Evidence-based Review of Non-surgical Management of Osteoarthritis

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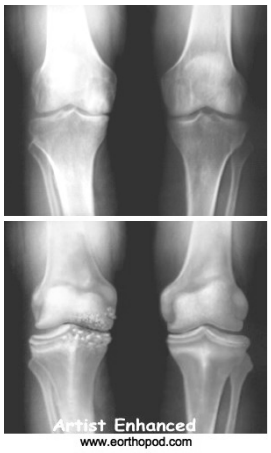
Objectives

1. Understand the basic epidemiology of OA
2. Understand challenges facing OA therapy development

Osteoarthritis

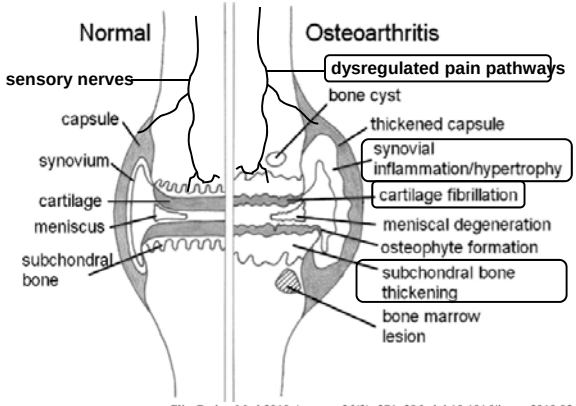
- 30-40 million people in USA
- Increasing prevalence
- Progressive cartilage degeneration and failure of whole joint
- Risk Factors include: age, weight, biomechanics
- No current DMOADs
- Varying disease presentations



OA is Highly Prevalent in the US

- **Most common cause of knee pain in people >50yrs old**
- **Aging and obesity significantly increase risk of symptomatic OA**
- **30-50% over age 65 suffer from OA**
- **Over 80% >65yrs old have radiographic OA in at least one joint**
- **Knee pain is common, incidence is increasing, only half have signs of radiographic OA**

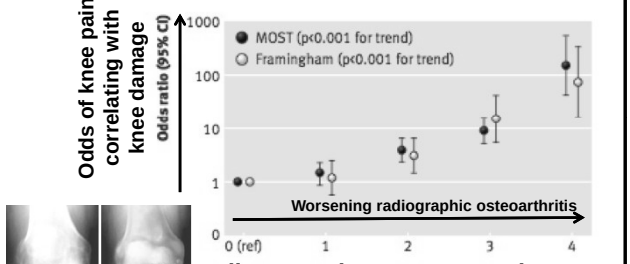
OA Pathophysiology: Total Joint Failure

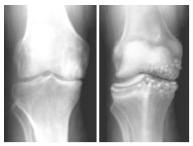


Clin Geriatr Med. 2010 August ; 26(3): 371–386. doi:10.1016/j.cger.2010.03.002.

Structural Joint Deformity Correlates with Pain in Knee OA

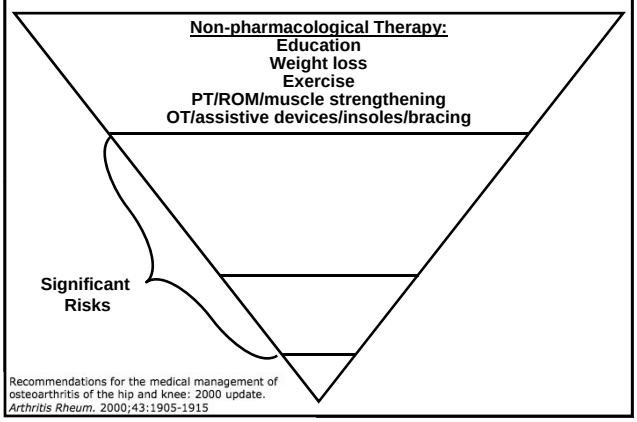
T. Neogi, *et al*. BMJ 2009; 339: b2844





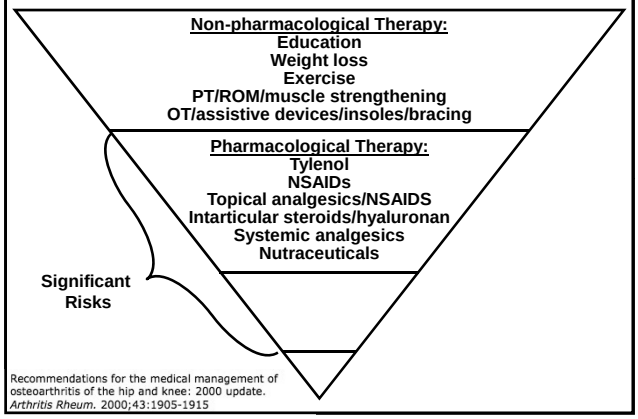
Kellgren and Lawrence grade
(radiological assessment of OA and structural deformity in knees of patients with discordant knee pain)

Current OA Therapeutic Options

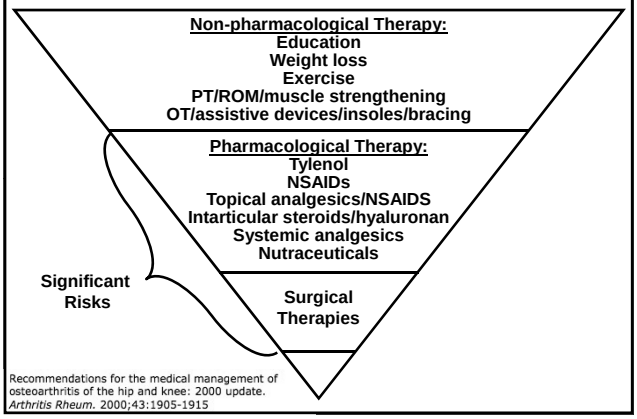


Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. *Arthritis Rheum.* 2000;43:1905-1915

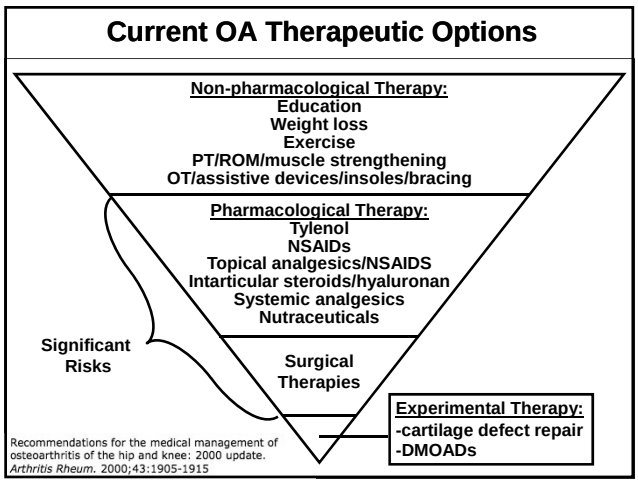
Current OA Therapeutic Options



Current OA Therapeutic Options



Current OA Therapeutic Options



Unmet Needs in Research for OA Therapeutics

- **Identifying phenotypic subsets of OA patients**
- **Defining the onset of disease relative to clinical diagnosis**
- **Understanding disease pathophysiology**
- **Disease Modifying OA Drug (DMOAD)**

Challenges in OA Clinical Trials

- Defining the onset of OA relative to clinical diagnosis—when does OA start?
  - Targeting preventive or corrective therapies?
- Multiple phenotypes
- High rate of placebo effect in OA (20-40%)
- Study outcomes:
  - Improvements in pain, function and/or tissue damage?

Difficulties in Developing Management Guidelines in OA

- How do we define "improvement"?
  - Pain
  - Functional assessment/scores
  - QALY's
  - ADLs
  - Tissue changes (cartilage volume, etc.)
- Do interventions offer prevention of worsening pain/function or improvement in pain/function?

Difficulties in Developing Management Guidelines for OA

- Multiple agencies with recommendations
  - EULAR
  - OARSI
  - ACR
  - Japanese
  - French
  - Orthopedics
- Different methods to determine guideline validity
- Heavy reliance on "expert opinion"
- Literature variations by hip, knee and/or hand OA interventions

Hochberg et al, Arthritis Care and Research Vol 64, No. 4, April 2012

Arthritis Care & Research
Vol. 64, No. 4, April 2012, pp 465–474
DOI 10.1002/acr.21596

SPECIAL ARTICLE

American College of Rheumatology 2012 Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee

MARC C. HOCHBERG,[1] ROY D. ALTMAN,[2] KARINE TOUPIN APRIL,[3] MARIA BENKHALTI,[3] GORDON GUYATT,[4] JESSIE McGOWAN,[3] TANVEER TOWHEED,[5] VIVIAN WELCH,[3] GEORGE WELLS,[3] AND PETER TUGWELL[3]

Guidelines and recommendations developed and/or endorsed by the American College of Rheumatology (ACR) are intended to provide guidance for particular patterns of practice and not to dictate the care of a particular patient. The ACR considers adherence to these guidelines and recommendations to be voluntary, with the ultimate determination regarding their application to be made by the physician in light of each patient's individual circumstances. Guidelines and recommendations are intended to promote beneficial or desirable outcomes but cannot guarantee any specific outcome. Guidelines and recommendations developed or endorsed by the ACR are subject to periodic revision as warranted by the evolution of medical knowledge, technology, and practice.

The American College of Rheumatology is an independent, professional, medical and scientific society which does not guarantee, warrant, or endorse any commercial product or service.

ACR OA Guidelines 2012: HAND OA (PHARMACOLOGICAL TX)

- **Conditionally Recommended:**
  - **Topical capsaicin**
  - **Topical NSAIDs**
  - **Oral NSAIDs (<75yrs old, no contraindications)**
  - **Tramadol**
- **Conditionally Recommended to NOT use:**
  - **Intra-articular injections**
  - **Opiates**

Hochberg et al, Arthritis Care and Research Vol 64, No. 4, April 2012

ACR OA Guidelines 2012: HAND OA (NON-PHARMACOLOGICAL TX)

- **Evaluate to perform ADL's**
- **Instruct in joint protection techniques**
- **Assistive devices to perform ADL's**
- **Thermal modalities**
- **Splinting for 1st CMC OA**

Need a good occupational therapist skilled in hand OA treatments!

Hochberg et al, Arthritis Care and Research Vol 64, No. 4, April 2012

Overview of Hand OA Therapy Recs

1. **DIP/IP vs. 1st CMC disease = different disease entities? (different treatments/outcomes)**
2. **Minimal options for pharmacological treatment, even for pain control**
3. **Very few RCT studies comparing these therapies, very little strong supporting evidence**

MY RESPONSE:

- **ADL's are important!**
  - **Goal is improving patient well-being including FUNCTIONAL improvements.**
  - **Not everyone's biggest issue is pain—for many, decreased function is the problem**
- **Hand OA requires a collaborative treatment approach**
- **Can JOINT PROTECTION prevent PROGRESSION?**
- **Splint, DON'T inject, 1st CMC OA.**

ACR OA Guidelines 2012: KNEE OA (NON-PHARMACOLOGICAL TX)

- **STRONGLY RECOMMEND: EXERCISE**
  - **Aerobic exercise (land or aquatic)**
  - **Severely dysfunctional—start with aquatic**
- **STRONGLY RECOMMEND: WEIGHT LOSS**
  - **Independently improves pain and function**
- **NOTE: These are the only "*strongly recommended*" recommendations that the ACR makes for any form of OA**

Hochberg et al, Arthritis Care and Research Vol 64, No. 4, April 2012

ACR OA Guidelines 2012: KNEE OA (NON-PHARMACOLOGICAL TX)

- **Conditionally Recommend:**
  - **Self-management programs focusing on psychosocial interventions**
  - **PT: thermal, manual therapy, with exercise**
  - **Medially-directed patellar taping for laterally deviated patella**
  - **Tai chi**
  - **Walking aids, if useful**
  - **Insoles: medial wedge for lateral compartment OA, lateral wedge for medial compartment OA**

Hochberg et al, Arthritis Care and Research Vol 64, No. 4, April 2012

RESPONSE:

- **Strongly recommended:**
  - **DIET**
  - **EXERCISE**
- **Both are independently demonstrated to result in sustained clinical improvement in OA pain and function in *weight bearing OA*.**
- **Collaborative treatment approach**

Weight Loss and Exercise Improve OA Pain and Function

Research

Preliminary Communication

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

Stephen P. Messier, PhD; Shannon L. Mihalko, PhD; Claudine Legault, PhD; Gary D. Miller, PhD; Barbara J. Nicklas, PhD; Paul DeVita, PhD; Daniel P. Beavers, PhD; David J. Hunter, MBBS, PhD; Mary F. Lyles, MD; Felix Eckstein, MD; Jeff D. Williamson, MD; J. Jeffery Carr, MD; Ali Guermazi, MD, PhD; Richard F. Loeser, MD

JAMA. 2013;310(12):1263-1273. doi:10.1001/jama.2013.277669

IDEA Trial: Study Design

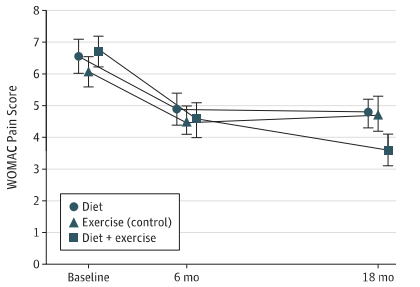
- Single blind, single center, 18mo randomized controlled trial
- 3 group randomization:
  - Diet alone
  - Exercise alone (Exercise is comparison group)
  - Diet + Exercise
- Inclusion criteria:
  - 55yrs old or more, mild to moderate knee OA, BMI 27 to 41, sedentary lifestyle
  - No study-influenced changes in meds

IDEA Trial: Study Design

Diet	Exercise	Diet + Exercise
• Goal: 10-15% weight loss over 6-18mo • Energy intake deficit 800-1000Kcal/day • 2 meal replacement shakes/day • 3rd meal guided recipes	3x weekly: 15min walking ↓ 20min weights ↓ 15min walking ↓ 10min cool down	Combined

JAMA. 2013;310(12):1263-1273. doi:10.1001/jama.2013.277669

Figure 2. Mean WOMAC Pain Scores Across the 18-Month Intervention Period



No. of patients			
Diet	152	115	124
Exercise	149	119	127
Diet + exercise	152	130	120

JAMA. 2013;310(12):1263-1273. doi:10.1001/jama.2013.277669

RESULTS At 18 months, 399 participants (88%) completed the study. Compared with exercise participants, knee compressive forces were lower in diet participants and IL-6 levels were lower in diet and diet + exercise participants.

	18-mo Outcomes, Mean (95% CI)				
	Exercise (E)	Diet (D)	D + E	Difference, E vs D	Difference, E vs D+E
Weight loss, kg	−1.8 (−5.7 to 1.8)	−8.9 (−12.4 to −5.3)	−10.6 (−14.1 to −7.1)		
Knee compressive forces, N	2687 (2590 to 2784)	2487 (2393 to 2581)	2543 (2448 to 2637)	200 (55 to 345)[a]	144 (1 to 287)
IL-6, pg/mL	3.1 (2.9 to 3.4)	2.7 (2.4 to 3.0)	2.7 (2.5 to 3.0)	0.43 (0.01 to 0.85)[a]	0.39 (−0.03 to 0.81)[a]
Pain	4.7 (4.2 to 5.1)	4.8 (4.3 to 5.2)	3.6 (3.2 to 4.1)	−0.11 (−0.81 to 0.59)	1.02 (0.33 to 1.71)[a]
Function	18.4 (16.9 to 19.9)	17.4 (15.9 to 18.9)	14.1 (12.6 to 15.6)	0.98 (−1.24 to 3.20)	4.29 (2.07 to 6.50)[a]
SF-36 physical	41.9 (40.5 to 43.2)	42.4 (41.1 to 43.7)	44.7 (43.4 to 46.0)	−0.55 (−2.53 to 1.43)	−2.81 (−4.76 to −0.86)[a]

[a]Differences were significant.

CONCLUSIONS AND RELEVANCE Among overweight and obese adults with knee OA, after 18 months, participants in the diet + exercise and diet groups had more weight loss and greater reductions in IL-6 levels than those in the exercise group; those in the diet group had greater reductions in knee compressive force than those in the exercise group.

JAMA. 2013;310(12):1263-1273. doi:10.1001/jama.2013.277669

IDEA Trial: Clinical Relevance

- Weight loss improves OA pain and function
- Mild to moderate weight loss (Goal 10-15% reduction) improves pain
- Diet plus exercise better than either alone
- Diet interventions are significant to achieve weight loss (significant calorie restriction)
- Exercise is not overtly rigorous (walking, 20min weights)

ACR OA Guidelines 2012: KNEE OA (PHARMACOLOGICAL TX)

- Conditionally Recommend:
  - Acetaminophen (modest effect)
  - Oral/topical NSAIDs
  - Tramadol
  - IA corticosteroids
- NOT RECOMMENDED:
  - Nutritional supplements (glucosamine/chondroitin)
  - Topical capsaicin

Hochberg et al, Arthritis Care and Research Vol 64, No. 4, April 2012

ACR OA Guidelines 2012: KNEE OA (PHARMACOLOGICAL TX)

- If inadequate response to acetaminophen (<4g/d), attempt oral/topical NSAIDs (>75yrs old = topical) or intra-articular steroids (frequency every 3-4months)
- Conditionally recommended as alternatives:
  - Tramadol
  - Duloxetine
  - IA hyaluronan

Hochberg et al, Arthritis Care and Research Vol 64, No. 4, April 2012

MY RESPONSE:

- Combine Acetaminophen + NSAIDs?
- NSAID toxicities in the OA population present risk
- Summary: medications should NOT be the mainstay of weight bearing OA treatment
  - Medications are NOT "strongly recommended" largely due to a lack of convincing supporting data and/or appropriate clinical trials

NSAIDS for Weight-Bearing OA

- Hx of symptomatic/complicated UGI ulcer WITHOUT UGI bleed within the last year:
  - Strongly recommend COX2 selective inhibitor or standard NSAID + PPI
  - No preference for any particular NSAID
- Hx of UGI bleed within the year:
  - COX2 plus PPI
- In general, chronic NSAID use should be considered for co-treatment with a PPI.
- NO NSAIDS with GFR <30, 30-60: risk/benefit

Hochberg et al, Arthritis Care and Research Vol 64, No. 4, April 2012

MY RESPONSE:

- Great care with NSAIDs not to do more harm than good (conditionally, not strongly recommended)
- Which NSAID?
  - Longer acting, q12hrs offers more options for PRN use and clinical effect (naprosyn, diclofenac)
- Ibuprofen and ASA: ASA given for CVS protection may be less effective when used with ibuprofen
- NOT use COX2 selective inhibitors in patients with significant CVS risks (strongly rec)

Hochberg et al, Arthritis Care and Research Vol 64, No. 4, April 2012

What about patients who fail pharmacological and non-pharmacological therapy?

- Total joint replacement (TKR, THR)
- What if they can't have TKR?
  - Pain control: Opiods (strongly recommended)
    - American Pain Society/American Association of Pain Medicine Use of Opiods in Management of Chronic Non-Cancer Pain Recommendations
  - Duloxetine (conditionally recommended)
  - Acupuncture
  - Transcutaneous Electrical Stimulation

Hochberg et al, Arthritis Care and Research Vol 64, No. 4, April 2012

Non-pharmacological therapy: HIP OA

Table 5. Nonpharmacologic recommendations for the management of hip osteoarthritis (OA)

We strongly recommend that patients with hip OA should do the following:
Participate in cardiovascular and/or resistance land-based exercise
Participate in aquatic exercise
Lose weight (for persons who are overweight)
We conditionally recommend that patients with hip OA should do the following:
Participate in self-management programs
Receive manual therapy in combination with supervised exercise
Receive psychosocial interventions
Be instructed in the use of thermal agents
Receive walking aids, as needed
We have no recommendations regarding the following:
Participation in balance exercises, either alone or in combination with strengthening exercises
Participation in tai chi
Receiving manual therapy alone

Hochberg et al, Arthritis Care and Research Vol 64, No. 4, April 2012

Pharmacological therapy: HIP OA

Table 6. Pharmacologic recommendations for the initial management of hip OA*

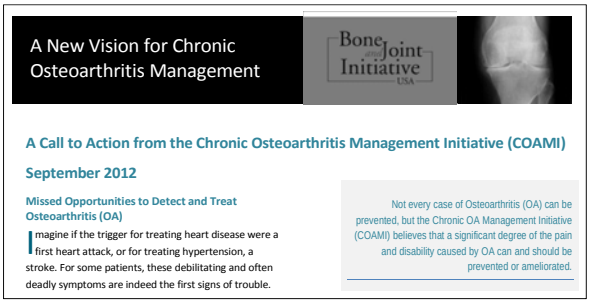
We conditionally recommend that patients with hip OA should use one of the following:
- Acetaminophen
- Oral NSAIDs
- Tramadol
- Intraarticular corticosteroid injections

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

We have no recommendation regarding the use of the following:
- Topical NSAIDs
- Intraarticular hyaluronate injections
- Duloxetine
- Opioid analgesics

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

Management or Prevention?



1. Approaching OA management by advocating preventative strategies such as in other chronic diseases (DMII, CVS, etc.)
2.Development of standardized OA screening tools (like the A1C)
3.Defining "Pre-OA" conditions and risk stratification of phenotypes prone towards OA
4.Promotion of self-management strategies (DM, CVS)

How can we apply these guidelines to clinical practice?

Principles of modern OA Management: Role of Exercise and Weight Loss

- **The only "Strongly Recommended" treatments by the ACR for weight bearing OA**
- **A priority management strategy for patients who have obesity and OA**
- **Necessary for pre-op for TKR and THR**
  - **See Dr. Andrew Glasman's MedNet presentation**

Principles of Modern OA Management: NSAIDs

- Great care with chronic use
- Assess for bleeding risk, monitor appropriately
- Cardiovascular and renal issues
- Age-related toxicity (>75yrs old)
- Topical NSAIDs over orals

Principles of Modern OA Management: Opiates

- Not recommended for hand OA
- Only recommended for weight bearing OA in the context that they cannot get a replacement
- Worsening outcomes with opiates used for OA pain
- Should conform to established recommended guidelines for treatment of chronic, non-cancerous pain

Principles of Modern OA Management: Hand OA

- Difficult to treat
- Assess whether function is the primary problem or if pain is the primary problem.
  - Many patients have worse function than pain!
- Mutlimodal approach
- OSU developing academic-based OT research in this area

Principles of Modern OA Management: Phenotypes

- New phenotypes are emerging in OA patients
- Different phenotypes may require different treatment approaches:
  - Younger patients with early, mild-moderate OA and obesity
  - Older patients without obesity
  - Alignment and joint morphology
  - Severity of OA
- Target the patients for PREVENTION

Principles of Modern OA Management: Future Directions

- **Which treatments might prevent progression?**
- **Should pain treatments be targeted to increase exercise goals?**
- **Role of systemic inflammation in OA pathogenesis (elevated ESR, hsCRP, etc)?**
- **Can Exercise and/or weight loss prevent progression?**
- **DMOADs vs. improved pain control?**

Summary:

- **OA management exists, but is not overwhelmingly effective with any single agent/treatment modality**
- **A commitment to education of the patient is a top priority. Expectations must be managed.**
- **Diet and Exercise are primary treatment modalities in weight bearing OA**
- **Medications are not the only effective strategies for any form of OA**
- **Recommendations must be based on an individualized approach to osteoarthritis care**