

Making Decisions With Your Osteoarthritis Patients

Expert

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Introduction: Approaches to Osteoarthritis Management

- Applying knowledge of pathophysiology and pain mechanisms
- Making an early diagnosis
- Understanding the guidelines
- Using evidence-based approaches and guidelines
- Making the appropriate pharmacologic choices
- Reinforcing use of non-pharmacologic approaches
- Understanding directions for future management

What Clinicians Know About Osteoarthritis: Results of a Medscape Clinical Practice Assessment

- Educational activity consisting of 20 multiple choice questions
- Data from 430 orthopedists and 183 rheumatologists completing the activity
- Four knowledge gaps were identified:
 - Role of inflammation in osteoarthritis pathogenesis
 - Familiarity with current guidelines for osteoarthritis management
 - Pharmacologic properties of different osteoarthritis therapy formulations
 - Role of non-pharmacologic interventions in osteoarthritis

Global Burden of Osteoarthritis

Hip and knee osteoarthritis was ranked 11th highest contributor to global disability



1% global-age standardized prevalence with hip osteoarthritis

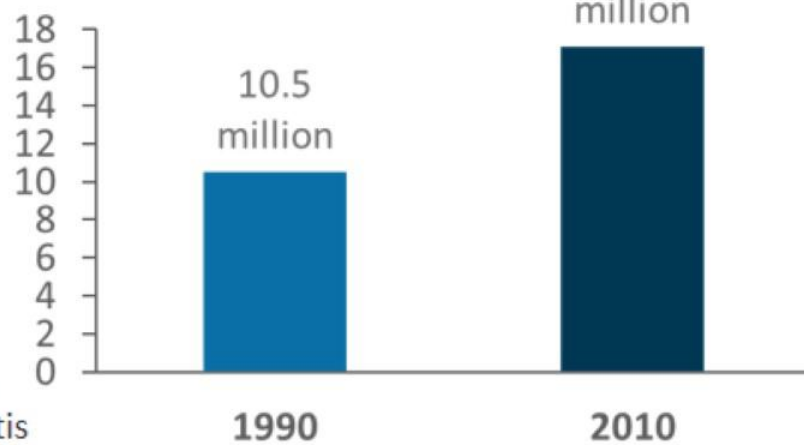


4% global standardized prevalence with knee osteoarthritis



Aging and obesity will increase demand for health services to treat osteoarthritis

Years of Life Lived With Hip and Knee Osteoarthritis Increased From 1990–2010



4.8% prevalence



2.8% prevalence

Considerable Global Burden of Osteoarthritis

Incidence of symptomatic osteoarthritis per year per 100,000 population^[a]

- Knee: 164-250 new cases
- Hand: 100 new cases
- Hip: 47-88 new cases

Lifetime risk of developing symptomatic knee osteoarthritis^[b]

- About 45% overall
- 57% in people with a history of knee injury
- 61% in obese individuals

Of total worldwide disability burden caused by osteoarthritis, 83% related to knee osteoarthritis^[c]

a. Arden N, et al. *Best Pract Res Clin Rheumatol*. 2006;20:3-225.

b. Murphy L, et al. *Arthritis Rheum*. 2008;59:1207-1213.

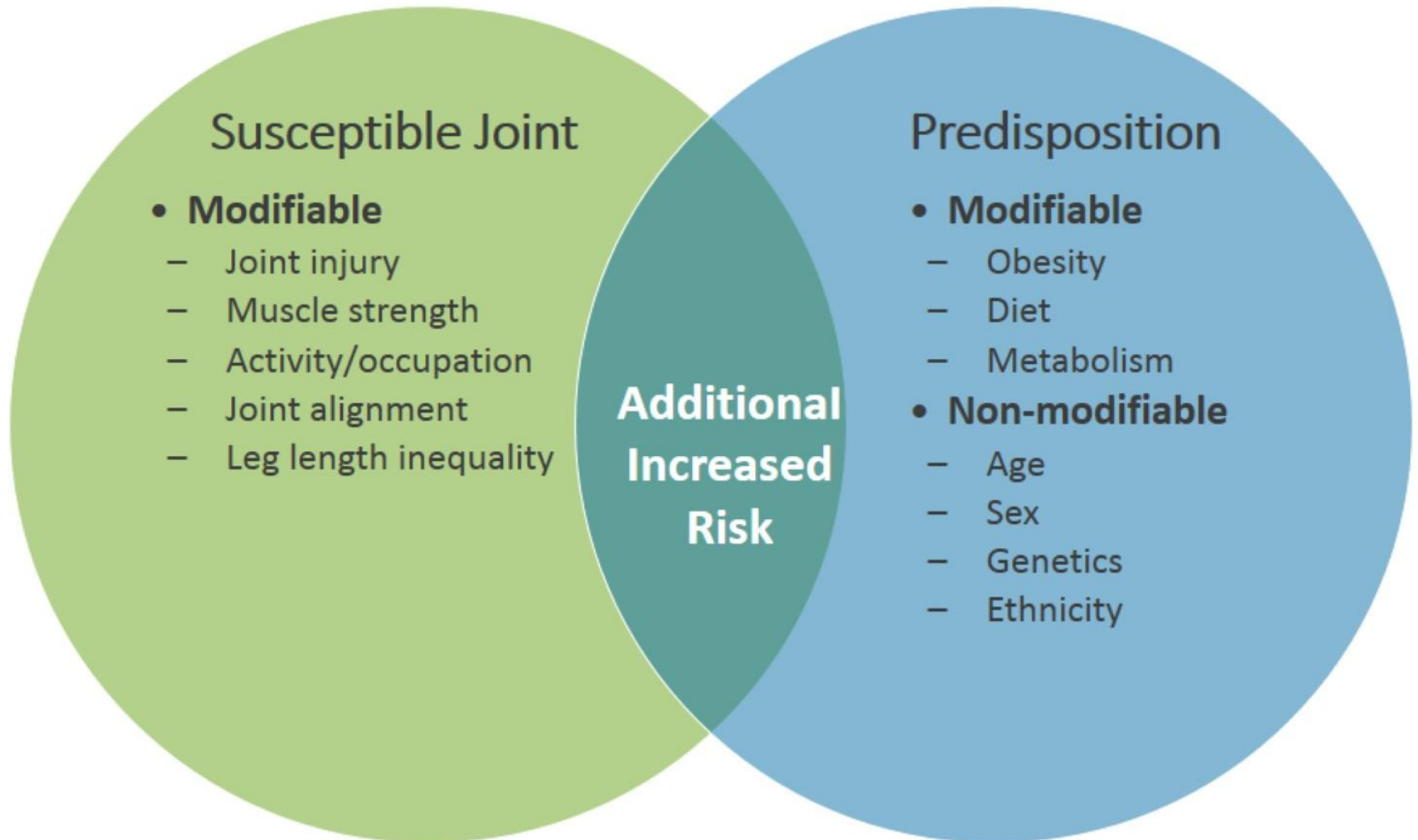
c. Vos T, et al. *Lancet*. 2012;380:2163-2196.

Disability Due to Osteoarthritis Is Increasing

	2005	2015	Change, %
DALYs for all ages, thousands	9562.5	12,886.2	34.8
Age-standardized rate, per 100,000	180.4	187.4	3.9

- Of all the noncommunicable diseases worldwide, osteoarthritis was associated with the greatest increase in DALYs between 1990 and 2015

Multiple Risk Factors for Knee Osteoarthritis



What Are the Signs and Symptoms of Osteoarthritis?

- A heterogeneous disease with many subsets
- Generalized or regional
- Symptoms can vary
- Pain is the principle feature
- Limited stiffness is typical
- Disability is common



Image courtesy of Paul Goyette / CC-BY-SA-2.0

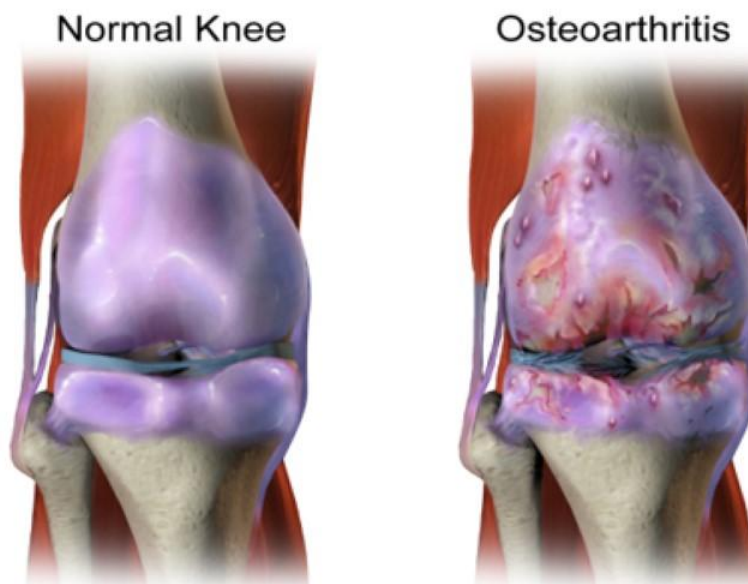
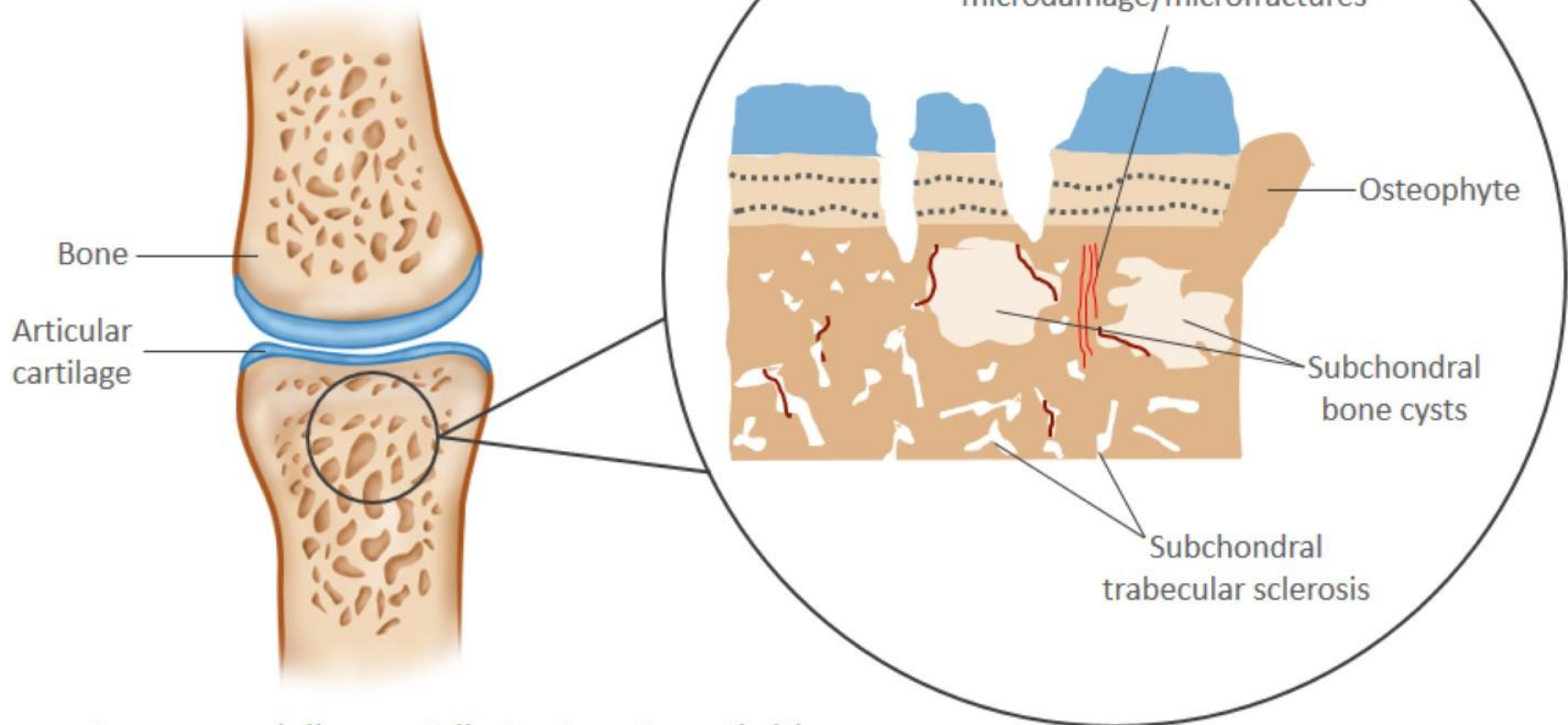


Image courtesy of BruceBlais / CC BY-SA 4.0

What Is Osteoarthritis?

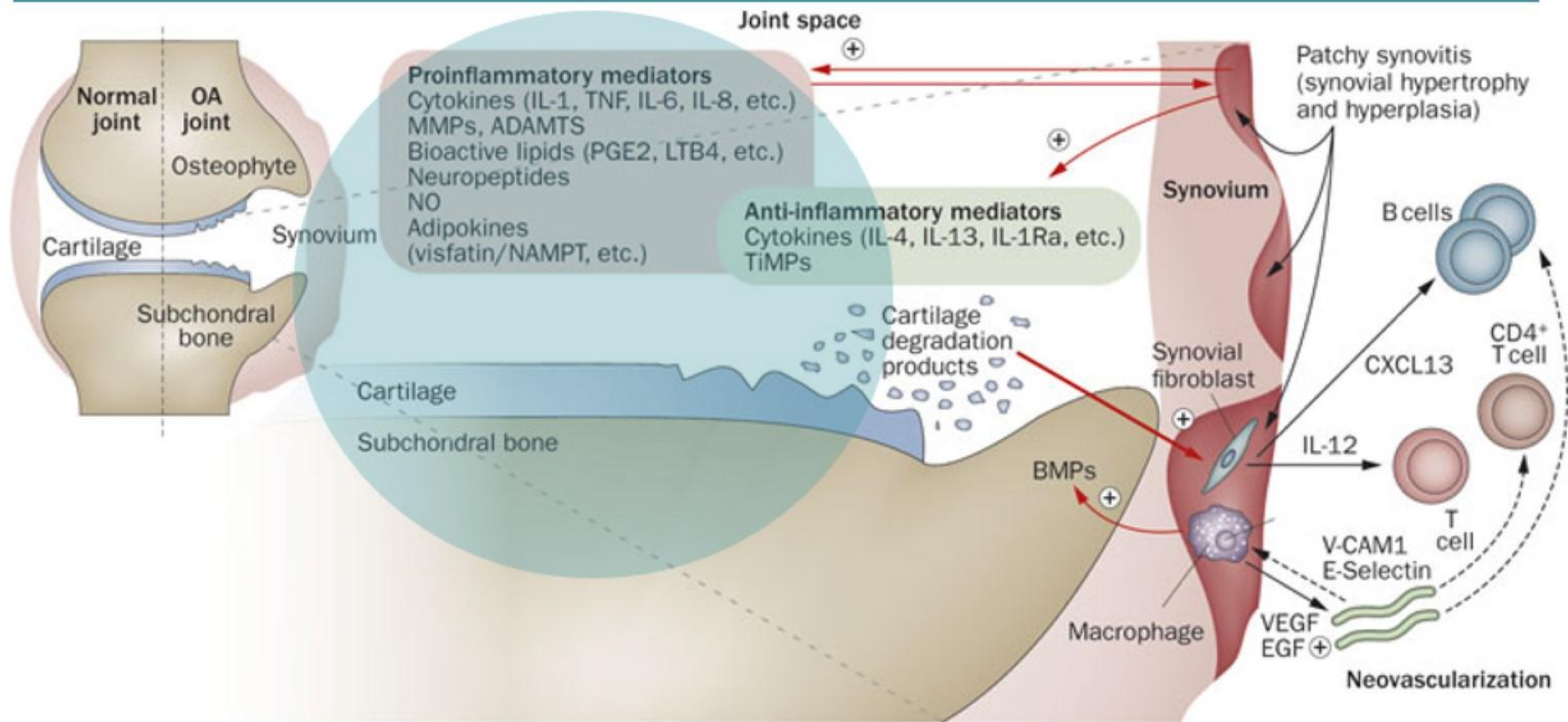
In knee osteoarthritis:

- Thinning of the cartilage
- Response within bone



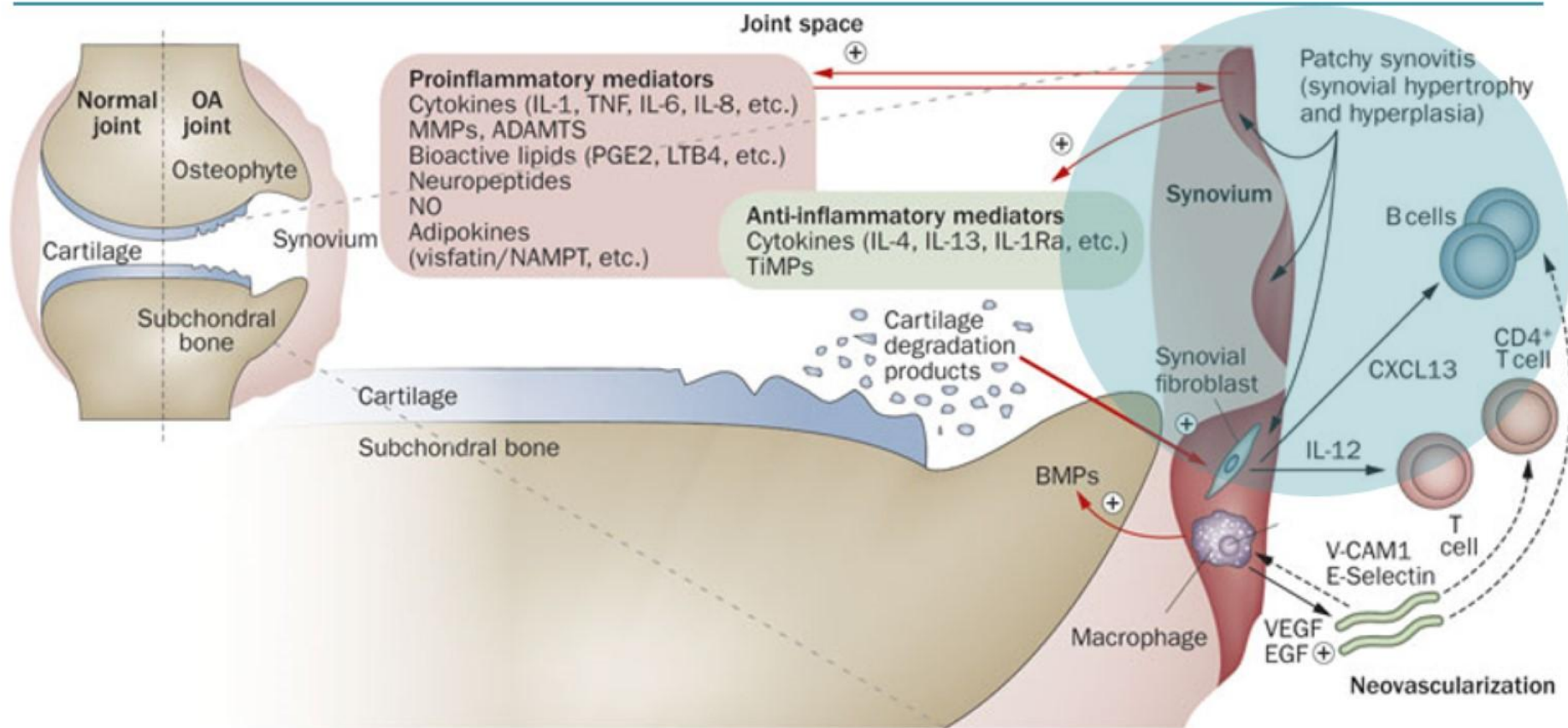
Bone remodeling contributes to osteoarthritis

Early Osteoarthritis: Role of Inflammation I



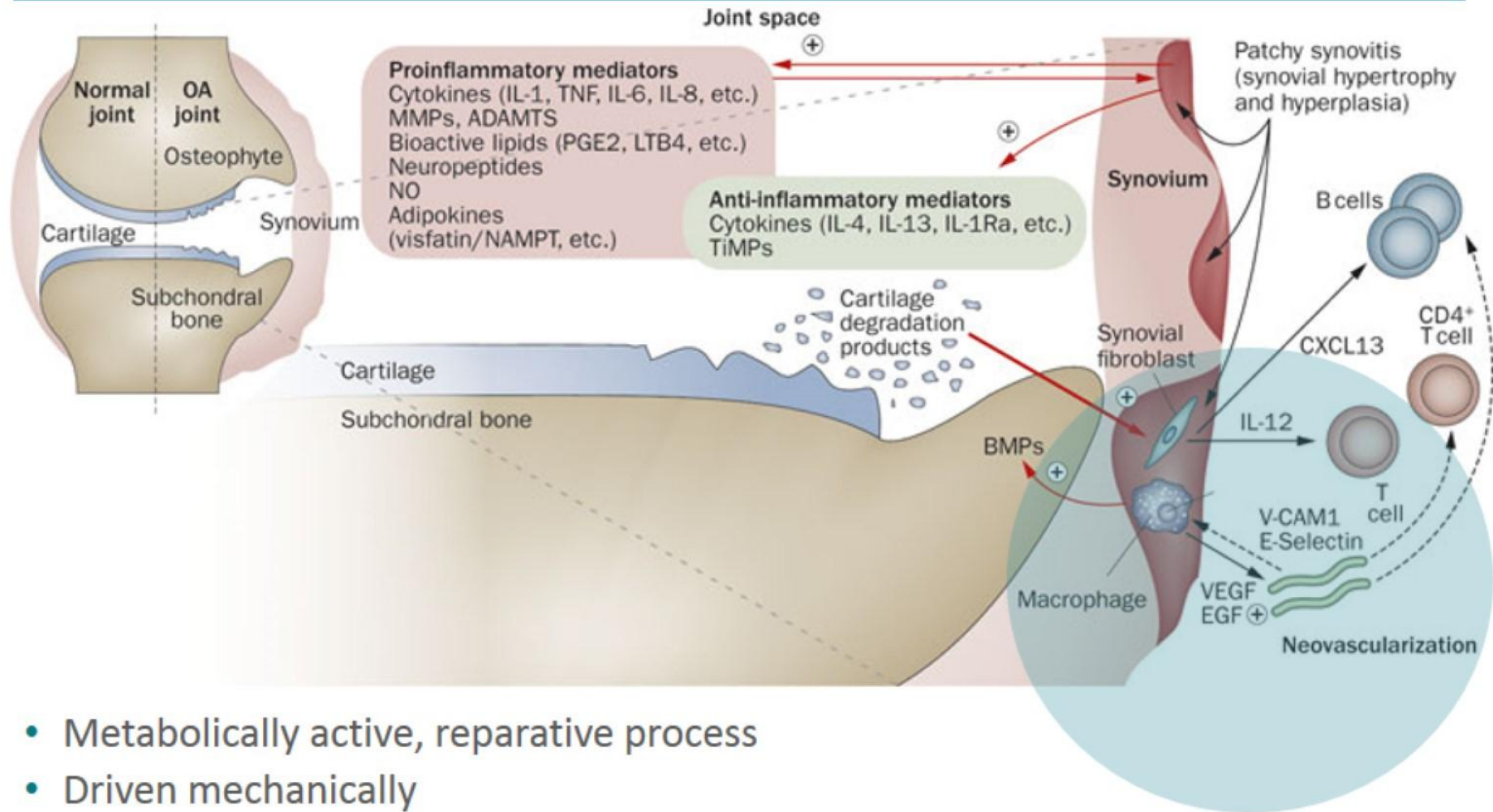
- Metabolically active, reparative process
- Driven mechanically
- Mediated biochemically: inflammatory and neuropeptide pathways

Early Osteoarthritis: Role of Inflammation II



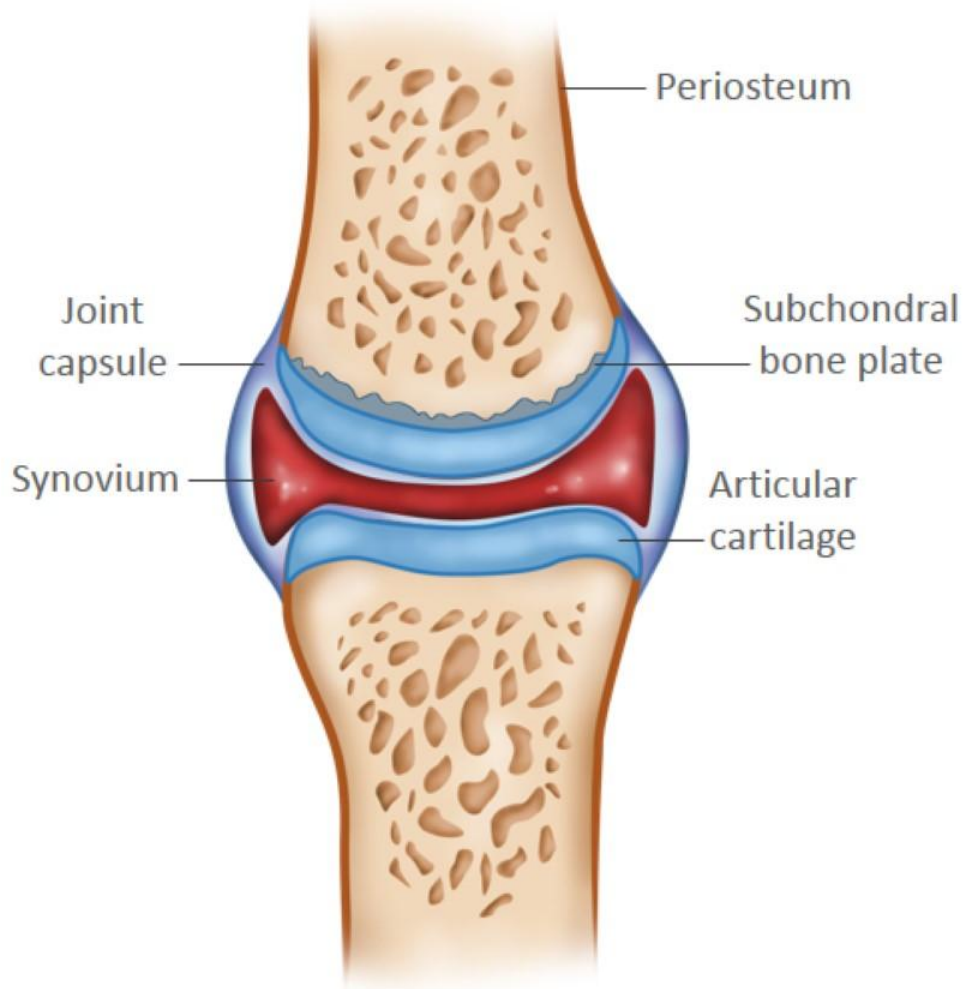
- Metabolically active, reparative process
- Driven mechanically
- Mediated biochemically: inflammatory and neuropeptide pathways

Early Osteoarthritis: Role of Inflammation III



- Metabolically active, reparative process
- Driven mechanically
- Mediated biochemically: inflammatory and neuropeptide pathways

Pain in Osteoarthritis



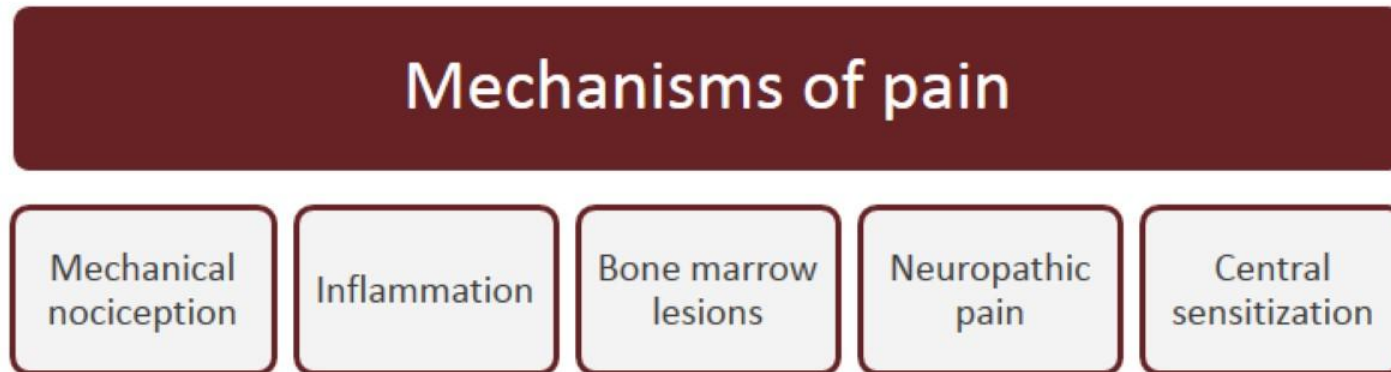
- Raised intraosseous pressure
- Periarticular strain
- Capsular stretching
- Periosteal elevation
- Synovitis
- Inflammation
- Neuropeptides

Central Sensitization in Osteoarthritis Pain

- As the disease progresses, consider central sensitization, where nociceptive inputs can trigger a prolonged increase in excitability of neurons in central pathways
- A variety of studies indicate that hypersensitivity of the CNS plays a significant role in a subgroup of patients with osteoarthritis pain
- The presence of central sensitization may alter treatment choices in later disease
- Some of the other approaches used in the earlier stages of disease, such as oral, injectable, and topical agents, can still be useful in later disease, but the central sensitization process should be considered in all patients

Pain in Osteoarthritis: Considerations

- Sources of pain: articular, periarticular



- Response to pain management will be influenced by these factors

Osteoarthritis: Presentation and Diagnosis

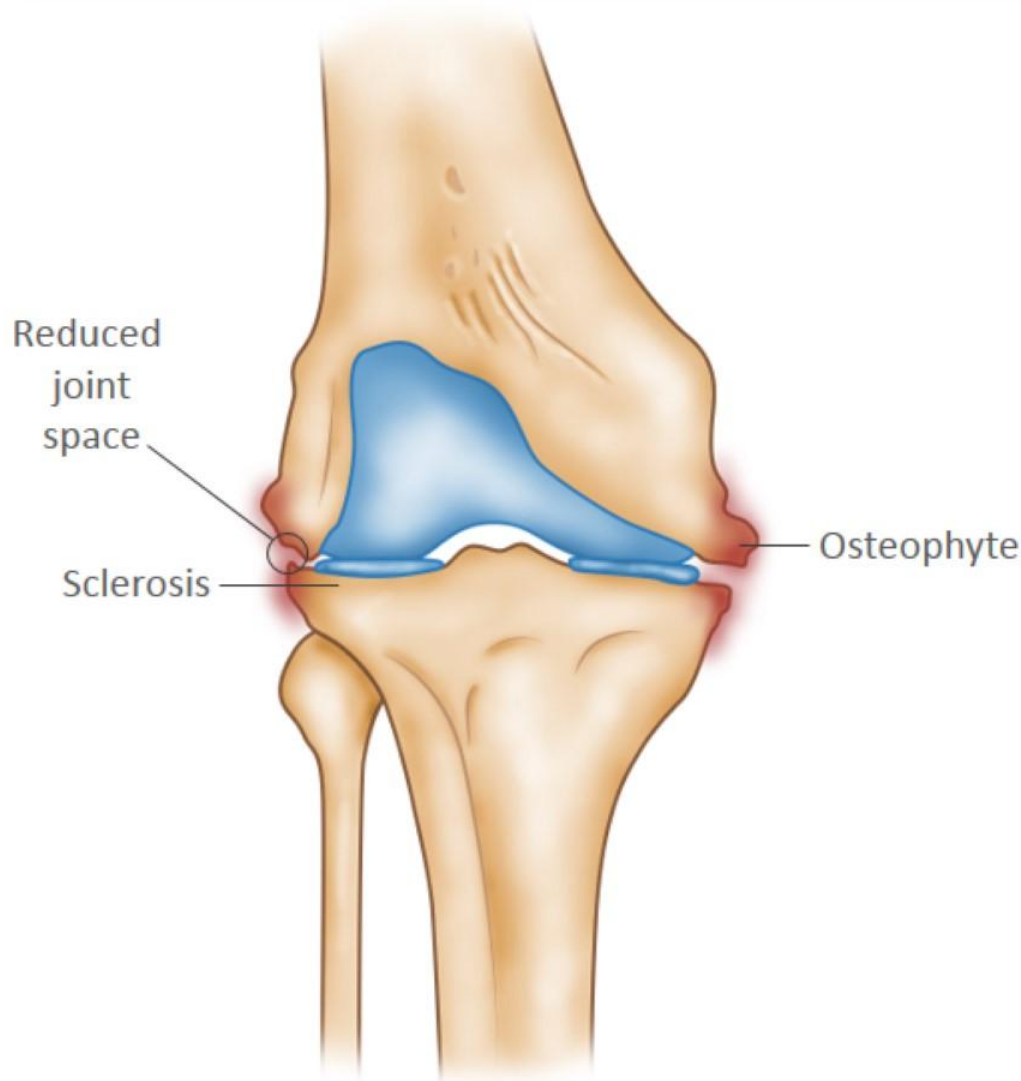
NICE Guideline 2014

- Diagnose osteoarthritis clinically without investigations if a person is 45 years or older and has:
 - Activity related joint pain
 - Morning stiffness < 30 minutes

Atypical features possibly indicating an alternative or additional diagnosis:

- History of trauma
- Prolonged morning joint-related stiffness
- Rapid worsening of symptoms
- Presence of a hot swollen joint, may indicate alternative or additional diagnoses

Investigations: Severe Osteoarthritis



When severe, x-rays show:

- Joint space narrowing
- Osteophyte formation
- Subchondral sclerosis

Usually defined by pathologic or radiologic criteria rather than clinical features

Osteoarthritis: Diagnosis and Management

Osteoarthritis is the beginning, not the end, of the diagnosis

No single patient is the same:

- Pattern of joints affected
- Additional medical risks
- Diseases
- Body weight
- Biomechanics

- Reduce disease progression through exercise, weight management, and control of comorbidities
- Manage symptoms, especially pain
- Limit adverse effects of interventions

As yet, there are no disease-modifying drugs

Various Sets of Guidelines and Recommendations for Osteoarthritis Treatment

- NICE Clinical Guideline UK^[a]
- American College of Rheumatology^[b]
- EULAR recommendations^[c]
- OARSI guidelines^[d]

a. NICE website. Osteoarthritis: care and management: Clinical guideline [CG177].

b. Hochberg MC, et al. *Arthritis Care Res (Hoboken)*. 2012;64:465-474.

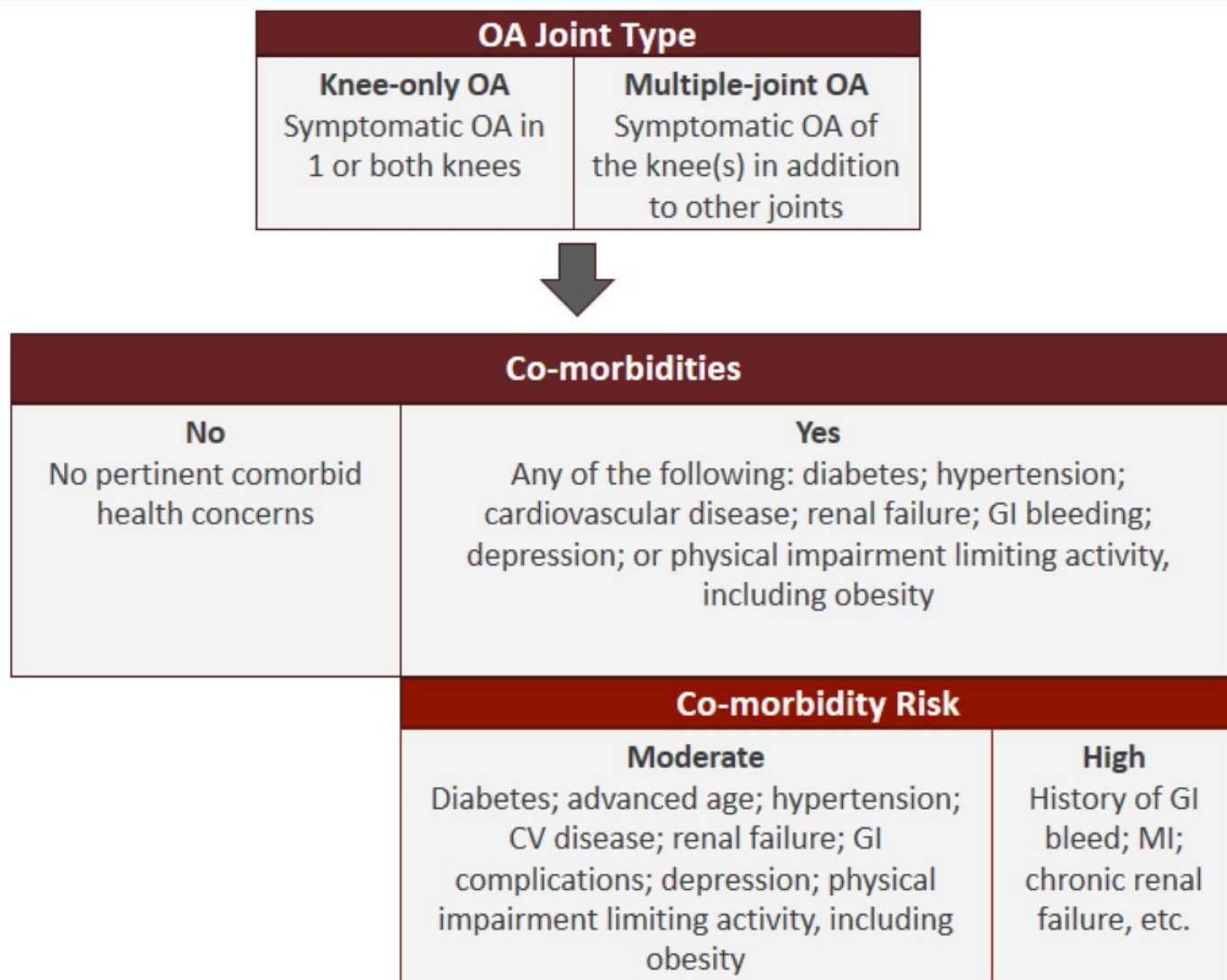
c. Fernandes L, et al. *Ann Rheum Dis*. 2013;72:1125-1135.

d. McAlindon TE, et al. *Osteoarthritis Cartilage*. 2014;22:363-388.

Points About Guidelines

- Guidelines are recommendations
- Treatments are patient specific
- Developed by current evidence and opinion
- The evidence base is changing all the time
- There are inconsistencies between guidelines
- Useful as a platform on which to base best practice

OARSI Guidelines: Osteoarthritis Stratification Into Subtypes



OARSI Guidelines for the Non-Surgical Management of Knee Osteoarthritis

Treatments Appropriate for All Individuals



Recommended Treatments Appropriate for Osteoarthritis Type

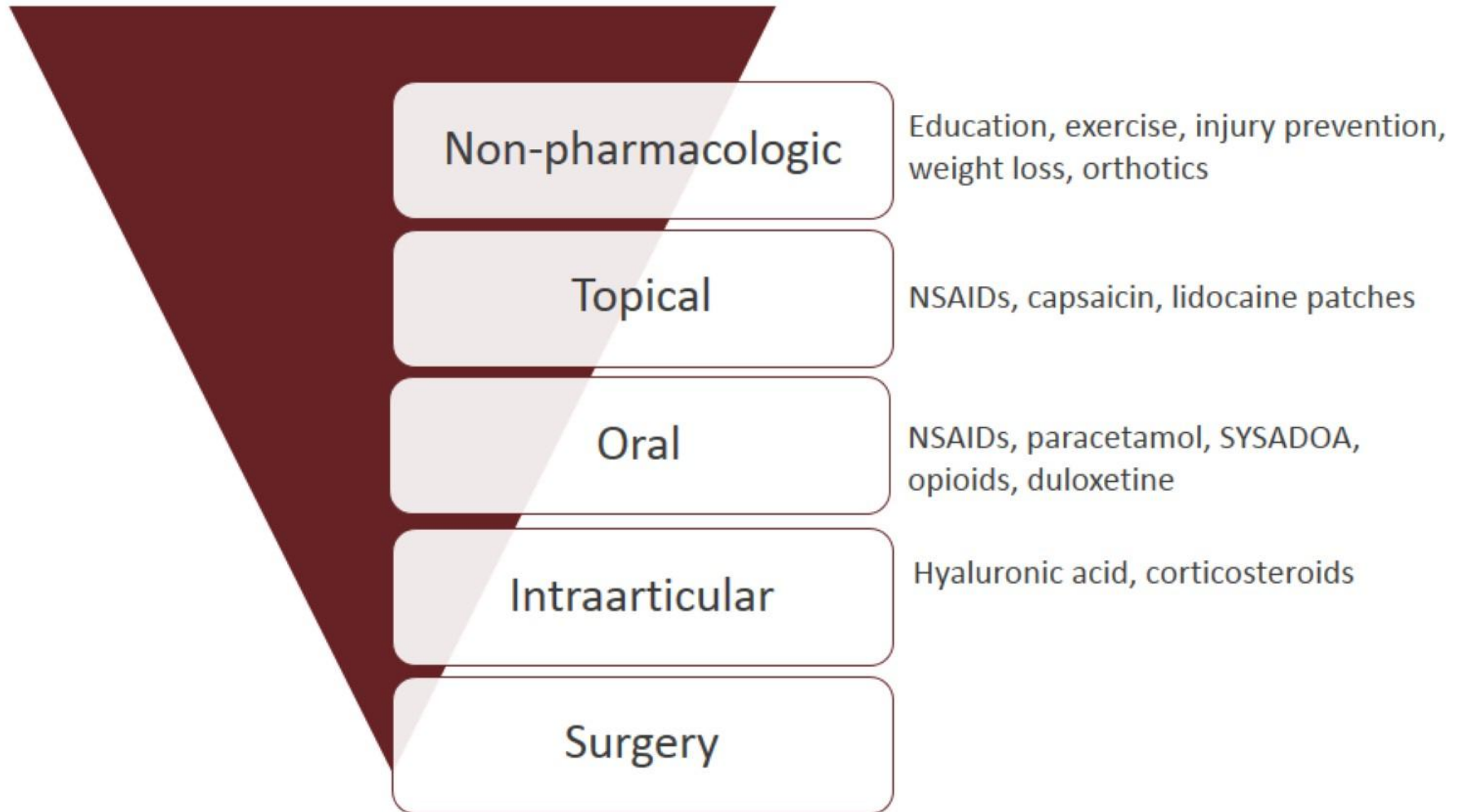
Knee only osteoarthritis without comorbidities

Biomechanical interventions, walking cane, intraarticular corticosteroids, topical NSAIDs, oral COX-2 inhibitors, capsaicin, oral non-selective NSAIDs, duloxetine, acetaminophen

Knee only osteoarthritis with comorbidities

Biomechanical interventions, walking cane, intraarticular corticosteroids, topical NSAIDs

Stepwise Approach to Treatment



OARSI Guidelines: Appropriateness Scores for Management Approaches to Knee Osteoarthritis

Non-pharmacologic	Median Score (scale 1-9)	Appropriate (no comorbidities)
Weight management	8	✓
Strength training	8	✓
Self-management and education	8	✓
Exercise (land-based)	8	✓
Exercise (water-based)	7	✓
Biomechanical interventions	7	✓
Cane (walking stick)	7	✓
Crutches	6	?
Acupuncture	5	?
Balneotherapy	5	?
TENS	5	?
Ultrasound	4	?
Electrotherapy/neuromuscular electrical stimulation	3	X

✓ = Yes, appropriate
 ? = Uncertain evidence
 X = Not appropriate

OARSI Guidelines: Appropriateness Scores for Pharmacologic Treatment of Knee Osteoarthritis

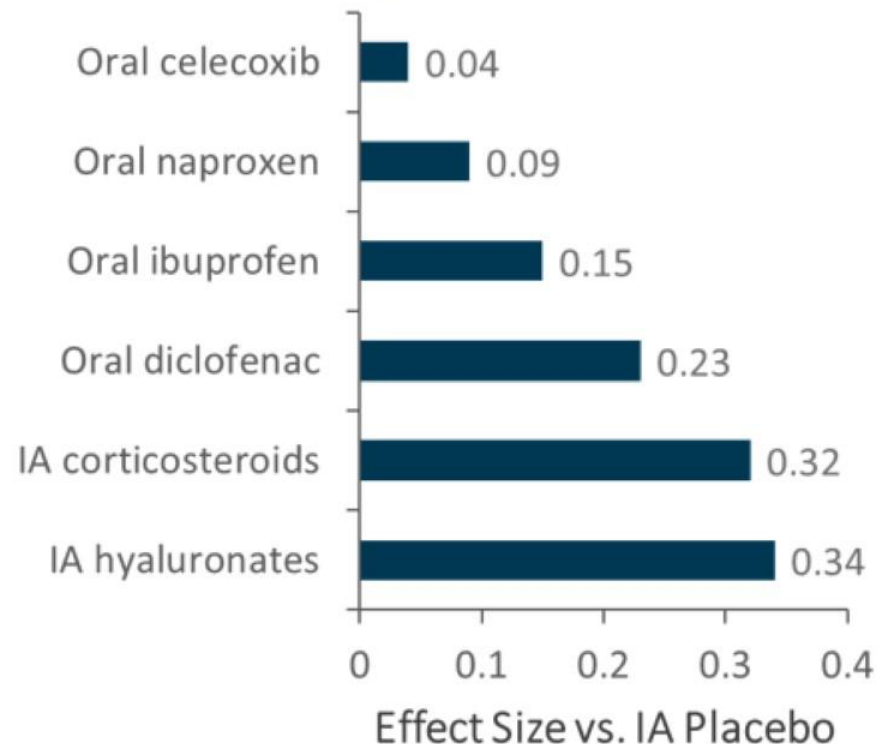
Pharmacologic treatments	Median Score (scale 1-9)	Appropriate (no comorbidities)
NSAIDs (topical)	8	✓
Acetaminophen (paracetamol)	7	✓
Capsaicin	7	✓
Corticosteroids (intraarticular injection)	7	✓
Duloxetine	7	✓
Glucosamine: symptom relief	5.5	?
Chondroitin: symptom relief	5	?
Hyaluronic acid (intraarticular injection)	5	?
Rosehip	5	?
Opioids: oral	4	?
Avocado soybean unsaponifiables	4	?
Diacerein	4	?
Opioids: transdermal	4	?
Chondroitin: disease modification	3	X
Glucosamine: disease modification	3	X
Risedronate	3	X

✓ = Yes, appropriate
 ? = Uncertain evidence
 X = Not appropriate

Injections: Advantages and Disadvantages

- Deliver higher concentration of agent to joint
- Can have short half life in joint
- Can have adverse effects
- There is a need for safe effective agents that remain in joint

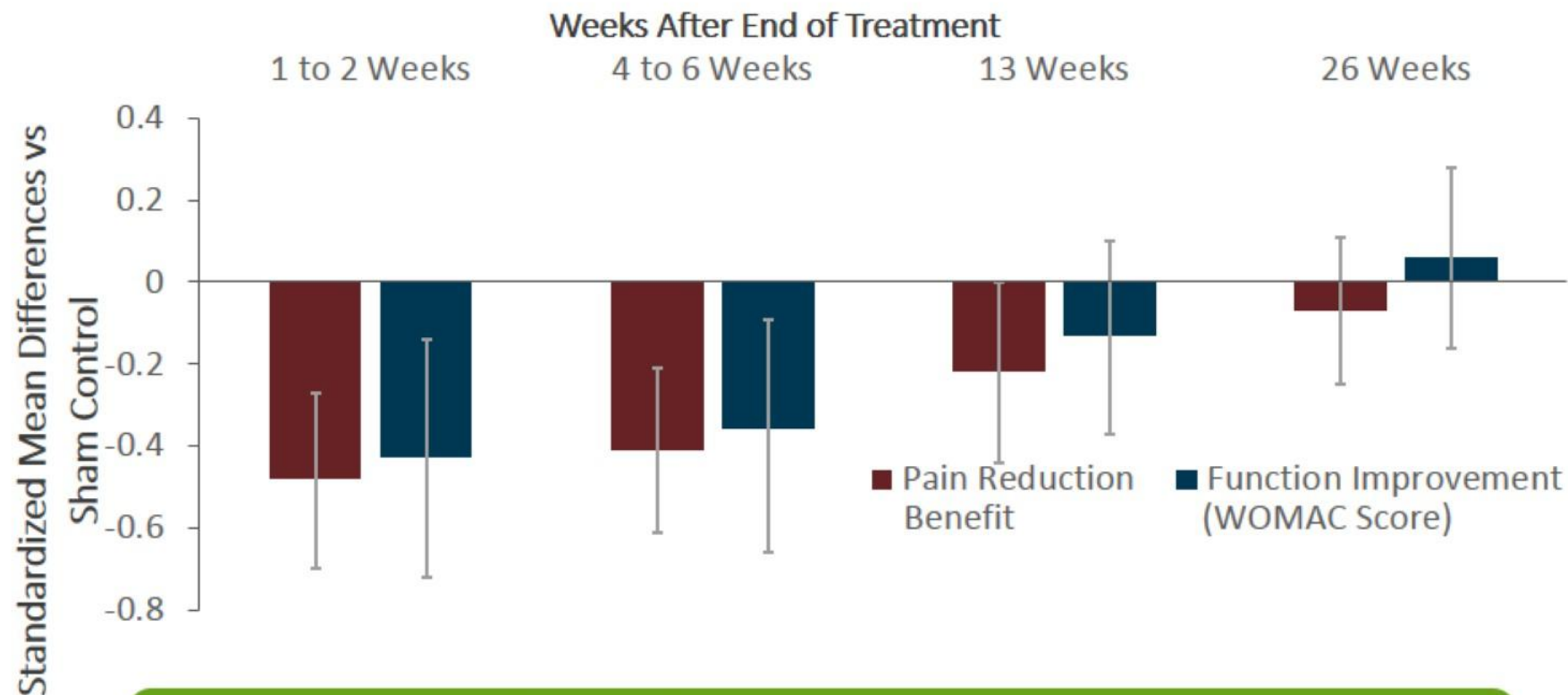
Network Meta-analysis of 137 Studies
Comprising 33,243 Participants



Intraarticular treatments were superior to NSAIDs, possibly due to integrated intraarticular placebo effect

Corticosteroids and Potential Injection Therapies for Knee Osteoarthritis

Meta-analysis of 27 Trials of ICS in Knee OA (N=1767)^[a]



Evidence base is still limited for: Hyaluronic acid preparations, platelet-rich plasma, Intraarticular biologics (eg, anti-TNF)^[b,c]

a. Jüni P, et al. *Cochrane Database Syst Rev*. 2015;CD005328.

b. Iannitti T, et al. *Drugs R D*. 2011;11:13-27.

c. Ayhan E, et al. *World J Orthop*. 2014;5:351-361.

Traumeel® and Zeel® T Combination in Knee Osteoarthritis

Traumeel®^[a]

- A fixed combination of 14 botanical and mineral components, which include mountain arnica, belladonna, and Echinacea, as well as other botanical extracts and minerals
- Comparable effectiveness to NSAIDs in reducing symptoms of inflammation, accelerating recovery, and improving mobility, with a favorable safety profile

Zeel® T^[b]

- A combination of 14 natural ingredients, including mountain arnica, bloodroot, coenzyme A D6 and sulfur
- Comparable efficacy to COX-2 inhibitors in patients with mild-to-moderate knee osteoarthritis

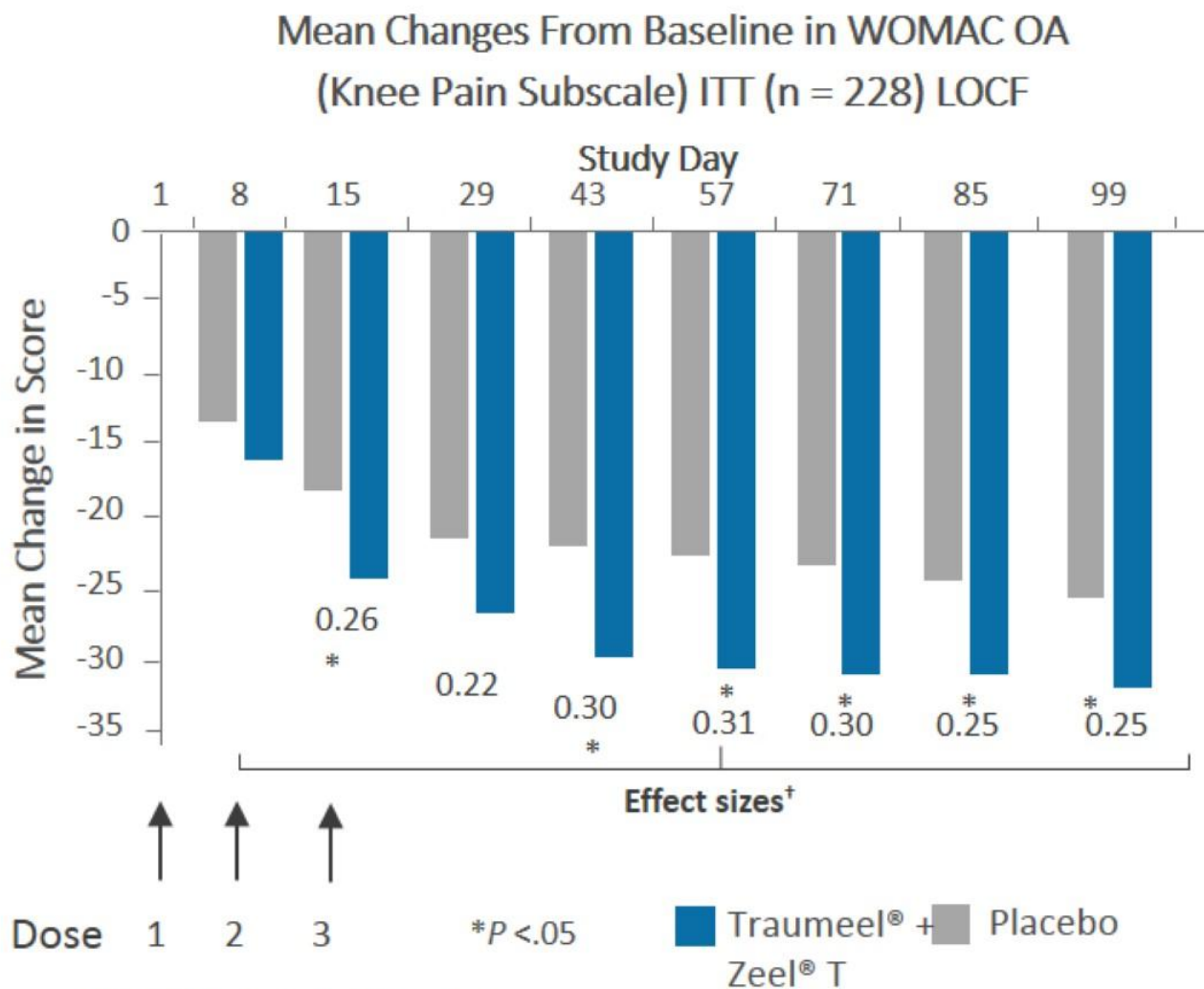
a. Schneider C. *Int J Gen Med.* 2011;4:225-234.

b. Birnesser H, et al. *Explore.* 2007;3:16-22.

Traumeel® and Zeel® T Combination: MOZaRT Study

- Patients and methods: Patients with osteoarthritis of the knee were randomly assigned to 3 weekly intraarticular injections of either Traumeel® and Zeel® T or saline
- Primary efficacy variable: change in knee pain from baseline to study end at week 17 as measured by WOMAC OA Pain Subscale (Section A, 1-5) 100 mm VAS (WOMAC pain section)
 - Effect sizes were calculated for comparison to meta-analysis data
- Safety assessment: monitoring vital signs, target-knee physical examinations, adverse events, concomitant medications, and regulatory databases (PSURs/DSURs)

Traumeel[®] and Zeel[®] T Risk-Benefit Estimation



[†]Statistically normalized (Hedges g) effect sizes
Lozada C, et al. EULAR 2015; Abstract 4268.

Complementary and Alternative Medicine Use in Patients With Arthritis

- 83% to 91% of patients with arthritis in primary or specialty care have tried complementary alternative medicines

Percentage of OA Patients Using CAM in a US Sample in 2001

Type of CAM	Ever		Current	
	Primary Care (n = 400)	Specialty Care (n = 300)	Primary Care (n = 400)	Specialty Care (n = 300)
Special diets	12.8	12.7	9.0	9.0
Vitamins and minerals	30.5	33.0	22.8	26.0
Supplements	31.0	42.7	22.0	25.3
Ointments or topical rubs	61.8	63.3	38.3	32.3
Body treatments	27.3	33.3	10.8	11.7
Movement	22.3	32.0	14.5	21.7
Spiritual	39.0	39.0	36.8	35.0
Mind-body therapies	27.5	30.0	23.5	25.3

Management of Osteoarthritis: Holistic Approach

- It is vital to consider the whole patient
- Emphasis should be on education and empowerment in order to change the destiny of the patient to promote best outcome
- Most difficult challenges often lie in doing the simple things well by lifestyle changes
- Regular exercise, weight loss, and biomechanics are a vital component in the global management of all patients with osteoarthritis

What Do Clinicians Need to Bear in Mind?

- Osteoarthritis is a complex, metabolically active, heterogeneous disease with many disease subsets
- Early diagnosis is vital
- Diagnosis includes identification of risks and comorbidities
- Management is customized to the patient

Concluding Remarks

- All patients should be educated about the disease and self-efficacy enhanced
- Weight management and exercise are vital
- Disease-modifying drugs have still not been identified
- Pharmacologic approaches aim to control pain
- The risk-benefit ratio and subsequent patient choice influence the selection of appropriate interventions

Abbreviations

ADAMTS = alpha disintegrin and metalloproteinase with thrombospondin motifs

BMP = bone morphogenetic protein

CAM = complementary and alternative medicine

CCL2 = CC-chemokine ligand 2

CNS = central nervous system

COX2 = cyclooxygenase-2

CV = cardiovascular

CXCL13 = CXC-chemokine ligand 13

DALY = disability-adjusted life year

DSUR = Development Safety Update Report

EGF = endothelial growth factor

EULAR = European League Against Rheumatism

GI = gastrointestinal

Abbreviations (cont)

GM-CSF = granulocyte-macrophage colony-stimulating factor

IA = intra-articular

IL = interleukin

IL-1Ra = IL-1 receptor antagonist

ITT = intention to treat

LIF = leukemia inhibitory factor

LOCF = last observation carried forward

LTB4 = leukotriene B4

MI = myocardial infarction

MMP = matrix metalloproteinase

NAMPT = nicotinamide phosphoribosyl transferase

NICE = National Institute for Health and Care Excellence

NO = nitric oxide

NGF = nerve growth factor

Abbreviations (cont)

NSAID = nonsteroidal anti-inflammatory drug

OA = osteoarthritis

OARSI = Osteoarthritis Research Society International

PGE2 = prostaglandin E2

PSUR = Periodic Safety Update Report

SYSADSOA = symptomatic slow-acting drugs for osteoarthritis

TENS = transcutaneous electrical stimulation

TIMP = tissue inhibitor of metalloproteinase;

TNF = tumor necrosis factor

VAS = visual analogue scale

VCAM-1 = vascular cell adhesion molecule 1

VEGF = vascular endothelial growth factor

WOMAC OA = Western Ontario and McMaster Universities Osteoarthritis