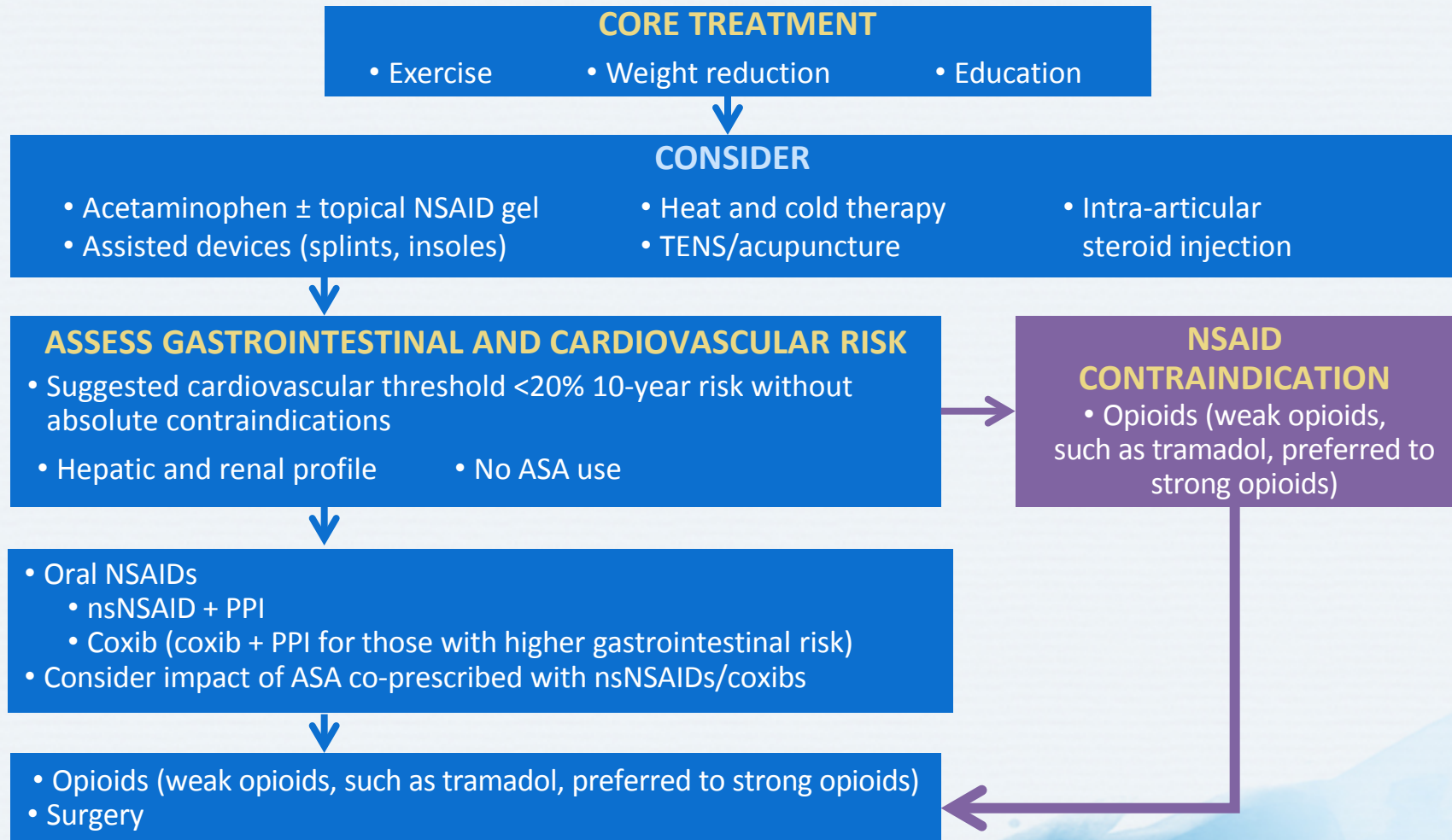
# Selected Osteoarthritis Management Guidelines

Organization	Year	Joints		
		Hand	Hip	Knee
ESCEO <sup>1</sup>	2014			X
OARSI <sup>2</sup>	2014			X
NICE <sup>3</sup>	2014	X	X	X
AAOS <sup>4</sup>	2013			X
South Africa <sup>5</sup>	2013	X	X	X
ACR <sup>6</sup>	2012	X	X	X
Chinese Orthopaedic Association <sup>7</sup>	2010	X	X	X
Croatian Society for Rheumatology <sup>8</sup>	2010		X	X
EULAR <sup>9</sup>	2010			X
Mexico <sup>10</sup>	2008		X	X
EULAR <sup>11</sup>	2007	X		
EULAR <sup>12</sup>	2005		X	

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

Bruyère O et al. *Semin Arthritis Rheum* 2014; pii:S0049-0172(14)00108-5; 2. McAlindon TE et al. *Osteoarthritis Cartilage* 2014; 22(3):363-88; 3. National Institute for Health and Care Excellence. 2014; 4. Jevsevar DS et al. *J Bone Joint Surg Am* 2013; 95(20):1885-6; 5. Hodgkinson B et al. *S Afr Med J* 2013;103(8 Pt 2):576-85; 6. Hochberg MC et al. *Arthritis Care Res (Hoboken)* 2012; 64(4):465-74; 7. Chinese Orthopaedic Association. *Orthop Surg* 2010; 2(1):1-6; 8. Grazio S et al. *Reumatizam* 2010; 57(1):36-47; 9. Zhang W et al. *Ann Rheum Dis* 2010;69(3):483-9; 10. Secretaria de Salud. 2008; 11. Zhang W et al. *Ann Rheum Dis* 2007;66(3):377-88; 12. Zhang W et al. *Ann Rheum Dis* 2005;64(5):669-81.

# Management of Osteoarthritis Flowchart



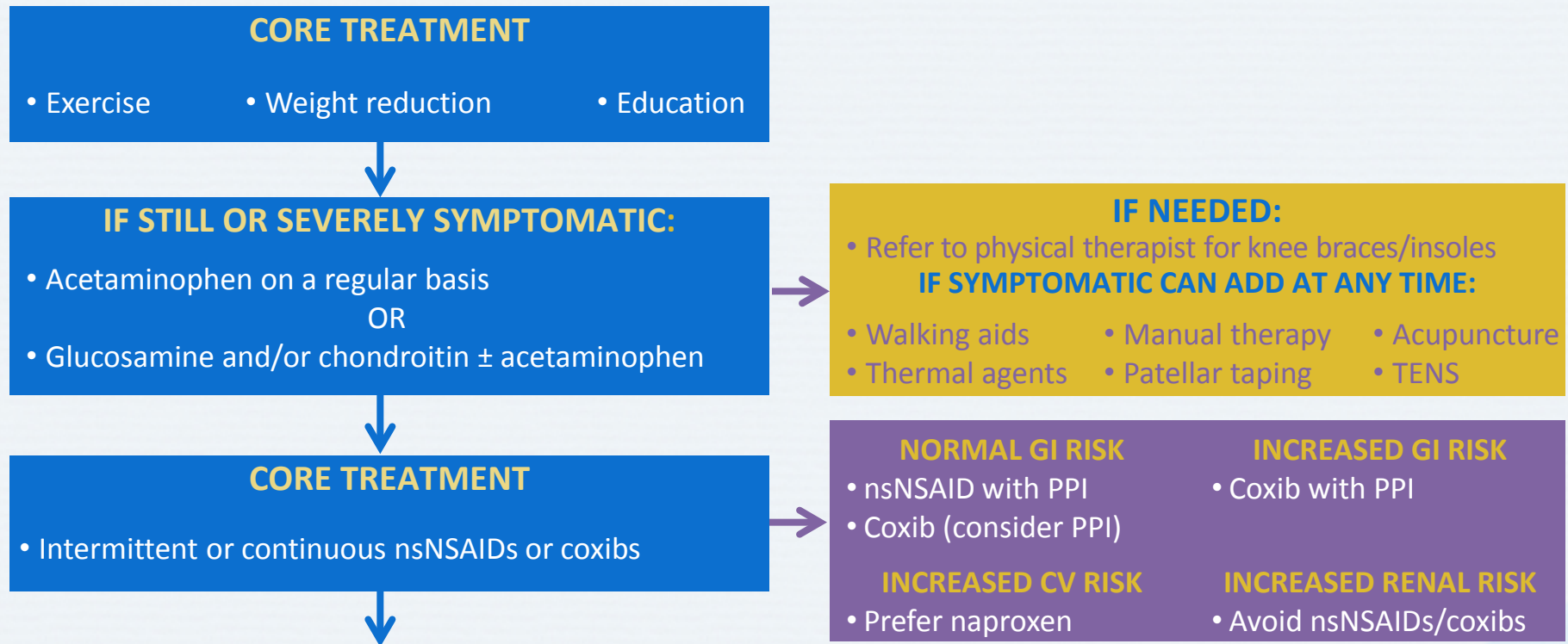
ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug;

nsNSAID = non-specific non-steroidal anti-inflammatory drug; PPI = proton pump inhibitor; TENS = transcutaneous electrical nerve stimulation

Adapted from: Adebajo A. *BMC Fam Pract* 2012; 13:23.



# ESCEO Algorithm for the Management of Osteoarthritis

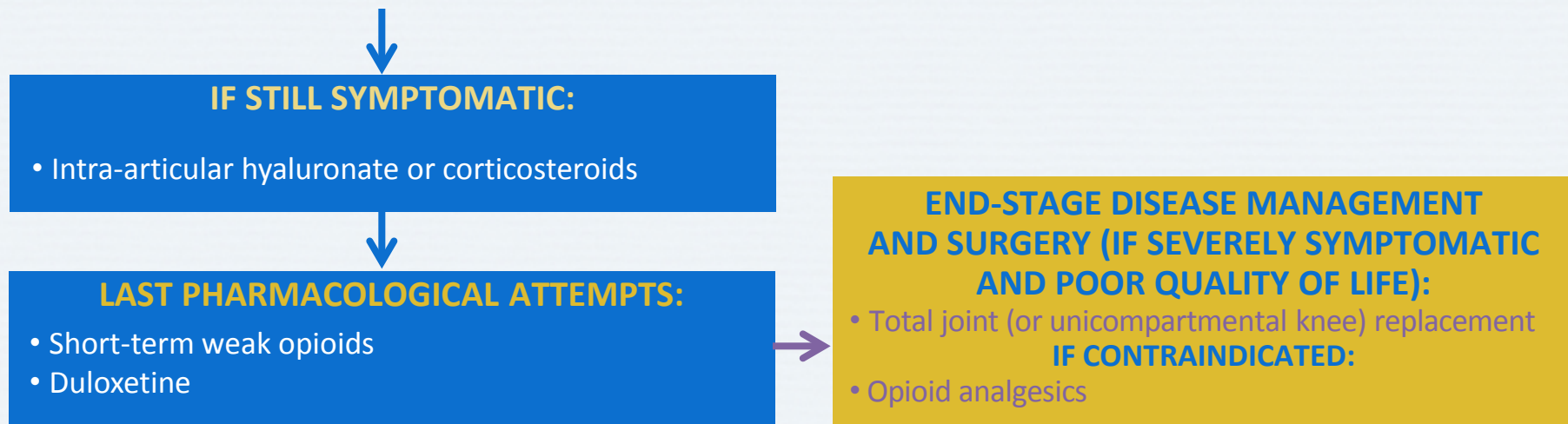


Coxib = COX-2-specific inhibitor; ESCEO = European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis; nsNSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug; PPI = proton pump inhibitor; TENS = transcutaneous electrical nerve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



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

# IASP Guidelines for the Pharmacological Management of Osteoarthritis

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## Systemic Treatments

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

## Local Treatments

- Intra-articular corticosteroids or hyaluronic acid injection

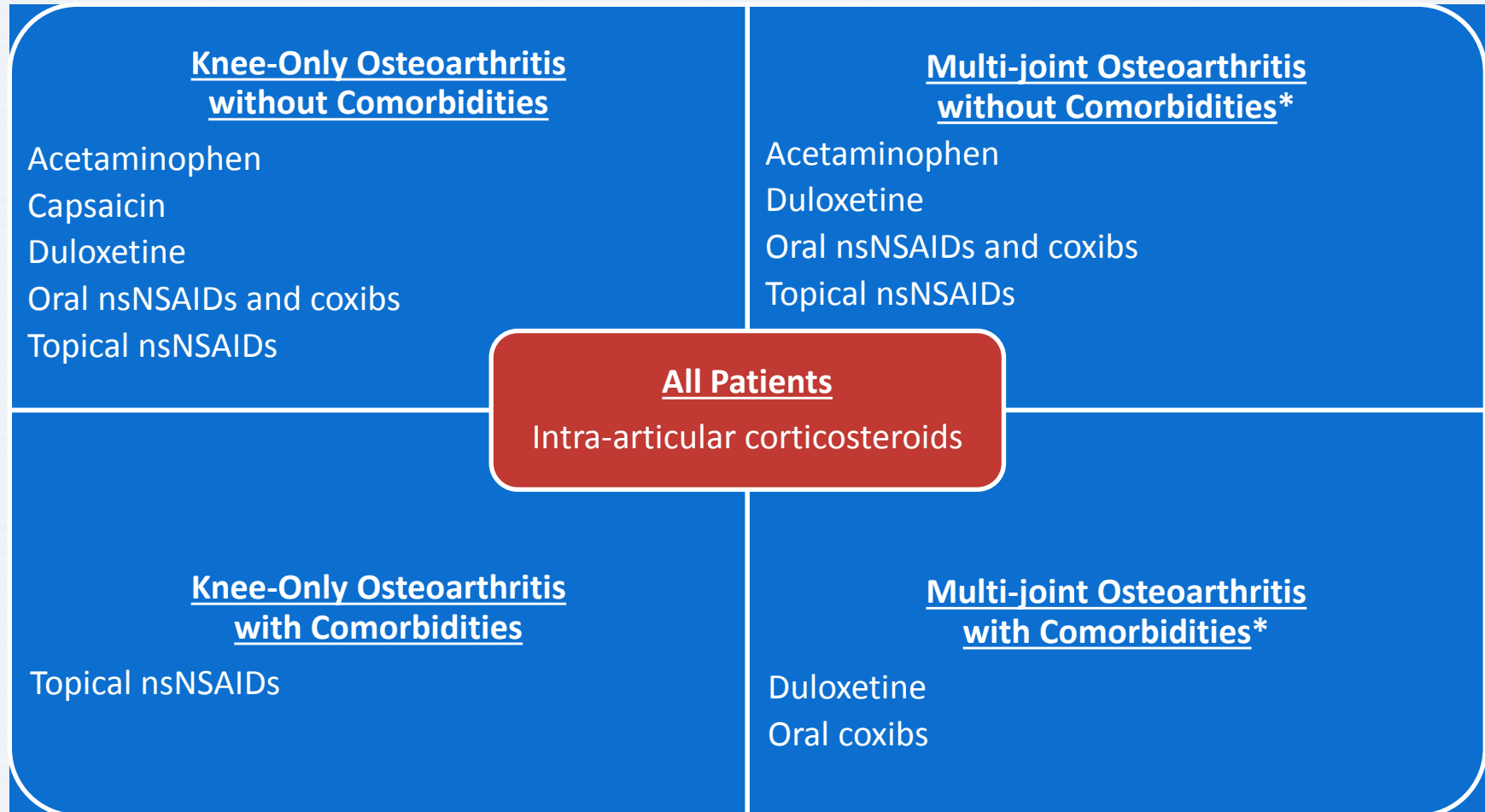
**Coxib** = COX-2-specific inhibitor; **IASP** = International Association for the Study of Pain;

**IL** = interleukin; **nsNSAID** = non-specific non-steroidal anti-inflammatory drug

International Association for the Study of Pain. *Osteoarthritis-Related Pain*.

Available at: <http://www.kamloopsphysiotherapy.ca/resources/Osteoarthritis.pdf>. Accessed: August 13, 2013.

# OARSI: Pharmacological Treatment for Knee Osteoarthritis



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)

McAlindon TE *et al. Osteoarth Cartil* 2014; 22(3):363-88.

# ACR Guidelines for the Pharmacological Management of Hand Osteoarthritis

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**ACR conditionally recommends using  $\geq 1$  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 Guidelines for the Pharmacological Management of Hip Osteoarthritis

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**ACR conditionally recommends using  $\geq 1$  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 Guidelines for the Pharmacological Management of Knee Osteoarthritis

---

**ACR conditionally recommends using  $\geq 1$  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



# EULAR Guidelines for the Pharmacological Management of Osteoarthritis

Pharmacotherapy	Hand	Hip	Knee
Acetaminophen $\leq 4$ g/day	✓	✓	✓
Oral NSAIDs at lowest effective dose and shortest duration	✓	✓	✓
Intra-articular injection of corticosteroid	✓	✓	✓
Opioid analgesics	x	x	✓
SYSADOAs	x	x	✓

EULAR = European League Against Rheumatism; NSAID = non-steroidal anti-inflammatory drug;

SYSADOA = symptomatic slow acting drugs for osteoarthritis

Jordan K et al. *Ann Rheum Dis* 2003; 62(12):1145–55; Zhang W et al. *Ann Rheum Dis* 2005; 64(5):669–81; Zhang W et al. *Ann Rheum Dis* 2007; 66(3):377–88.

# 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

# Measuring Treatment Response in Ankylosing Spondylitis: ASAS

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## ASAS20

- Improvement of  $\geq 20\%$  and absolute improvement of  $\geq 10$  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  $\geq 20\%$  worsening

# ACR Criteria for Assessing Treatment Response in Rheumatoid Arthritis

20% improvement in  
tender and swollen joints



20% improvement in  $\geq 3$  of the  
following:

- Physician global assessments
- Patient global assessments
- Pain
- Disability
- Acute-phase reactant

# Quality Measures that Focus on Rheumatoid Arthritis: PQRI

Number	Measure title	Description	Measure developer	Patient-level measure
106	DMARD Therapy	% of patients (≥18 years) prescribed, dispensed, or administered ≥1 ambulatory prescription for a DMARD	NCQA	Yes
176	TB Screening	% 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	AMA-PCP/ NCQA	Yes
177	Periodic Assessment of Disease Activity	% of patients with an assessment and classification of disease activity within 12 months	AMA-PCP/ NCQA	Yes
178	Functional Status Assessment	% of patients for whom a functional status assessment was performed at least once within 12 months	AMA-PCP/ NCQA	Yes
179	Assessment and Classification of Disease Prognosis	% of patients who have an assessment and classification of disease prognosis at least once within 12 months	AMA-PCP/ NCQA	Yes
180	Glucocorticoid Management	% 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	AMA-PCP/ NCQA	Yes

**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**

*2010 PQRI Measure List.* Available at: [http://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/PQRS/downloads/2010\\_PQRI\\_MeasuresList\\_111309.pdf](http://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/PQRS/downloads/2010_PQRI_MeasuresList_111309.pdf). Accessed: August 15, 2013.

# Quality Measures that Focus on Rheumatoid Arthritis: MDS

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- 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**

Centers for Medicare & Medicaid Services. *Nursing Home Quality Initiative*. Available at: <http://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/NursingHomeQualityInits/index.html?redirect=/NursingHomeQualityInits>. Accessed: August 5, 2013;

Saliba D et al. *Development and Validation of a Revised Nursing Home Assessment Tool: MDS 3.0*. Available at: <http://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/NursingHomeQualityInits/downloads/MDS30FinalReport.pdf>. Accessed: August 5, 2013.



# Assessing Treatment Response in Osteoarthritis: WOMAC™

Pain subscale	Physical function subscale	Stiffness subscale
<ol style="list-style-type: none"> <li>1. Walking on a flat surface</li> <li>2. Going up/down stairs</li> <li>3. While sleeping</li> <li>4. Sitting/lying down</li> <li>5. Standing upright</li> </ol>	<ol style="list-style-type: none"> <li>1. Descending stairs</li> <li>2. Ascending stairs</li> <li>3. Getting out of a chair</li> <li>4. Standing upright</li> <li>5. Bending</li> <li>6. Walking on a flat surface</li> <li>7. Getting in/out of car</li> <li>8. Shopping</li> <li>9. Putting on socks/stockings</li> <li>10. Getting out of bed</li> <li>11. Taking off socks/stockings</li> <li>12. Lying in bed</li> <li>13. Getting in/out of bath</li> <li>14. Sitting</li> <li>15. Getting on/off toilet</li> <li>16. Heavy domestic duties</li> <li>17. Light domestic duties</li> </ol>	<ol style="list-style-type: none"> <li>1. Morning stiffness</li> <li>2. Stiffness after sitting/lying/resting</li> </ol>

**WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index**

Bellamy N *et al.* *J Rheumatol* 1988; 15(12):1833-40; WOMAC™ Questionnaire. Available at:

[http://www.oarsi.org/pdfs/pain\\_indexes/WOMAC\\_QUESTIONNAIRE\\_INFORMATION.pdf](http://www.oarsi.org/pdfs/pain_indexes/WOMAC_QUESTIONNAIRE_INFORMATION.pdf). Accessed: August 5, 2013.

# Quality Measures that Focus on Osteoarthritis: PQRS

Item	Number 109	Number 142
Measure title	Function and Pain Assessment	Assessment for Use of Anti-Inflammatory or Analgesic OTC Medications
Description	Percentage of patients visits ( $\geq 21$ years) with a diagnosis of osteoarthritis with assessment for function and pain	Percentage of patients visits ( $\geq 21$ years) with a diagnosis of osteoarthritis with assessment for use of anti-inflammatory or analgesic over-the-counter medications
Measure developer	AMA-PCPI	AMA-PCPI
Reporting options	Claims-based Registry	Claims-based Registry
Patient-level measure	No	No

**AMA-PCPI = American Medical Association-sponsored Physician Consortium on Performance Improvement;**  
**PQRS = Physician Quality Reporting System**

Physician Quality Reporting System. Available at: [http://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/PQRS/index.html?redirect=/PQRS/15\\_MeasuresCodes.asp](http://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/PQRS/index.html?redirect=/PQRS/15_MeasuresCodes.asp). Accessed: August 15, 2013.

# Quality Measures that Focus on Osteoarthritis: MDS

---

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Saliba D *et al.* *Development and Validation of a Revised Nursing Home Assessment Tool: MDS 3.0*. Available at: <http://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/NursingHomeQualityInits/downloads/MDS30FinalReport.pdf>. Accessed: August 5, 2013.

# When to Refer Patients with Osteoarthritis

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

**\*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**

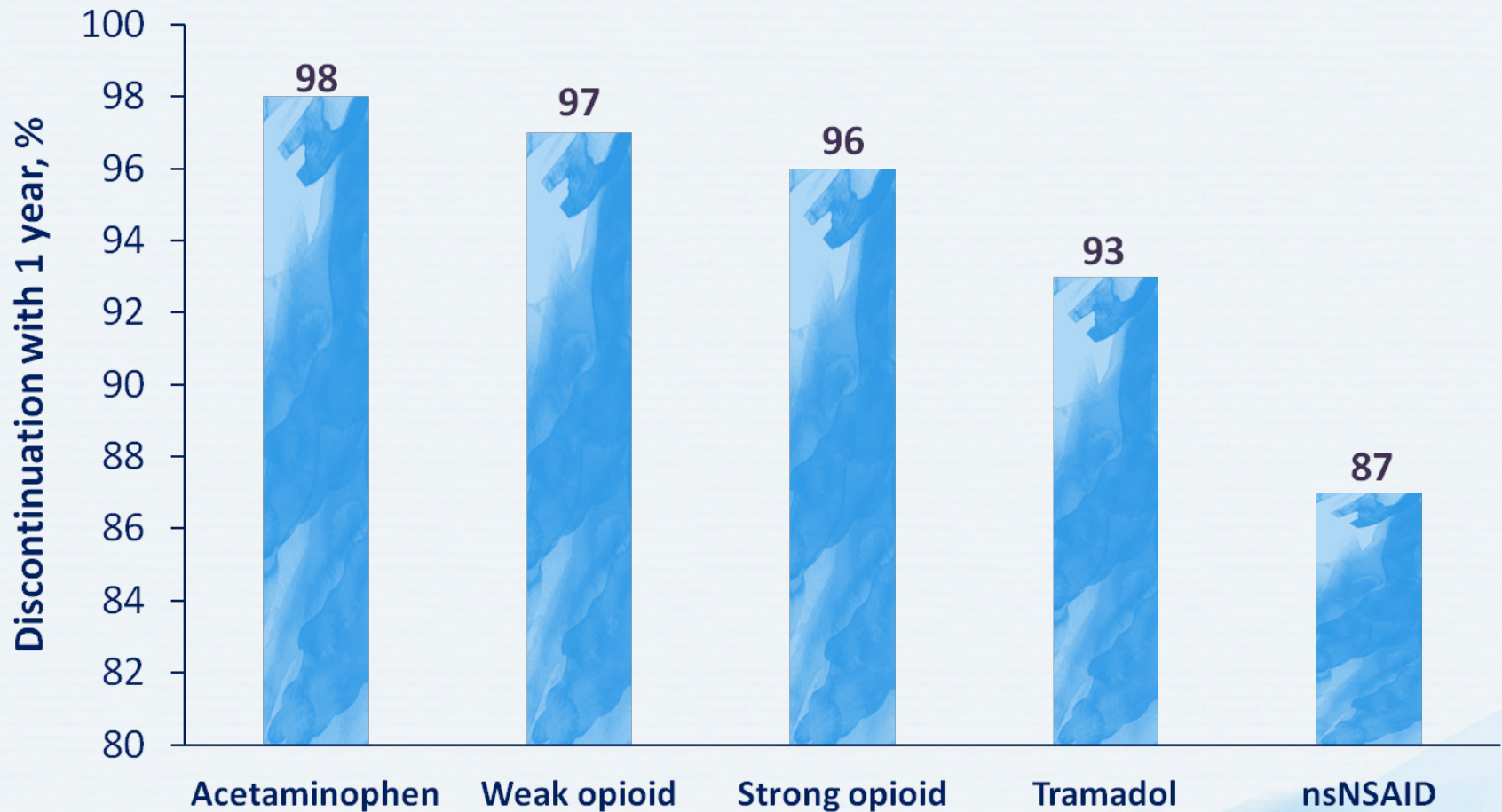
National Institute for Clinical Excellence. *Referral Advice: A Guide to Appropriate Referral From General to Specialist Services*. London, UK: 2001.

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# Adherence

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# Osteoarthritis and Non-adherence to Select Analgesics



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

Gore M *et al. Clin Ther* 2011; 33(12):1914-31.



# Strategies to Improve Adherence

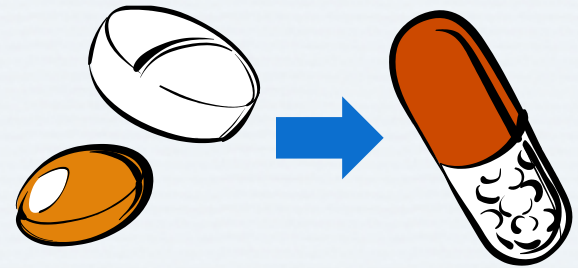
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- **S**implify regimen
- **I**mpart knowledge
- **M**odify patient beliefs and human behavior
- **P**rovide communication and trust
- **L**eave the bias
- **E**valuate adherence

# 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

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- 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

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## 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

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- 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



# Leaving the Bias

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

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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

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# Summary

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# Management of Chronic Joint Pain: Summary

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- 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