Osher Mini Med School: Osteoarthritis

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- No Disclosures

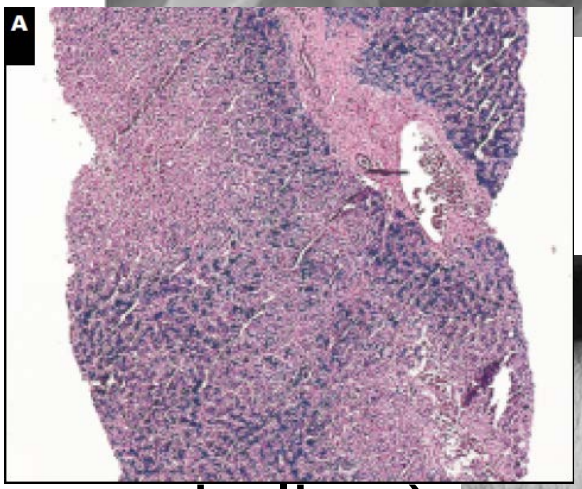
Outline

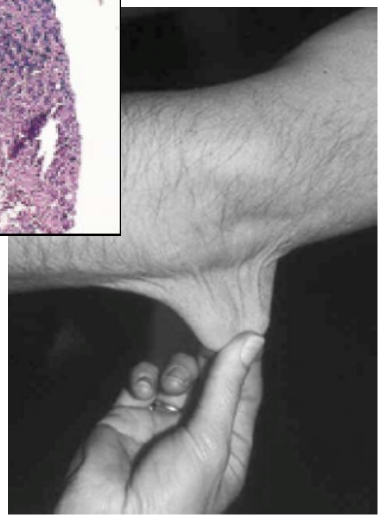
- Causes of OA
  - Knowledge gaps
- Treatment options
  - Medication
  - Non-Medication
  - “Holy Grail”: Disease Modifying Drug?

Osteoarthritis: Causes

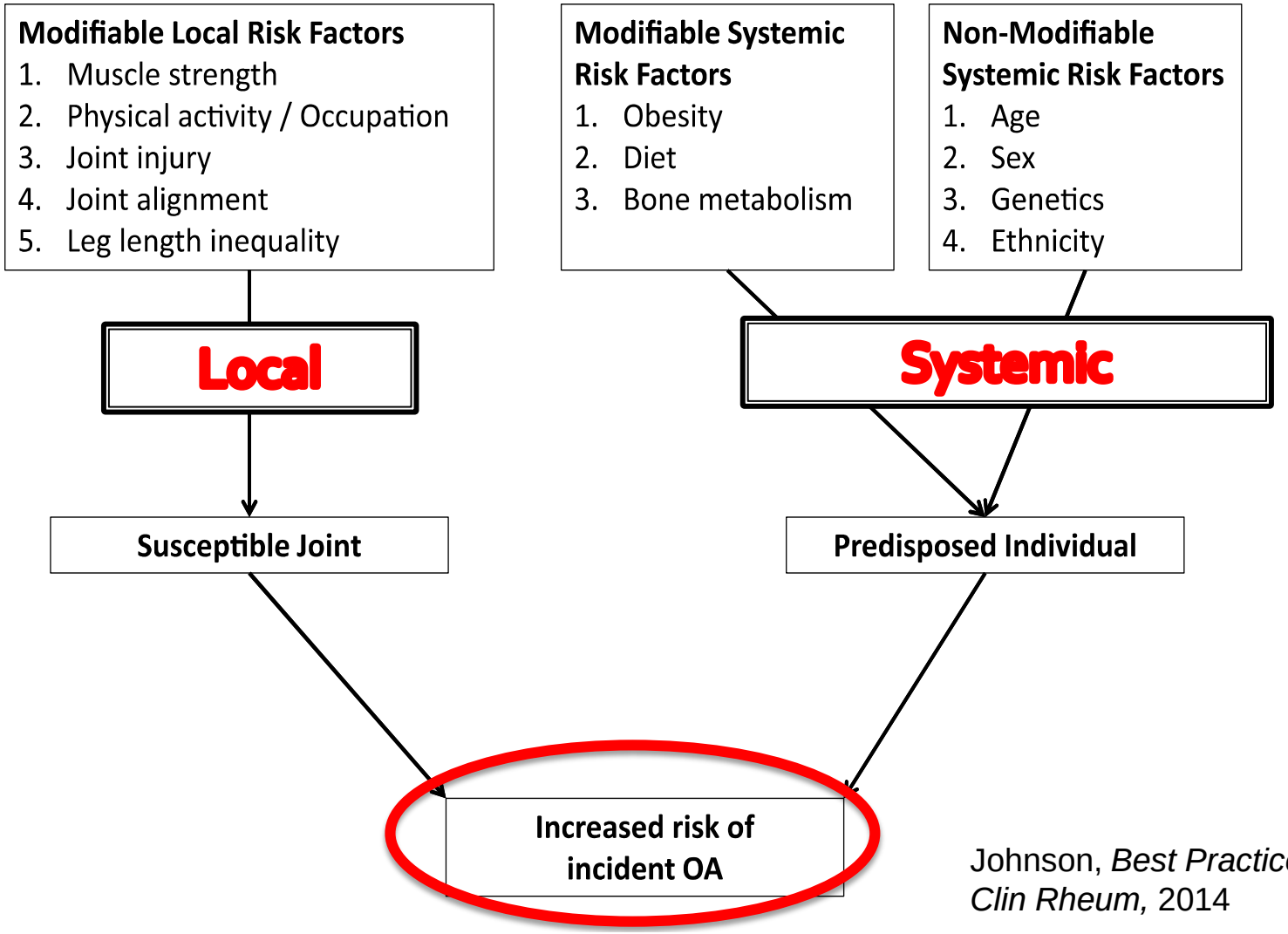
- Primary v Secondary OA

- Secondary OA:
- Congenital or acquired:
  - Dysplasia
  - Collagenopathy
  - Inflammatory arthritis
  - Metabolic disorders (iron metabolism)



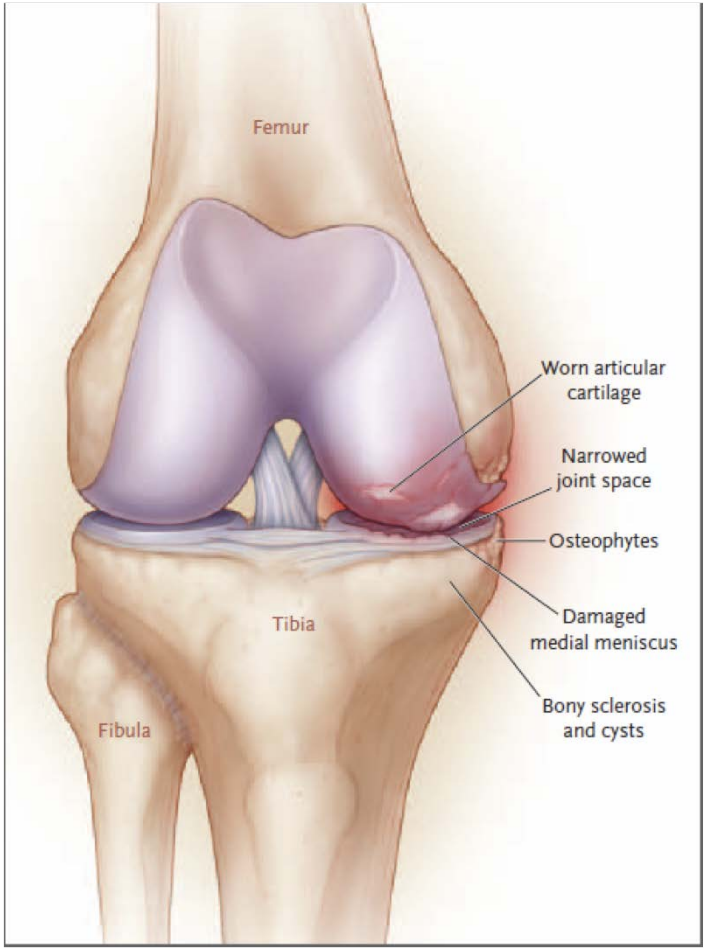


OA: Primary



Johnson, *Best Practice & Research Clin Rheum,* 2014

OA: Pathogenesis

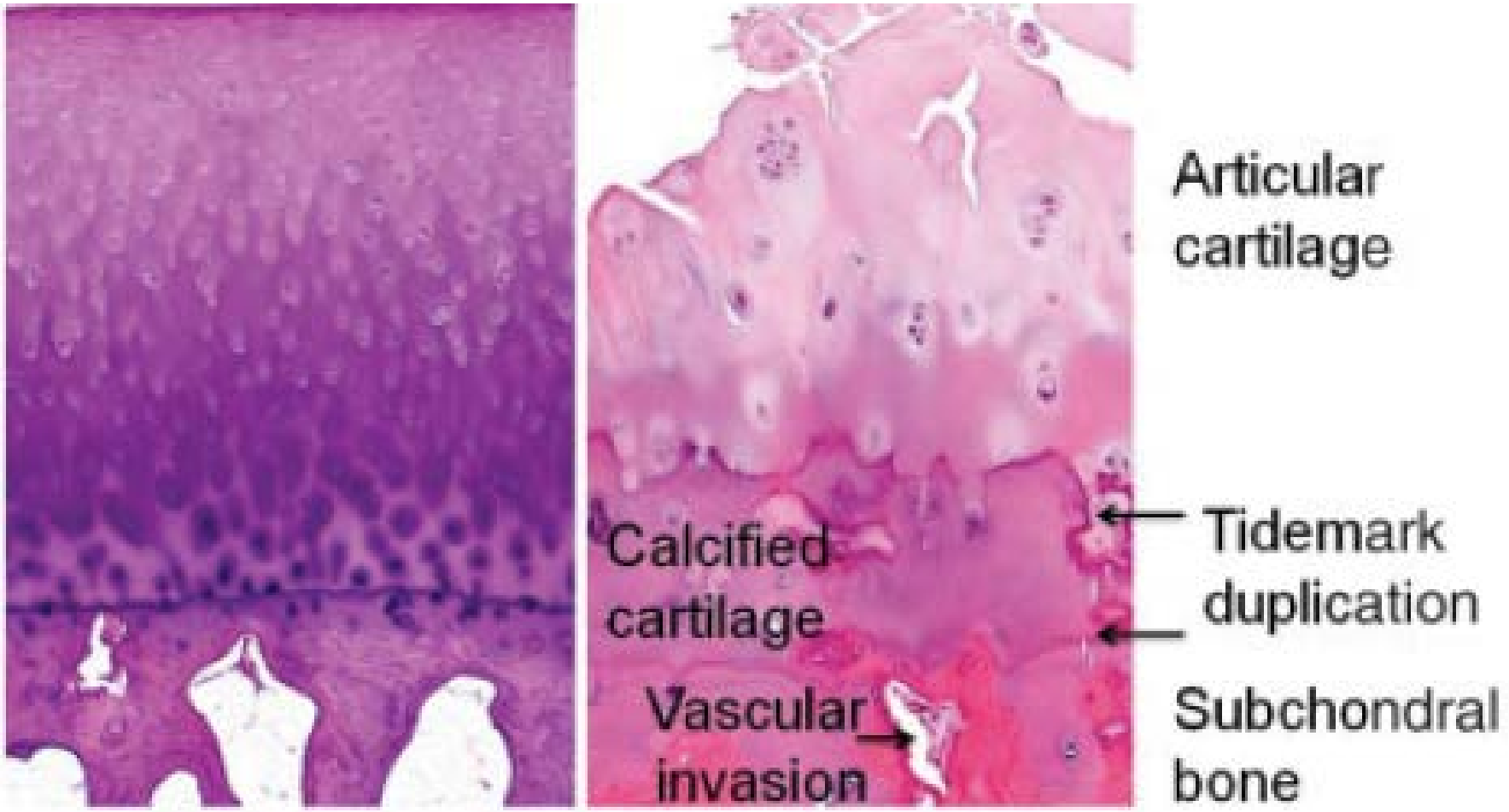


Felson, NEJM, 2006

Disease of the Whole Joint

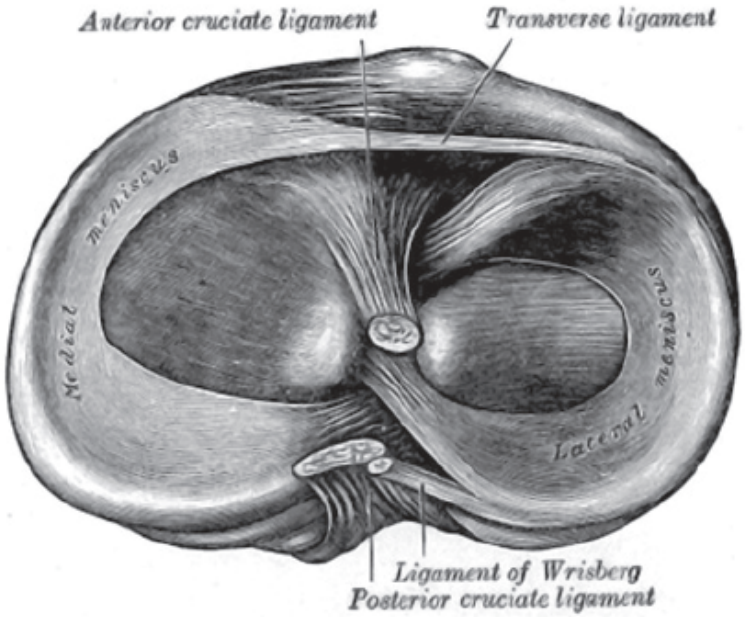
- Cartilage
- Bone
- Meniscus
- Soft Tissue Structures

OA pathogenesis: Subchondral Bone and Cartilage Changes



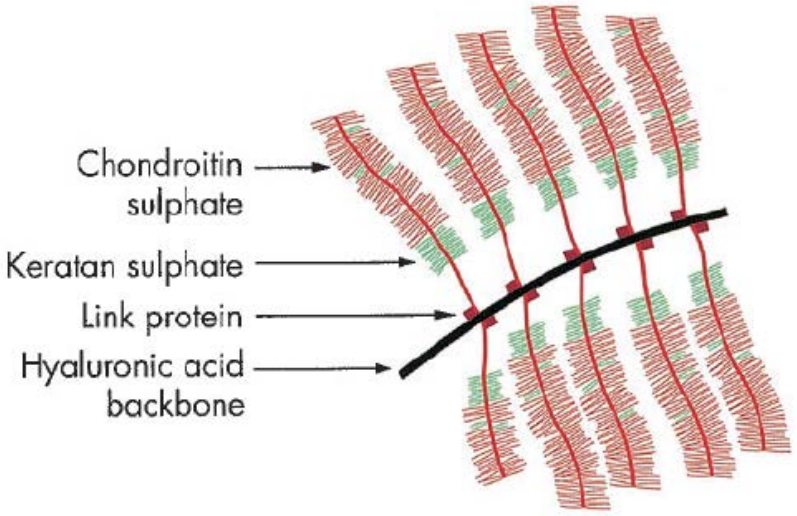
OA pathogenesis: Meniscus

- <u>Meniscal damage</u>
- Can be risk factor for accelerated incident OA
- X-ray: “joint space” = **meniscus**

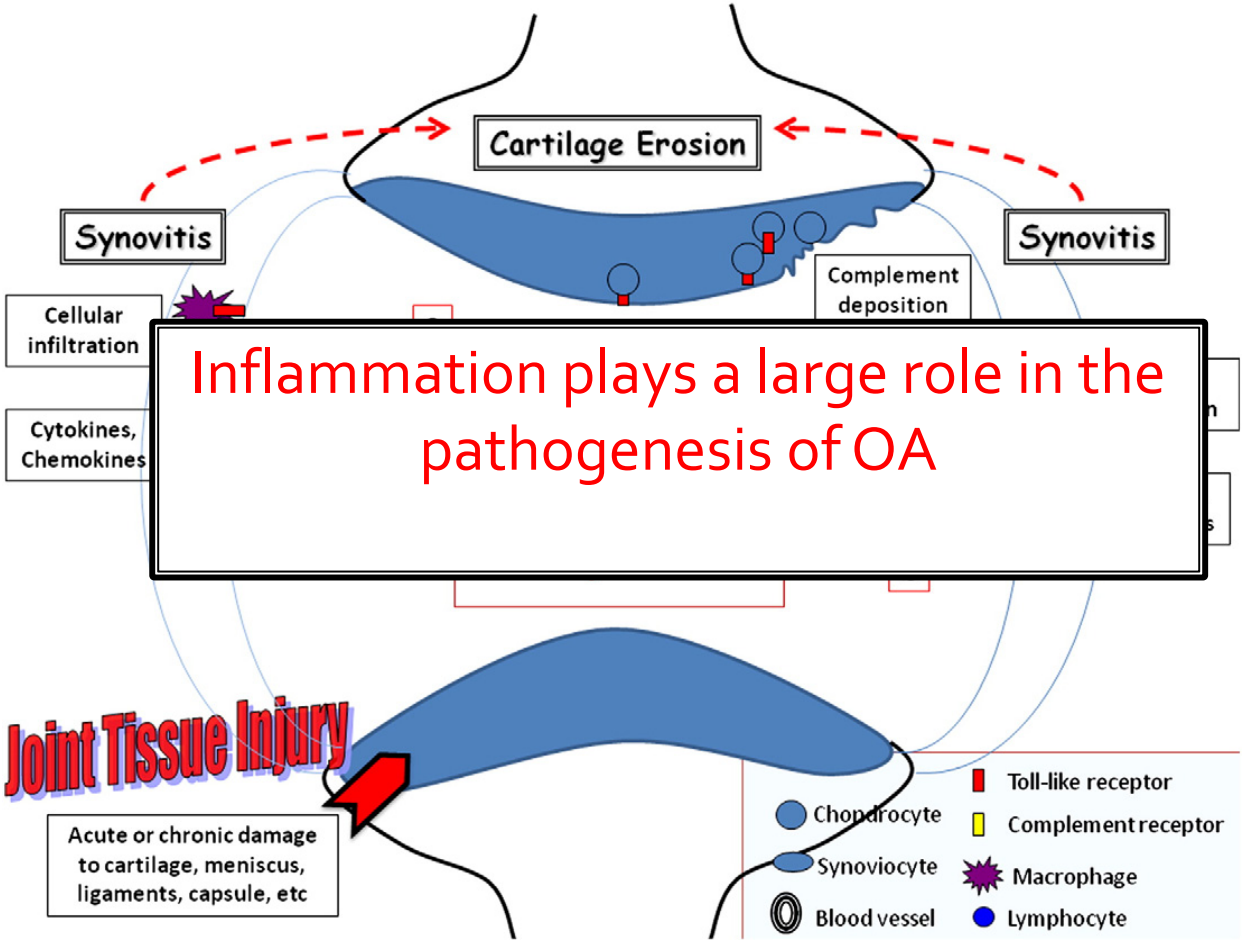


Cartilage Components

- Water
- Collagen
- Proteoglycan
  - = Core protein chain + glycosaminoglycans (GAGs)
  - GAGs= keratan sulfate, chondroitin sulfate, hyaluronic acid



Inflammation and OA



model of Toll-like Receptor (a) and complement activation (b) in the joint leading to synovitis and potentiation of cartilage erosion in OA. Joint tissue injury, either a

Scanzello, *Bone*, 2012

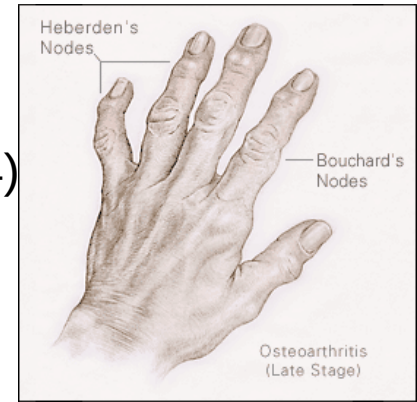
Genetics of OA

- **Complicated by heterogeneity of populations and OA disease**
- **Monozygotic twin studies**
  (Spector et al., Rheumatology, 2009)

	Heritability, % (95% CI)
DIP	65 (57, 73)
PIP	53 (44, 62)
CMC	68 (60, 75)
Hip	28 (15, 40)
Knee	37 (28, 48)

Macgregor, Rheum, 2009

- **SNP analysis**
  - IL1R antagonist gene variants
  - Higher risk of knee OA progression by SNP analysis (X. Wu et al., OA&C, 2013)
- **GWAS analyses**
  - Hand OA: ALDH1A2 gene variants (Styrkasdottir, 2014)
  - UK population, (Zeggini et al., Lancet 2012)



OA: Treatment

“It’s fine to discover cures, but remember chronic conditions are our bread and butter”

Case:

- 73 yo woman with Hx of severe knee DJD
- Hx of gastritis, responded to PPI in the past, not currently taking
- On ASA 81 mg
- Wants to know what medication(s) she can safely take regularly when in pain?

American College of Rheumatology 2012 Guidelines

Table 4. Pharmacologic recommendations for the initial management of knee OA*

We conditionally recommend that patients with knee OA should use one of the following:
- Acetaminophen
- Oral NSAIDs
- Topical NSAIDs
- Tramadol
- Intraarticular corticosteroid injections

We conditionally recommend that patients with knee OA should not use the following:
- Chondroitin sulfate
- Glucosamine
- Topical capsaicin

We have no recommendations regarding the use of intraarticular hyaluronates, duloxetine, and opioid analgesics

* No strong recommendations were made for the initial pharmacologic management of knee osteoarthritis (OA). For patients who have an inadequate response to initial pharmacologic management, please see the Results for alternative strategies. NSAIDs = nonsteroidal antiinflammatory drugs.

Recommendations are similar for hip osteoarthritis except no role for topical agents in hip OA

Use Acetaminophen first

Cymbalta is a last option

Hochberg MC, et al. Arthritis Care Res 2012

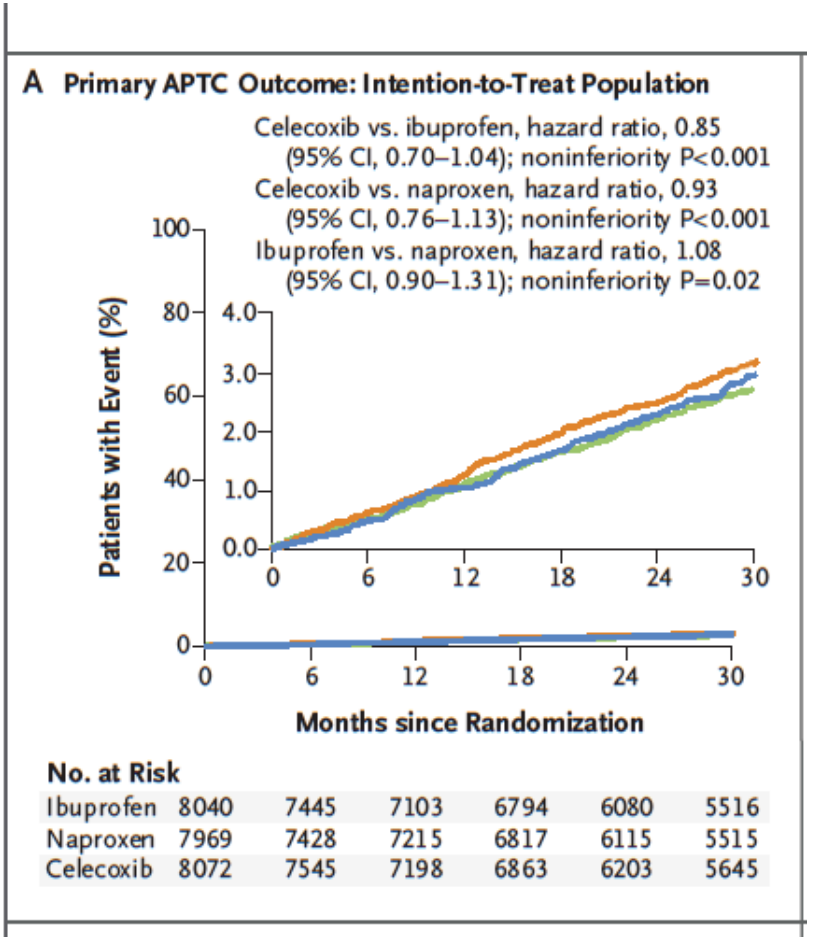
NSAID toxicity

GI TOXICITY

High risk
1. History of a previously complicated ulcer, especially recent
2. Multiple (>2) risk factors
Moderate risk (1–2 risk factors)
1. Age >65 years
2. High dose NSAID therapy
3. A previous history of uncomplicated ulcer
4. Concurrent use of aspirin (including low dose) corticosteroids or anticoagulants
Low risk
1. No risk factors
H. pylori is an independent and additive risk factor and needs to be addressed separately (see text and recommendations).

Our patient: **moderate** risk, use lower-dose NSAID with PPI

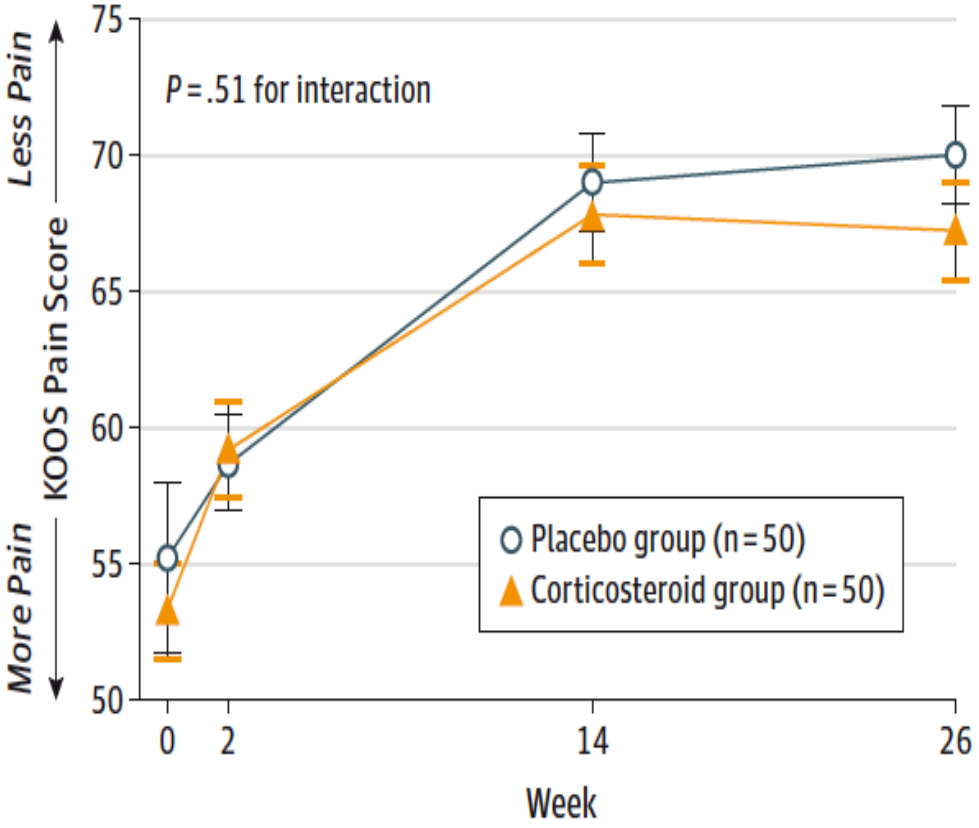
CARDIOVASCULAR RISK



Intra-articular Corticosteroids for Knee Osteoarthritis

Cochrane Meta-analysis

- Less pain at 1-4 weeks
- Effect decreases over time
- No effect after 6 mo.
- Adverse effects do not seem to be a problem*



Self reported pain assessed

Peter J, et al. Cochrane Database Syst Rev 2015.

Henriksen M, et al. JAMA Intern Med 2015,

Intra-articular Hyaluronic Acid for Knee Osteoarthritis

Viscosupplementation with hyaluronic acid (HA) - a natural constituent of joint fluid - to restore the viscoelasticity of synovial fluid

- Debatable efficacy based on data
  - Chevalier et al., Ann Rheum Dis 2010
  - Campbell et al, OA &C, 2007
- Slow acting – benefits appreciated at 5-13 weeks post injection
- Few adverse events reported: acute reaction of inflammation and synovitis

Bellamy N, et al. Cochrane Database Syst Rev, 2006

Opioids for the management of Osteoarthritis

Two Meta-analyses:

- Patients with osteoarthritis had improvement in pain and physical function from treatment with opioids although the effect size was relatively small (0.7 cm on a 10-cm visual pain scale, 0.6 units on a disability 0-10 scale)
- *Adverse events →limit opioid usefulness
- The long-term efficacy and safety unclear

Avouac J, et al. Osteoarthritis Cartilage 2007,
da Costa BR, et al. Cochrane Database Syst Rev 2014

Case:

- Our (same) patient would prefer not to take any “dangerous” medications, and would prefer more “natural” methods of pain relief.
- She would like to try the herbal medication Boswellia for pain
- What should she do?

Herbal medications for OA

- Boswellia
- Turmeric
- Cat's claw
- Avocado-soybean unsap.
- No known diet that halts OA

Counsel the patient:
-May be of benefit
-Costly?

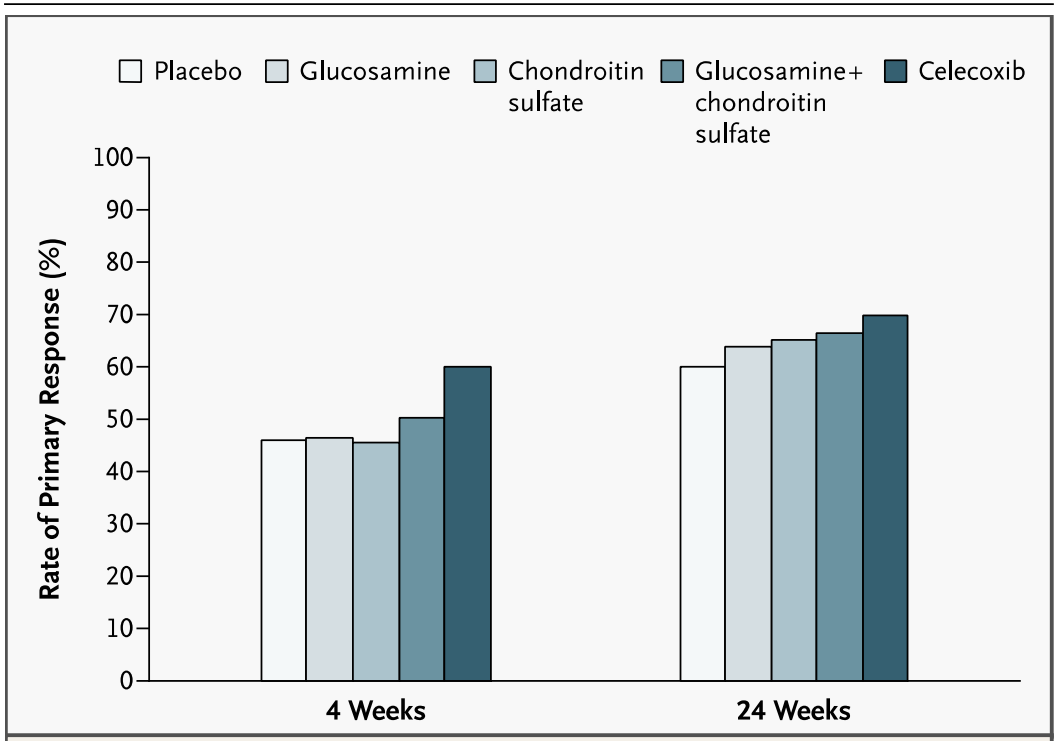
-Risk is unclear

- <u>Resources:</u>
  - Osher Centers for Integrative Medicine
  - **Memorial Sloan Kettering herbal references:**
    https://www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/integrative-medicine/herbs

Glucosamine/Chondroitin

Most past studies indicate no significant benefit in:

- Pain
- Function
- Joint Structure

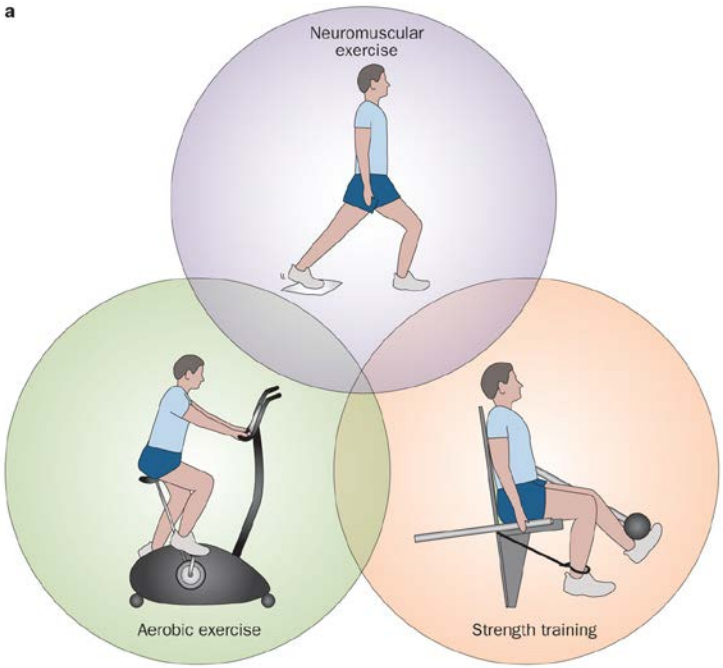


GAIT Study (Clegg DO et al., NEJM, 2006)

OA Treatment: Knee (and Hip)

- Treatment
  - Non-pharmacologic Rx of OA
  - Pharmacologic Rx of OA
  - Joint Injections for OA
  - **Mainstay: Combination of pharmacologic and non-pharmacologic therapy**

ACR : Knee (and Hip) OA Treatment



- Exercise
- Weight Loss
- Walking
- Tai Chi
- Accupuncture
- *Water Therapy*

Hochberg MC, et al., Arthritis Care Res 2012

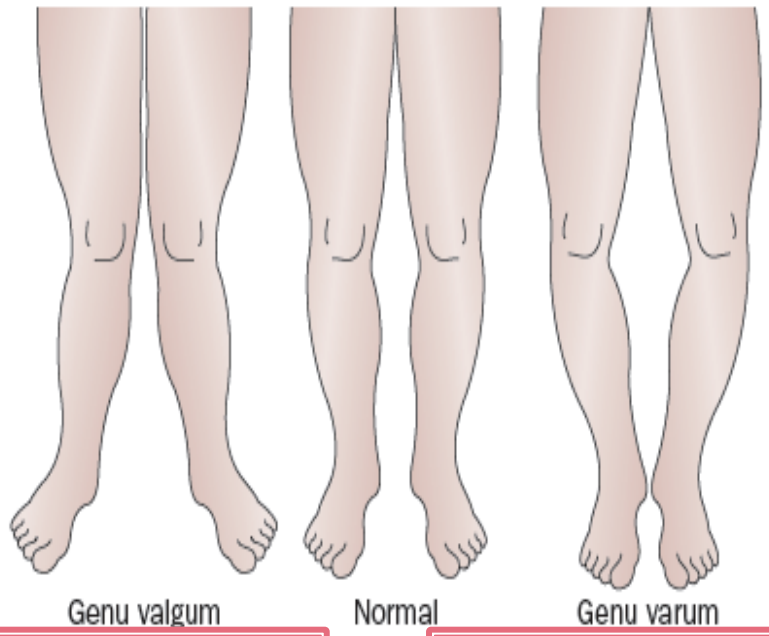
Exercise Decreases Pain in OA

- Improvement in pain with regular PT /gentle exercise program more than just weight loss alone (JAMA, 2013)
- Decrease in pain → increase in function

→"Move it or lose it"

- Effect on central pain pathways

Varus Deformity Biomechanics (Medial Knee OA)



Valgus: Knock-kneed

Varus: bow-legged

Varus Deformity Biomechanics

- Corrective Devices
  - Shift the weight-bearing axis towards the center of the affected varus knee→ towards **neutral** alignment
  - **<u>Directly Unload Medial Knee</u>**
  - Unloader Braces
  - Lateral Wedges
  - Canes
  - Flexible Shoes

- Methotrexate
- TNF-inhibitors
  - Etanercept (Enbrel)
  - Adalimumab (Humira)
- Hydroxychloroquine
- Strontium relanate
- Tanezumab

Regenerative Medicine

- PRPP (TGF-beta, PDF-GF,VEGF)

- Bone Marrow Matrix
- Adipose MSC
- Autologous BM Aspirate
- Allogeneic MSCs
- Umbilical cord derived MSCs

- Wide variation in methodology, poor clinical data to support use at this time

- More standardized methodology and outcome measures needed

Thank You!

OA Pathogenesis: Bone

OSTEOPHYTE

BUTTRESSING

Jacobson J A et al. Radiology 2008;248:737-747

Hand OA

DIP

CMC

PIP

-Increases with age, especially postmenopausal women
-Women > Men
-Heberden's and Bouchard's nodes→genetic predisposition

Hand OA: Pharmacologic

RECOMMEND

- Topical capsaicin
- Topical NSAIDs
- Oral NSAIDs
- Tramadol
- >75 years old→ Topical NSAIDs more than oral

DON'T RECOMMEND

- Intraarticular therapies
- Opioid Analgesics

Cane Use with Stairs

- Use stairs one at a time, use cane on **contralateral** side of the affected (bad) leg

- Going **up**: Advance with the good (unaffected) leg first
- Going **down**: descend with the BAD leg first, and contralateral cane at the same time

→"Up with the good, down with the bad."

Base of Thumb Splints

- Splints are used to support, stabilize, protect painful joint
- RCT : nighttime use decreased pain & hand disability compared with usual care at 1 year. (took time for effect)
- Avoid 24 hr use of splints → muscle atrophy.

Rannou F, et al. Ann Intern Med 2009, PMID 19451573

Water therapy: Improves pain

Analysis 2.3. Comparison 2 Aquatic exercise vs control immediately after treatment: knee OA, Outcome 3 Quality of life.

Review: Aquatic exercise for the treatment of knee and hip osteoarthritis

Comparison: 2 Aquatic exercise vs control immediately after treatment: knee OA

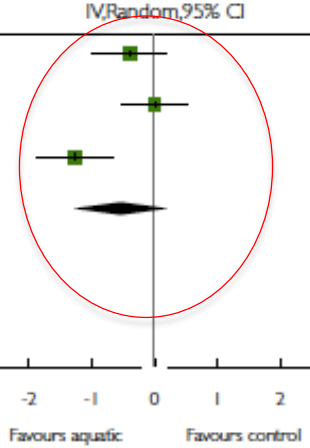
Outcome: 3 Quality of life

Study or subgroup	Aquatic N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Lim 2010	24	-46.8 (8.27)	20	-42.65 (12.18)		32.8 %	-0.40 [-1.00, 0.20]
Lund 2008	27	-43 (12.47)	27	-43.1 (12.47)		34.4 %	0.01 [-0.53, 0.54]
Wang 2011	26	-73 (12)	26	-57 (13)		32.8 %	-1.26 [-1.86, -0.66]
Total (95% CI)	**77**		**73**			**100.0 %**	**-0.54 [-1.28, 0.19]**

Heterogeneity: $Tau^2 = 0.34$; $Chi^2 = 9.77$, df = 2 (P = 0.01); $I^2 = 80\%$

Test for overall effect: Z = 1.44 (P = 0.15)

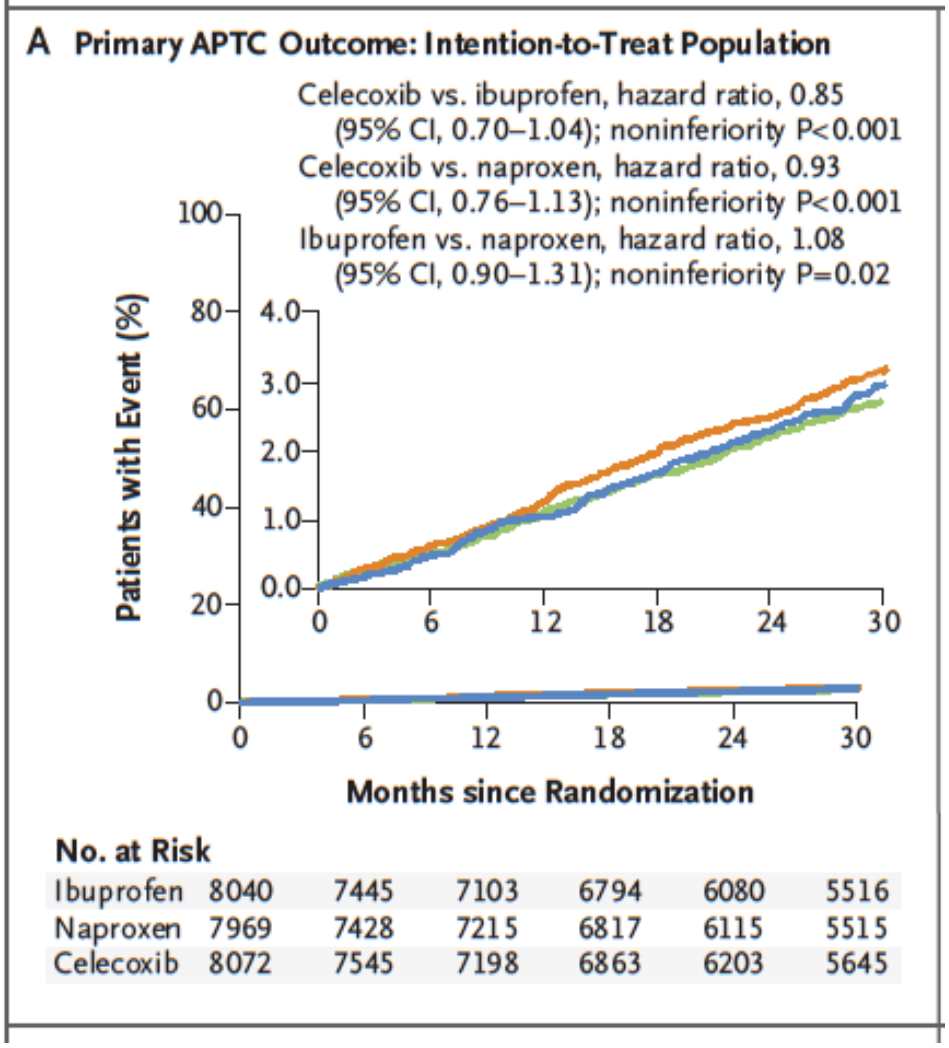
Test for subgroup differences: Not applicable



Cochrane, 2016

Water therapy helps with pain, not clear if effects are lasting

NSAIDs and Cardiovascular risk



- PRECISION trial
- Non-inferiority RCT of CV safety of celebrex v ibuprofen and naproxen
- Outcome: hemmoraghic death, nonfatal MI, nonfatal stroke

Nissen, et al.,NEJM, 2016