Management of Osteoarthritis

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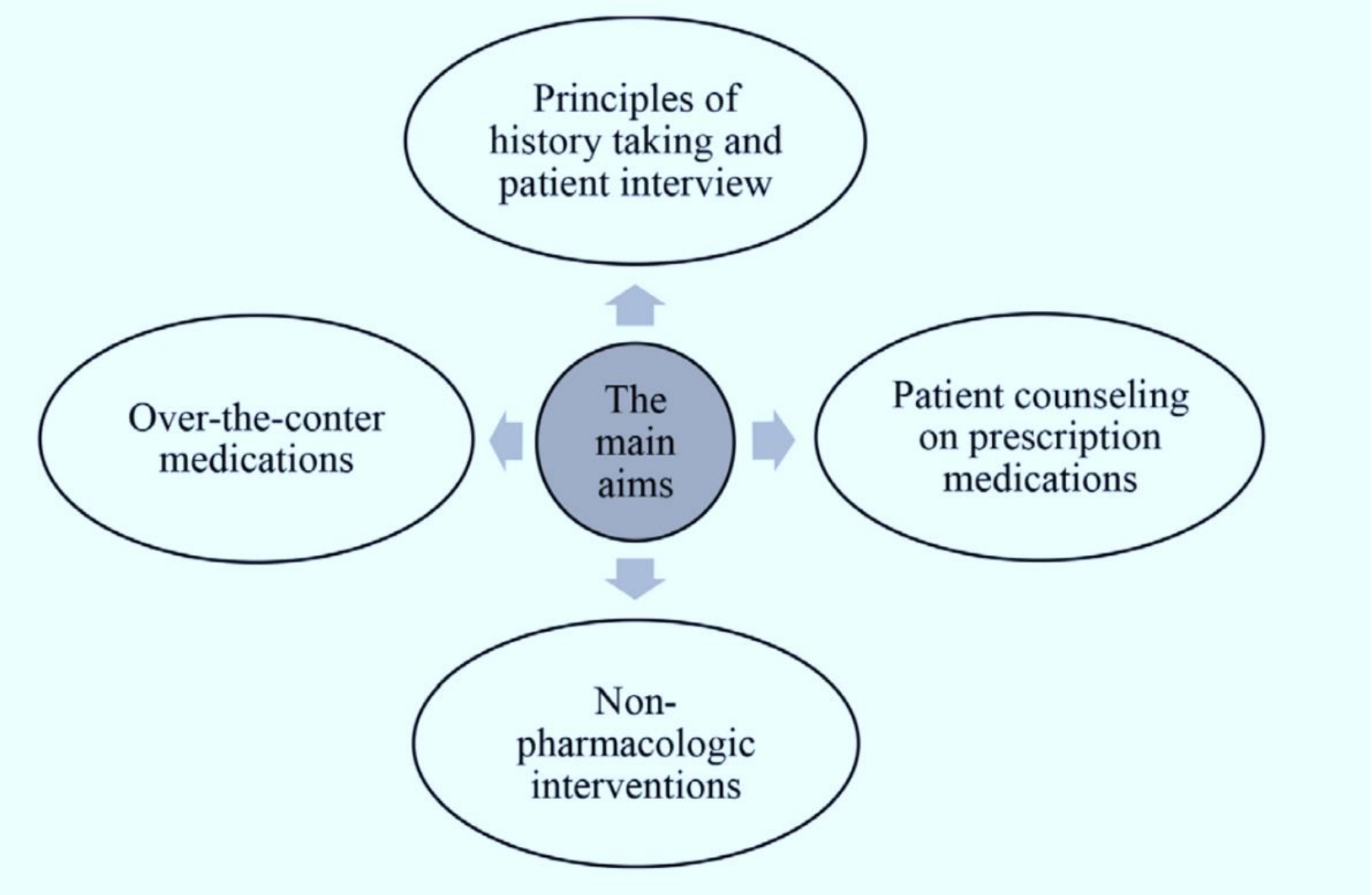
Learning Outcomes

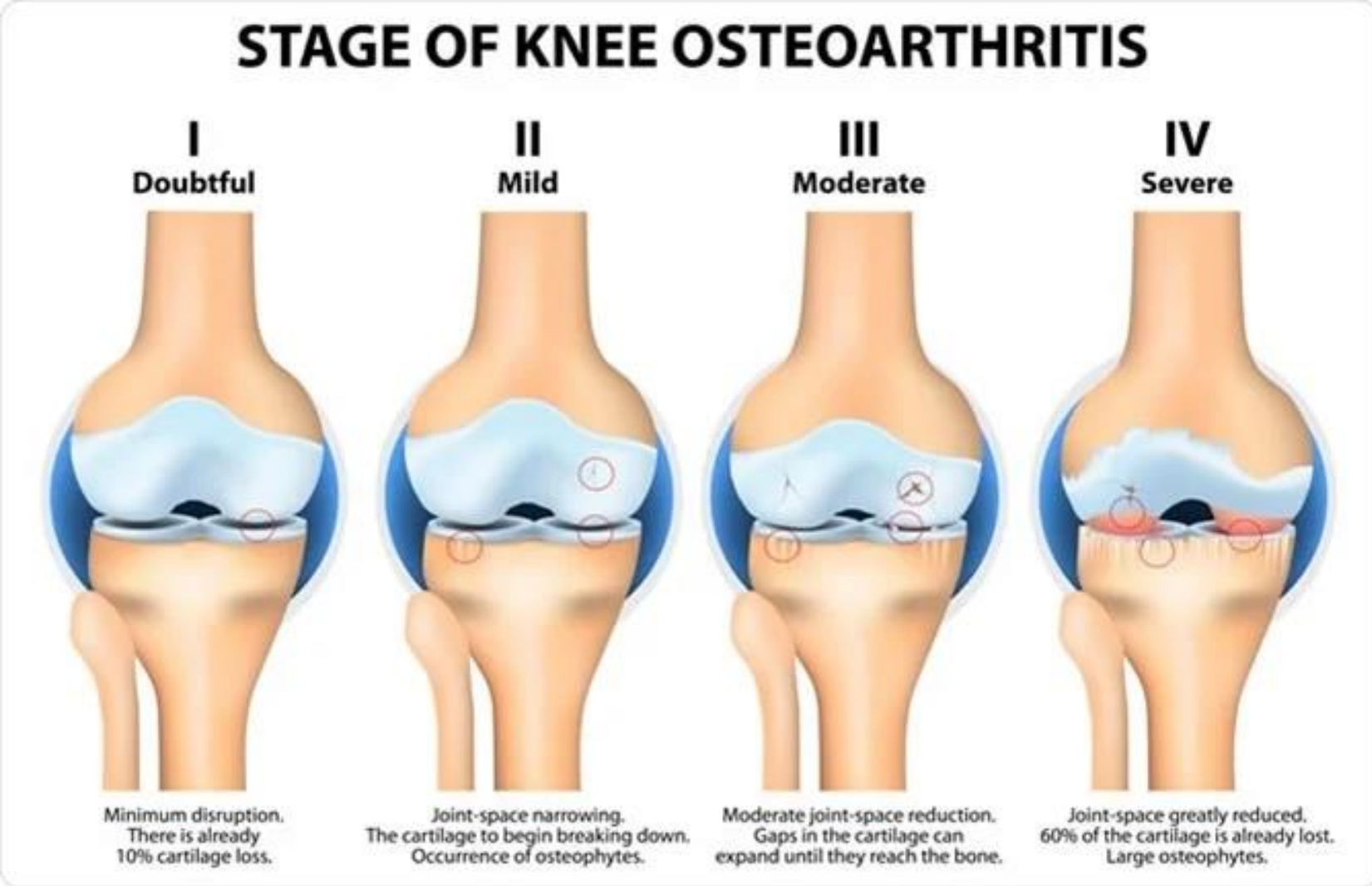


INTRODUCTION

- 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

- 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.

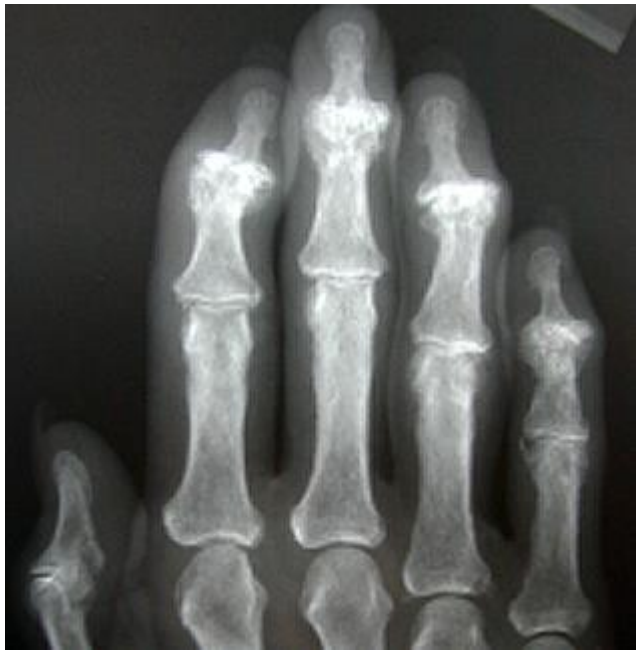
Principal manifestations of osteoarthritis

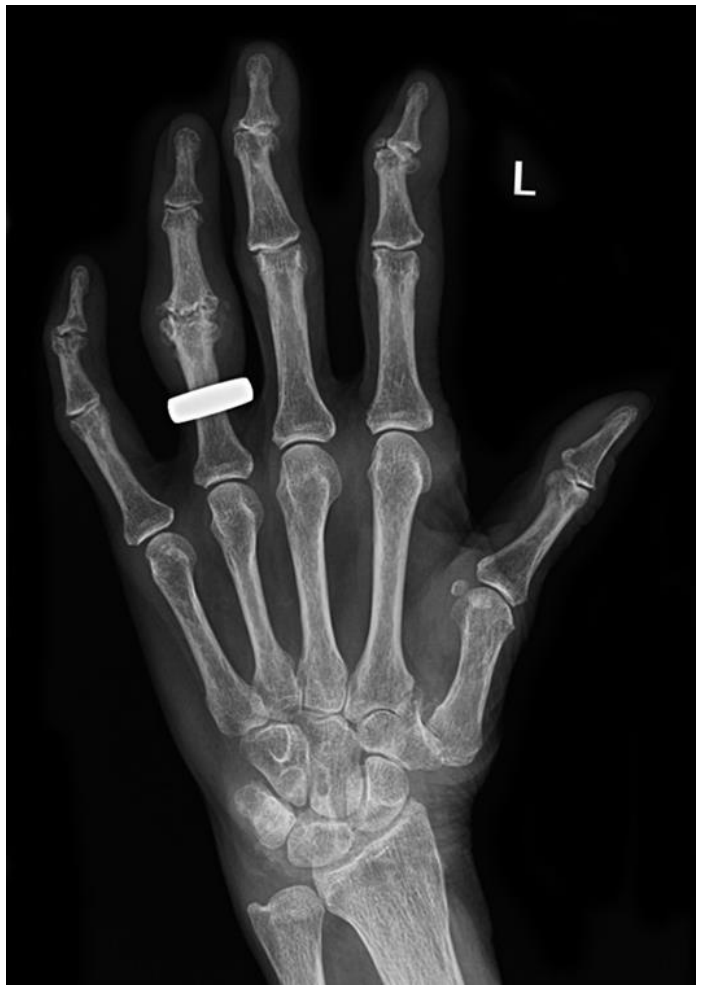
Patient characteristics	
Age of onset	▪ >40 years*
Symptoms	
Pain	▪ Affects one or a few joints at a time ▪ Insidious onset - slow progression over years ▪ Variable intensity ▪ May be intermittent ▪ Increased by joint use and relieved by rest ▪ Night pain in severe osteoarthritis
Stiffness	▪ Short-lived (<30 minutes) and early morning- or inactivity-related
Swelling	▪ Some (eg, nodal osteoarthritis) patients present with swelling and/or deformity
Constitutional symptoms	▪ Absent
Physical exam findings	
Appearance	▪ Swelling (bony overgrowth ± fluid/synovial hypertrophy) ▪ Attitude ▪ Deformity ▪ Muscle wasting (global - all muscles acting over the joint)
Palpation	▪ Absence of warmth ▪ Swelling (effusion if present is usually small and cool) ▪ Joint line tenderness ▪ Periarticular tenderness (especially knee, hip)
Range of motion	▪ Crepitus (knee, thumb bases) ▪ Reduced range of movement ▪ Weak local muscles

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).

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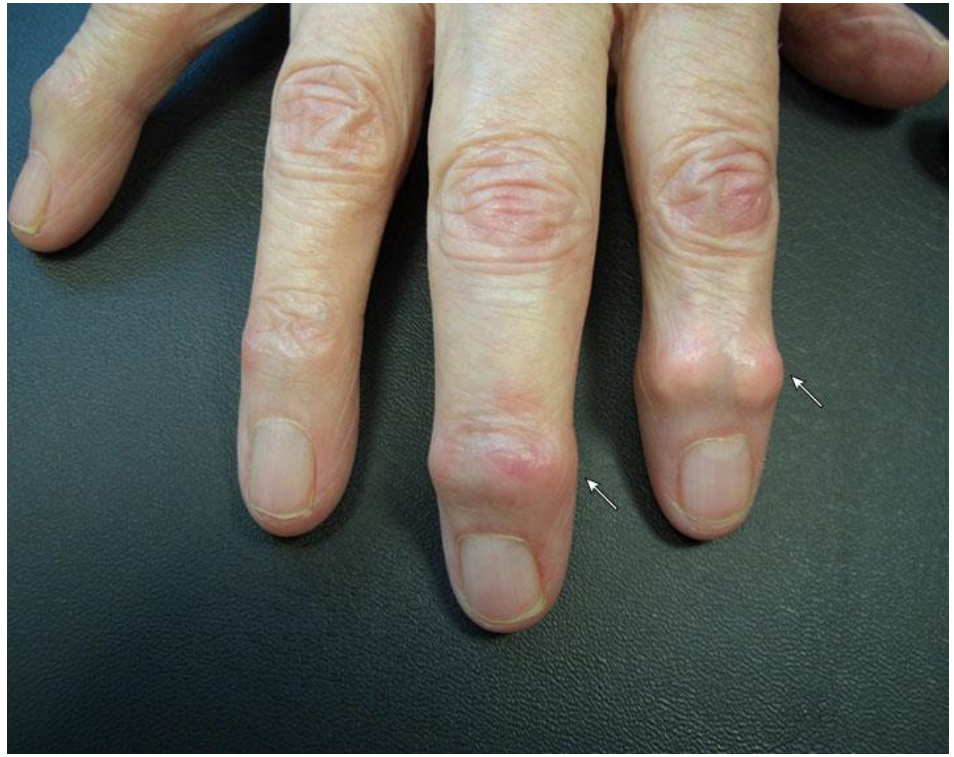
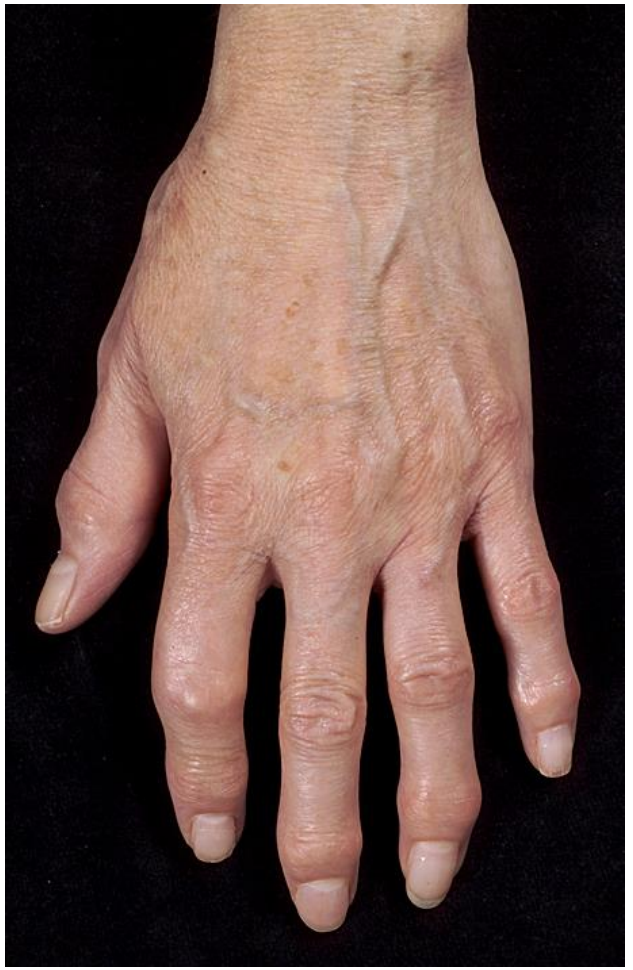
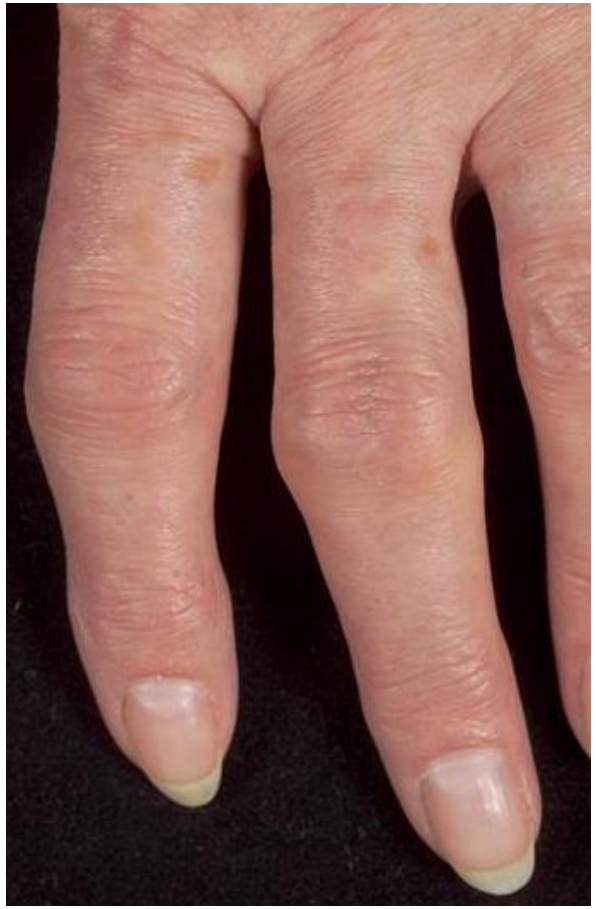


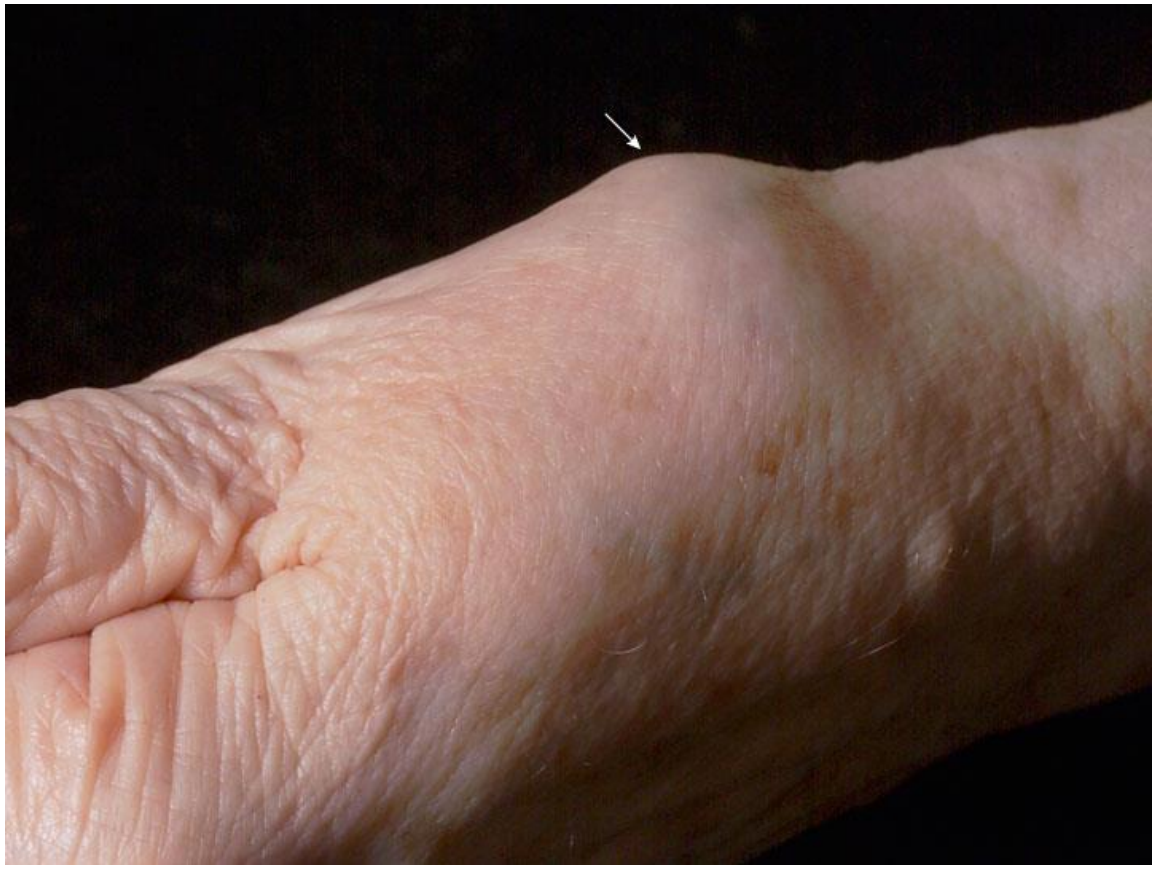
Heberden's nodes



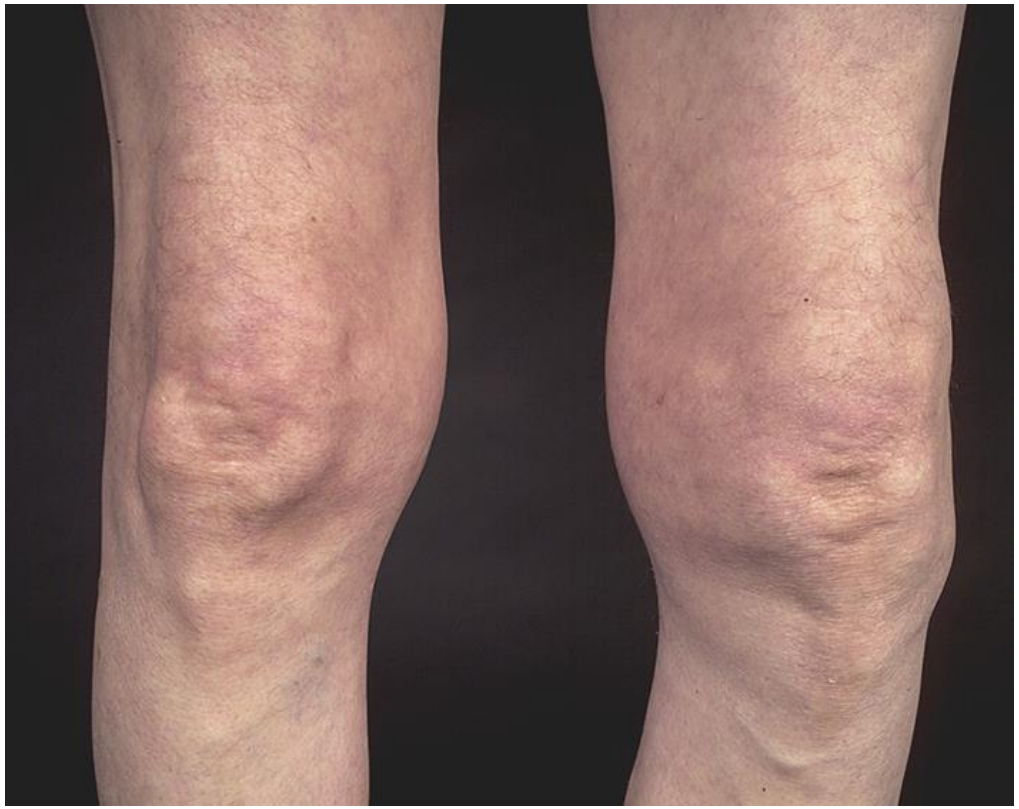
Deformity
Heberden's nodes



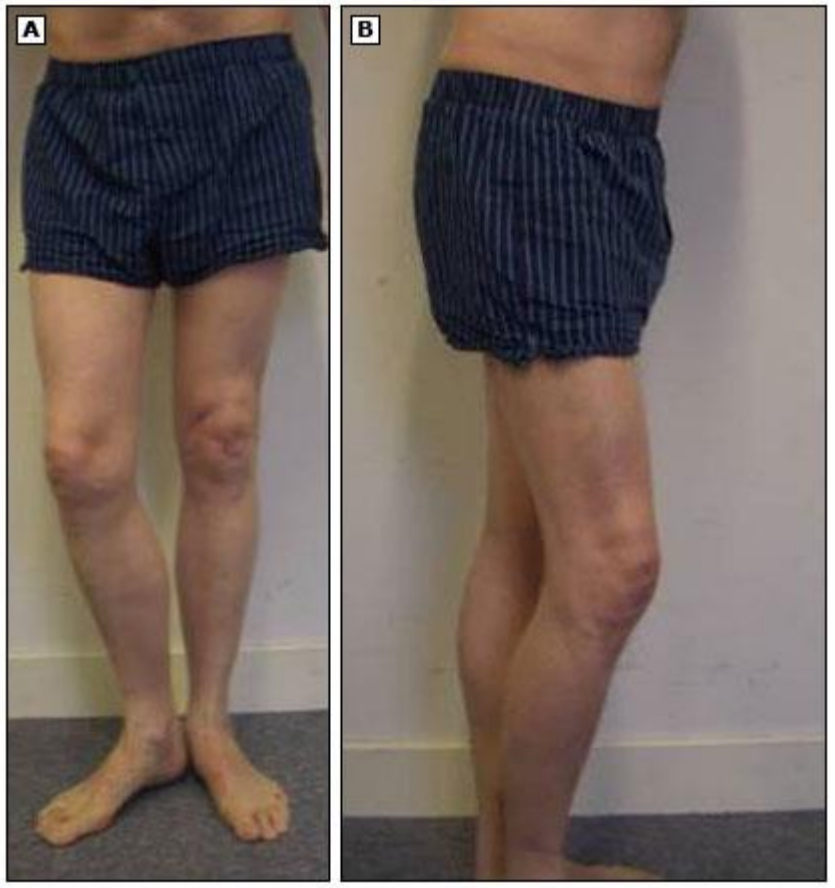
Erosive hand OA with marked radial deviation



Thumb-base osteoarthritis

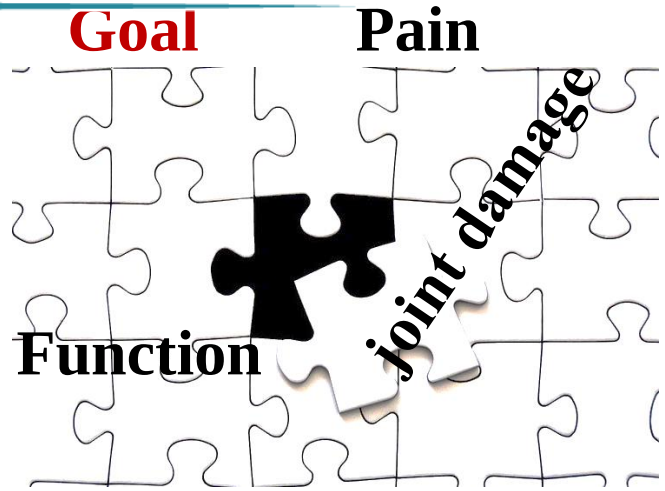


Unilateral knee OA



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

- 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

- 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

- 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

Weight loss

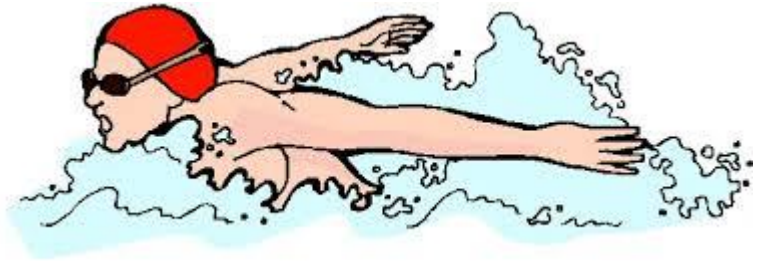
- Loss of at least 10 percent of body weight through a combination of diet and exercises has been associated with a 50 percent reduction in pain scores in overweight/obese patients with knee OA after **18 months.**

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

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

A combination of aerobic, strengthening, and aquatic exercises.



Zhang W, Nuki G, Moskowitz RW, et al. OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis Cartilage 2010; 18:476.

Non-pharmacologic therapy for the management of OA
Equipment

Braces, foot orthoses, and assistive devices when required

Pharmacologic therapy

- 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

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

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

General approach to pharmacotherapy

- 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

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

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

- 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 ≥1 hour following application. Wash hands immediately after application (unless hands are treated joint, then wait ≥1 hour to wash hands).
- Avoid sunlight to exposure areas.
- Avoid wearing clothes or gloves for ≥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

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

- 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

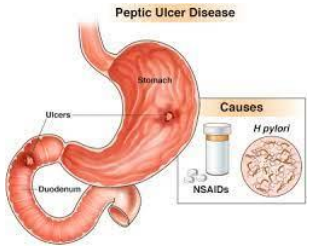
Drug	Usual analgesic dose (oral)	Maximum dose per day	Selected characteristics
Diclofenac	50 mg every 8 to 12 hours	150 mg for RA, labeling in United States permits up to 200 mg	•Dosing for free-acid preparation differs from doses listed here for sodium or potassium salts;
Indomethacin	25 to 50 mg every 8 to 12 hours	150 mg For rheumatologic conditions, labeling in United States permits up to 200 mg	More frequently associated with CNS side effects (eg, headache, altered mental status) compared with other NSAIDs
Meloxicam	7.5 to 15 mg once daily	15 mg	•Long duration of effect; relatively slow onset •Relative COX-2 selectivity and minimal effect on platelet function at lower daily dose of 7.5 mg
Piroxicam	10 to 20 mg once daily	20 mg	• Long-acting alternative for treatment of chronic pain and inflammation poorly responsive to other NSAIDs • **Prescribing generally limited to specialists with experience in treatment of chronic pain and inflammation**

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)	•Shorter-acting alternative to naproxen; useful in patients without cardiovascular risks
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	•Often preferred by for treatment of acute or chronic pain and inflammation in patients without relevant comorbidities or risks •Higher dose (eg, 500 mg base twice daily) may have less cardiovascular toxicity than comparable doses of other NSAIDs; •Naproxen sodium has a faster onset than naproxen base
Celecoxib	200 mg daily or 100 mg every 12 hours	400 mg	•Less risk of GI toxicity relative to nonselective NSAIDs; benefit negated by low-dose aspirin, which may require concurrent gastroprotection •No effect on platelet function **•Cardiovascular and kidney risks are dose-related and may be similar to nonselective NSAIDs** •May be tolerated by patients with AERD or pseudoallergic reactions (eg, asthma, rhinosinusitis) who cannot take other NSAIDs

Gastritis and Gastroduodenal Ulcer Associated with NSAIDs

- 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

- 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

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

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

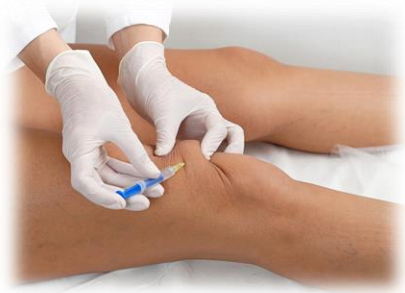
Acetaminophen

- 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

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

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

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

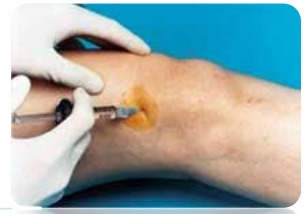
Intraarticular glucocorticoid

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

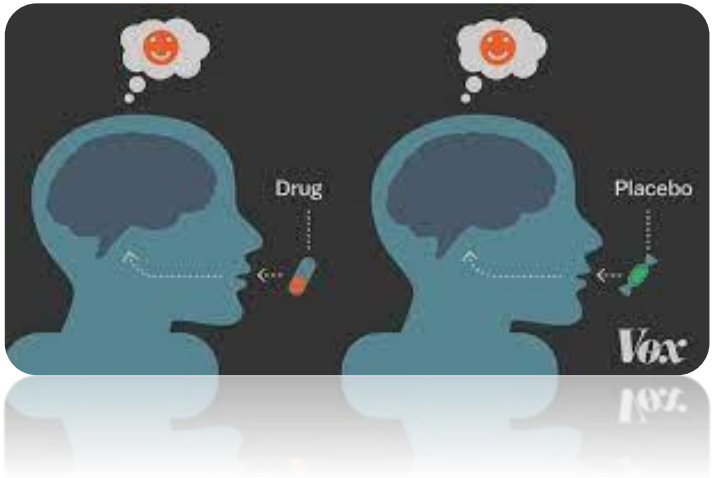
- The use of any intraarticular hyaluronic acid (HA) formulation is not recommended due to the lack of robust evidence demonstrating benefit, nd most evidence demonstrates only a small superiority over intraarticular placebo

- 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

- 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

- 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

>>>

- 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

- 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

Liu X, Machado GC, Eyles JP, et al. Dietary supplements for treating osteoarthritis: a systematic review and meta-analysis. Br J Sports Med 2018; 52:167.

Nutritional supplements in management of OA

- 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

Sulphate

- Needs to be stabilized with NaCL(salt) or KCL
- Can contain up to 30% salt if stabalised 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


NATURAL WORLD
Full Flex Plus
BioPerine
OptiMSM
Helps Cartilage Health and Joint Flexibility
60 CAPLETS


WWW.PURITAN.COM
Puritan's Pride
GLUCOSAMINE HYDROCHLORIDE
1000 mg
(Shellfish Free)
60 Tablets
DIETARY SUPPLEMENT


Health Aid
VEGAN
Glucosamine
Sulphate 500mg
2KCl
With Vitamin C which contributes to the normal function of cartilage
ONE-A-DAY
30 Tablets
VEGAN


NATURES AID
Glucosamine
Sulphate 2KCl

Glucosamine & diabetes

- 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

- 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

- 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

- 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?