

# Management of Osteoarthritis

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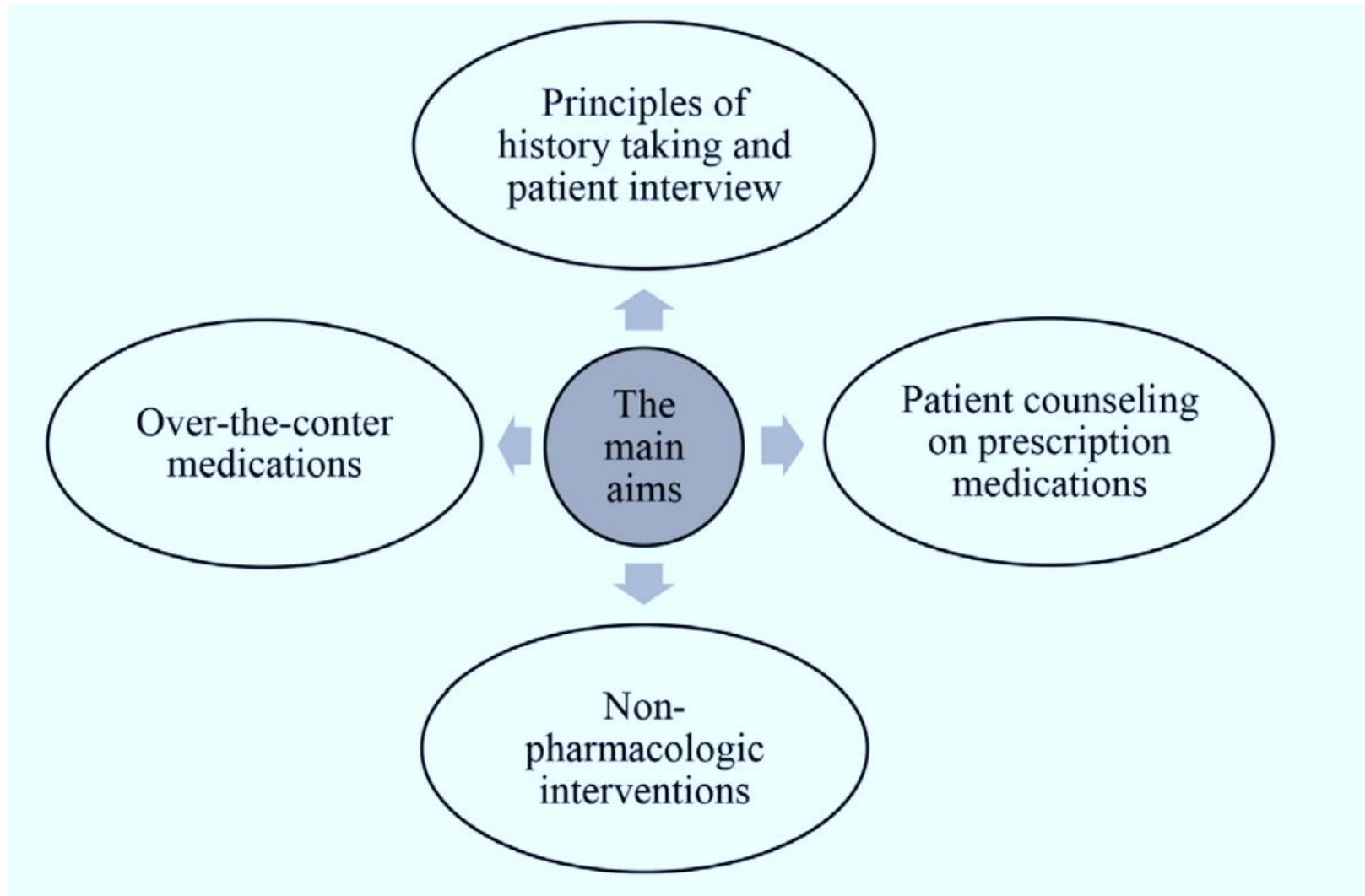
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# Learning Outcomes

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# INTRODUCTION

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- ❑ Osteoarthritis (OA) is the **commonest form of arthritis** and possesses marked variability of disease expression.
- ❑ Although most patients present with **joint pain and functional limitations**, the **age of disease onset**, **sequence** of joint involvement, and **disease progression** vary from person to person.
- ❑ OA ranges from an **asymptomatic**, incidental finding on clinical or radiologic examination to a **progressive disabling disorder** eventually culminating in "joint failure."

# CLINICAL MANIFESTATIONS

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- ❑ The primary symptoms of osteoarthritis (OA) are joint pain, stiffness, and locomotor restriction.
- ❑ Symptoms usually present in just one or a few joints in a middle-aged or older person.
- ❑ Other manifestations in patients with OA include sequelae such as muscle weakness, poor balance, and comorbidities such as fibromyalgia

# STAGE OF KNEE OSTEOARTHRITIS

**I**  
**Doubtful**



Minimum disruption.  
There is already  
10% cartilage loss.

**II**  
**Mild**



Joint-space narrowing.  
The cartilage to begin breaking down.  
Occurrence of osteophytes.

**III**  
**Moderate**



Moderate joint-space reduction.  
Gaps in the cartilage can  
expand until they reach the bone.

**IV**  
**Severe**



Joint-space greatly reduced.  
60% of the cartilage is already lost.  
Large osteophytes.

## Principal manifestations of osteoarthritis

Patient characteristics	
Age of onset	<ul style="list-style-type: none"><li>▪ &gt;40 years*</li></ul>
Symptoms	
Pain	<ul style="list-style-type: none"><li>▪ Affects one or a few joints at a time</li><li>▪ Insidious onset - slow progression over years</li><li>▪ Variable intensity</li><li>▪ May be intermittent</li><li>▪ Increased by joint use and relieved by rest</li><li>▪ Night pain in severe osteoarthritis</li></ul>
Stiffness	<ul style="list-style-type: none"><li>▪ Short-lived (&lt;30 minutes) and early morning- or inactivity-related</li></ul>
Swelling	<ul style="list-style-type: none"><li>▪ Some (eg, nodal osteoarthritis) patients present with swelling and/or deformity</li></ul>
Constitutional symptoms	<ul style="list-style-type: none"><li>▪ Absent</li></ul>
Physical exam findings	
Appearance	<ul style="list-style-type: none"><li>▪ Swelling (bony overgrowth ± fluid/synovial hypertrophy)</li><li>▪ Attitude</li><li>▪ Deformity</li><li>▪ Muscle wasting (global - all muscles acting over the joint)</li></ul>
Palpation	<ul style="list-style-type: none"><li>▪ Absence of warmth</li><li>▪ Swelling (effusion if present is usually small and cool)</li><li>▪ Joint line tenderness</li><li>▪ Periarticular tenderness (especially knee, hip)</li></ul>
Range of motion	<ul style="list-style-type: none"><li>▪ Crepitus (knee, thumb bases)</li><li>▪ Reduced range of movement</li><li>▪ Weak local muscles</li></ul>

OA: osteoarthritis.

\* Major joint injury and certain rare conditions may predispose to OA before the age of 40 years.

Adapted from: OARSI Primer (<http://primer.oarsi.org>).

UpToDate®







Heberden's nodes



Deformity  
Heberden's nodes





Erosive hand OA with  
marked radial deviation



Thumb-base osteoarthritis



Unilateral knee OA



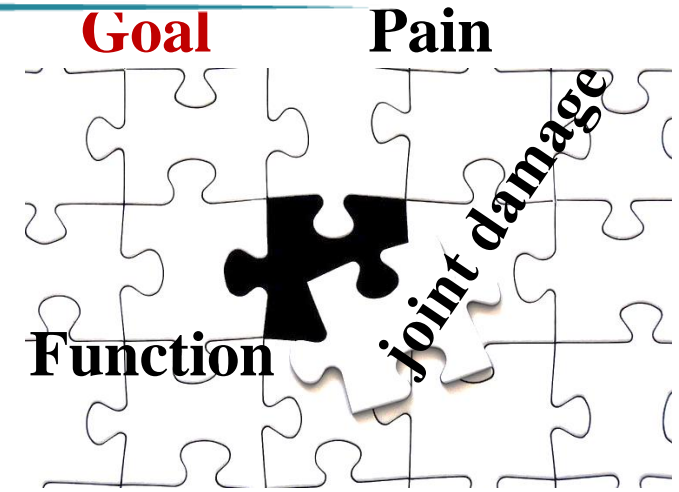
right hip OA, showing fixed flexion and external rotation deformity.



# Goal of treatment

❑ The goals of OA management are to

- Minimize pain
- Optimize function
- And beneficially modify the process of joint damage





# Approach

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- ❑ Due to the **modest effects** of the individual treatment options, a **combination** of therapeutic approaches is commonly used in practice and should prioritize therapies that are **safer**.





## Non-pharmacologic therapy

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- ❑ Non-pharmacologic interventions are the **mainstay** of OA management and should be **tried first**, followed by or in concert with medications to relieve pain when necessary.



Anchor  
Therapy



## Non-pharmacologic therapies include

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- ☐ **Weight** management
- ☐ **Exercises**
- ☐ **Braces** and foot **orthoses** for patients suitable to these interventions

And use of **assistive devices** when required

# Non-pharmacologic therapy for the management of OA

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## Weight loss

- ❑ Loss of at least 10 percent of body weight through a combination of diet and exercises has been associated with a 50 percent reduction in pain scores in overweight/obese patients with knee OA after 18 months.

Messier SP, Mihalko SL, Legault C, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. JAMA 2013; 310:1263.



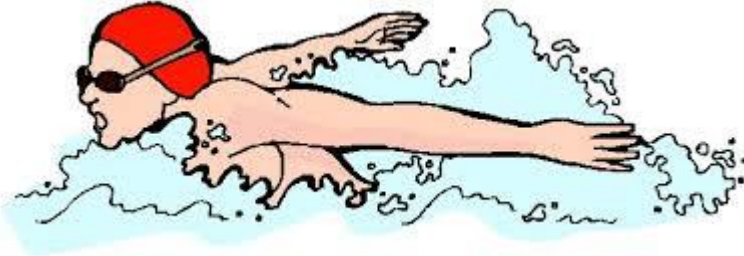


# Non-pharmacologic therapy for the management of OA

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- ❑ Exercises have effects of **similar magnitude** on pain and function compared with **NSAIDs**.

A combination of **aerobic, strengthening, and** aquatic exercises.



# Non-pharmacologic therapy for the management of OA

## Equipment

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**Braces, foot orthoses, and assistive devices when required**



# Pharmacologic therapy

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- ❑ Pharmacologic agents are used for patients with **symptomatic OA** who have **not responded adequately** to initial non-pharmacologic measures **or concomitantly** with these interventions.
- ❑ Pharmacologic therapy should only be used during periods when **symptoms are present**, since none of the interventions have been shown to be **disease-modifying**.



# Pharmacologic therapy

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**The main medications used in the pharmacologic management of OA include:**

- ☐ Oral and topical NSAIDs
- ☐ Topical capsaicin
- ☐ Duloxetine (prescription only)
- ☐ And intraarticular glucocorticoids & hyaluronate

# General approach to pharmacotherapy

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- ❑ In patients with one or a few joints affected, especially knee and/or hand OA, pharmacotherapy initiate with **topical NSAIDs** due to their **similar efficacy** compared with oral NSAIDs and their better safety profile.

# General approach to pharmacotherapy

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## Topical NSAIDs

- ❑ The risk of **gastrointestinal, renal, and cardiovascular toxicity** is much lower with topical NSAIDs as compared with its oral formulation due to the reduced systemic absorption (**5- to 17-fold** lower)
- ❑ The **tolerability profile** is **also better** with topical NSAIDs, with mild skin rashes being the most commonly reported side effect.

# Administration

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## Topical Diclofenac

❑ Lower extremity (eg, knee):

Gel 1% (OTC or Rx): **Apply 4 g** to each affected **area up to 4 times** daily; maximum dose per joint: **16 g/day**; maximum total body dose (all combined joints): **32 g/day**.

❑ Upper extremity (eg, hand):

Gel 1% (OTC or Rx): **Apply 2 g** to each affected area **up to 4 times daily**; maximum dose per joint: **8 g/day**; maximum total body dose (all combined joints): **32 g/day**.



# Administration

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- ❑ Apply to clean, dry, intact skin; do not apply to open wounds, eyes, or mucous membranes.
- ❑ Do not cover with occlusive dressings or apply heat, sunscreens, cosmetics, lotions, moisturizers, insect repellents, or other topical medications to affected area.
- ❑ Showering/bathing should be avoided for  $\geq 1$  hour following application. Wash hands immediately after application (unless hands are treated joint, then wait  $\geq 1$  hour to wash hands).
- ❑ Avoid sunlight to exposure areas.
- ❑ Avoid wearing clothes or gloves for  $\geq 10$  minutes after application.

# General approach to pharmacotherapy

## Capsaicin

- ❑ Topical capsaicin is a treatment option when **one or a few joints are involved** and other interventions **are ineffective** or **contraindicated**; however, its use may be limited by common local side effects.



# General approach to pharmacotherapy

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## **Oral NSAIDs are used in patients with:**

- ☐ Inadequate symptom relief from topical NSAIDs
- ☐ Symptomatic OA in multiple joints
- ☐ And/or patients with hip OA.



**vs**



## Oral NSAIDs

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- ❑ The use of NSAIDs in most patients is limited by the increased risk of **serious gastrointestinal, cardiovascular, and renal complications.**
- ❑ The **lowest effective dose** should be used to control the patient's symptoms on an **as-needed basis.**

# Recommended doses

Diclofenac acid **35 mg** is approximately equivalent to **38.5 mg** of diclofenac salts

Drug	Usual analgesic dose (oral)	Maximum dose per day	Selected characteristics
<b>Diclofenac</b>	50 mg every 8 to 12 hours	150 mg for RA, labeling in United States permits up to 200 mg	<ul style="list-style-type: none"> <li>• Dosing for free-acid preparation differs from doses listed here for sodium or potassium salts;</li> </ul>
<b>Indomethacin</b>	25 to 50 mg every 8 to 12 hours	150 mg For rheumatologic conditions, labeling in United States permits up to 200 mg	<ul style="list-style-type: none"> <li>• More frequently associated with <b>CNS side effects</b> (eg, headache, altered mental status) compared with other NSAIDs</li> </ul>
<b>Meloxicam</b>	7.5 to 15 mg <b>once daily</b>	15 mg	<ul style="list-style-type: none"> <li>• Long duration of effect; <b>relatively slow onset</b></li> <li>• Relative COX-2 selectivity and <b>minimal effect on platelet function</b> at lower daily dose of 7.5 mg</li> </ul>
<b>Piroxicam</b>	10 to 20 mg <b>once daily</b>	20 mg	<ul style="list-style-type: none"> <li>• Long-acting <b>alternative</b> for treatment of chronic pain and inflammation poorly responsive to other NSAIDs</li> <li>• <b>Prescribing generally limited to specialists with experience</b> in treatment of chronic pain and inflammation</li> </ul>

# Recommended doses

Drug	Usual analgesic dose (oral)	Maximum dose per day	Selected characteristics
Ibuprofen	400 mg every 4 to 6 hours or 600 to 800 mg every 6 to 8 hours	3200 mg (acute), 2400 mg (chronic)	<ul style="list-style-type: none"> <li>•Shorter-acting alternative to naproxen; <b>useful in patients without cardiovascular risks</b></li> </ul>
Naproxen	Base: 250 to 500 mg every 12 hours or 250 mg every 6 to 8 hours	Base: 1250 mg (acute); 1000 mg (chronic); may increase to 1500 mg during a disease flare	<ul style="list-style-type: none"> <li>•Often <b>preferred</b> for treatment of acute or chronic pain and inflammation in patients without relevant comorbidities or risks</li> <li>•Higher dose (eg, 500 mg base twice daily) may have less cardiovascular toxicity than comparable doses of other NSAIDs;</li> <li>•<b>Naproxen sodium has a faster onset than naproxen base</b></li> </ul>
Celecoxib	200 mg daily or 100 mg every 12 hours	400 mg	<ul style="list-style-type: none"> <li>•<b>Less risk of GI toxicity</b> relative to nonselective NSAIDs; benefit negated by low-dose aspirin, which may require concurrent gastroprotection</li> <li>•<b>No effect on platelet function</b></li> <li>•<b>Cardiovascular and kidney risks are dose-related and may be similar to nonselective NSAIDs</b></li> <li>•May be tolerated by patients with AERD or pseudoallergic reactions (eg, asthma, rhinosinusitis) who cannot take other NSAIDs</li> </ul>

# Gastritis and Gastroduodenal Ulcer Associated with NSAIDs

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- ❑ For traditional NSAIDs, **low and medium doses** were associated with a lower risk than were higher doses.
- ❑ These adverse effects are **less common with selective COX-2 inhibitors**.
- ❑ Several NSAIDs had a far higher than average risk, including **ketorolac** and **piroxicam**.
- ❑ Drugs with a **long half-life** or **slow-release formulation** were associated with higher risk, even accounting for dose.

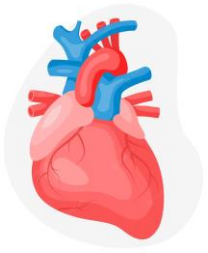




## Cardiovascular Effects of NSAIDs

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- ❑ The largest meta-analysis of observational studies available to date also clearly demonstrates that **higher doses of NSAIDs**, with the exception of naproxen, **increased the risk of serious cardiovascular events**.
- ❑ The effect of **dose and slow-release formulation** demonstrated that risk was a direct consequence of prolonged drug exposure.
- ❑ These adverse effects are more common with selective COX-2 inhibitors.



# General approach to pharmacotherapy

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## Duloxetine

- ❑ Duloxetine is used for patients with OA in **multiple joints** and **concomitant comorbidities** that may contraindicate oral NSAIDs and for patients with **knee OA** who have not **responded** satisfactorily to other interventions.

# General approach to pharmacotherapy

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## Acetaminophen

- ❑ Due to **safety concerns** pertaining to the use of acetaminophen (paracetamol) and **increased awareness** of its **negligible** and non-clinically **significant effects** on pain, this medication is no longer considered the first-line analgesic for the treatment **of knee and hip OA** by clinical guidelines.



# General approach to pharmacotherapy

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## Acetaminophen

- Although its **occasional use** for treatment of **mild OA** with occasional pain is recommended, its **lack of substantial efficacy** suggests that it should not be a primary treatment for **moderate to severe OA**.



# General approach to pharmacotherapy

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## Intra-articular glucocorticoid

- ❑ Intraarticular glucocorticoid injections **do not routinely used** due to the **short duration of its effects.**
- ❑ And evidence that it may have deleterious effects on the hyaline cartilage and may accelerate OA progression



- I. Wernecke C, Braun HJ, Dragoo JL. The Effect of Intra-articular Corticosteroids on Articular Cartilage: A Systematic Review. Orthop J Sports Med 2015; 3:2325967115581163.
- II. Kompel AJ, Roemer FW, Murakami AM, et al. Intra-articular Corticosteroid Injections in the Hip and Knee: Perhaps Not as Safe as We Thought? Radiology 2019; 293:656.
- III. McAlindon TE, LaValley MP, Harvey WF, et al. Effect of Intra-articular Triamcinolone vs Saline on Knee Cartilage Volume and Pain in Patients With Knee Osteoarthritis: A Randomized Clinical Trial. JAMA 2017; 317:1967.

# Intraarticular glucocorticoid

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## Choice of glucocorticoid preparation

- ❑ **Depot formulations** are designed to stay at the injection site and display **mostly local effects**, although systemic effects can occur.
  
- ❑ **The most commonly used depot glucocorticoids**
  - **Methylprednisolone** acetate
  - Triamcinolone **acetate**
  - And triamcinolone **acetonide**

# Intraarticular glucocorticoid

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## Variation of dose by anatomic location

- ❑ Glucocorticoid doses should vary with the **structure injected**.
- ❑ The UpToDate authors use triamcinolone acetonide
  - At standard doses of **40 mg** for a large joint (knee, shoulder),
  - **30 mg** for medium-sized joints (wrist, ankle, elbow)
  - And **10 mg** for small spaces

# Intraarticular glucocorticoid

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## Frequency of injection

- ❑ Intra-articular steroids are expected to result in clinical improvement of arthritis for **short duration**.
- ❑ Therefore, if arthritis recurs, joint injections can be repeated as many as **three times** in a **12-month period**.



# General approach to pharmacotherapy



## Hyaluronate

- ❑ The use of any intraarticular hyaluronic acid (HA) formulation is not recommended due to the **lack of robust evidence** demonstrating benefit, and most evidence demonstrates only a small superiority over intraarticular placebo
- ❑ Moreover, intraarticular HA is associated with **high costs** and potential side effects such as **pain flare-ups** and **joint infection**, although the latter is a rare complication.

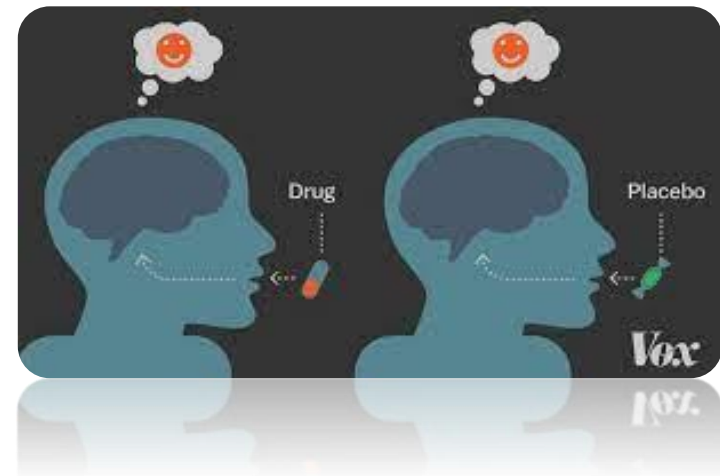
Rutjes AW, Jüni P, da Costa BR, et al. Viscosupplementation for osteoarthritis of the knee: a systematic review and meta-analysis. *Ann Intern Med* 2012; 157:180.  
Bannuru RR, Schmid CH, Kent DM, et al. Comparative effectiveness of pharmacologic interventions for knee osteoarthritis: a systematic review and network meta-analysis. *Ann Intern Med* 2015; 162:46.



# Role of placebo effect

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- According to a meta-analysis of trials including a placebo group, the overall effect size estimate of placebo for **pain** (defined as change from baseline to endpoint) was **0.51** (95% CI 0.46 to 0.55) for all trials, though there was significant **variation among distinct types of placebo**.



# Role of placebo effect

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❑ A number of determinants are able to evoke a placebo response. Among them, there are factors related to the intervention such as:

- The route of delivery
- Frequency of administration
- Color and cost
- How new the intervention is
- And others related to the health professional-patient relationship (context effect).

# Role of placebo effect

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- ❑ Interventions delivered by **invasive routes** (ie, intraarticular injections and acupuncture) were associated with more robust placebo effects compared with oral or topical placebos.
- ❑ In addition to alleviating pain, improvements in other common clinical OA outcomes have also been observed with placebo such as **stiffness and joint function**.

## Role of placebo effect

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- ❑ The landmark GAIT trial (Glucosamine/Chondroitin Arthritis Intervention) compared the effects of glucosamine, chondroitin sulfate, the combination of them, celecoxib, and oral placebo and has demonstrated that **at least 20** percent improvement in pain assessed by the Western Ontario and McMaster Universities (WOMAC) questionnaire.

# Nutritional supplements in management of OA

- ❑ Glucosamine and chondroitin
- ❑ Avocado soybean
- ❑ Fish oil
- ❑ Curcumin



## Nutritional supplements in management of OA

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- ❑ These nutritional supplements are not routinely recommend due to lack of **clear evidence** demonstrating a **clinically important benefit** from these supplements.
- ❑ However, may have **small effects** on symptoms, and patients with **mild disease** who may benefit more from these therapies.

# Nutritional supplements in management of OA

- ❑ Some meta-analyses also suggested that glucosamine sulfate (**1500 mg/day**) and chondroitin (**800 mg/day**) may have small effects in **delaying structural progression of OA** with long-term use (two to three years).



Be careful about serving size





# Glucosamine Sulphate vs hydrochloride

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## Sulphate

- Needs to be stabilized with NaCL(salt) or KCL
- Can contain up to 30% salt if stabilised with NaCL
- Typically contains around 75% glucosamine
- Glucosamine 2KCL does not contain salt
- Sourced from shellfish

## Hydrochloride

- A more **concentrated**
- Typically contains around 83% glucosamine
- Far **lower in salt**
- More naturally stable
- Doesn't require added salt
- Doesn't require preservatives
- Sourced from **vegetables**



# Glucosamine & diabetes

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- Glucosamine is likely safe in patients with well-controlled diabetes (HbA1c less than 6.5%) taking one or two oral antidiabetic medications or controlled by diet only.
- In patients with higher HbA1c levels or those taking insulin, monitor blood glucose levels closely/more frequently.

# Nutritional supplements in management of OA

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- With **role of placebo effect** in mind and in line with the prerequisite of **"do no harm"**
- Finally :we do not recommend **these supplements routinely** to all patients; however, we do not discourage their use for patients who **are keen to** take them, especially if **symptomatic benefit is achieved** with their use.

## Take home message

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- ❑ Non- pharmacologic interventions are **mainstay** of osteoarthritis management.
- ❑ **10 percent** weight reduction ➡ **50% pain reduction.**
- ❑ None of medicines are disease modifying and their use is limited to **symptomatic conditions.**
- ❑ **Topical NSAIDs** demonstrate similar efficacy with lower toxicity compare to Oral NSAIDs.

## Take home message

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- ❑ Acetaminophen is not **recommended anymore**.
- ❑ NSAIDs with a **long half-life** or slow-release formulation were associated with higher risk, even accounting for dose.
- ❑ The use of any intraarticular hyaluronic acid (HA) formulation is not recommended due to the **lack of robust evidence** demonstrating benefit.
- ❑ Use of supplements is not **routinely recommended** for all patients.



**Thanks for attention  
Any question?**