

# Keepin' the Joints Jumpin'

## — An Integrative Approach to the Patient with Osteoarthritis



August 2011

# Overview

- What is OA?
- What is the impact of OA?
- Treatment
  - Slowing progression
  - Treating symptoms

(Hidden agenda: there are many more options than just NSAIDs, and lots of reasons not to use those.)

# Osteoarthritis

Second most common  
chronic illness in  
America



# So what is Osteoarthritis?

## ■ Findings:

- Progressive loss of cartilage
- Thickening of subchondral bone, bone spur formation
- ± Inflammation of the synovium

## ■ And what patients experience:

- loss of range of motion
- pain in the joints

# Diagnosis

- Clinical diagnosis: correctly identify 99% of patients with knee osteoarthritis
  - 3 symptoms: pain on use, short-lived morning stiffness, functional limitation
  - 3 signs: crepitus, restricted movement, bony enlargement
- EULAR 2009 (note xrays are not required)

## Osteoarthritis



Healthy knee joint

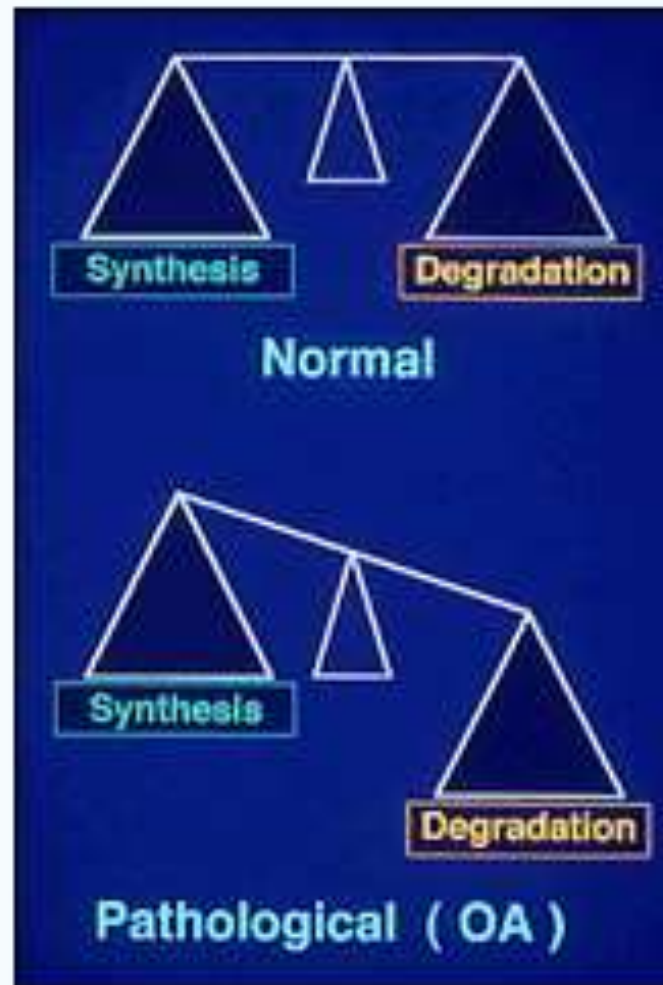


Hypertrophy and spurring  
of bone and erosion of cartilage



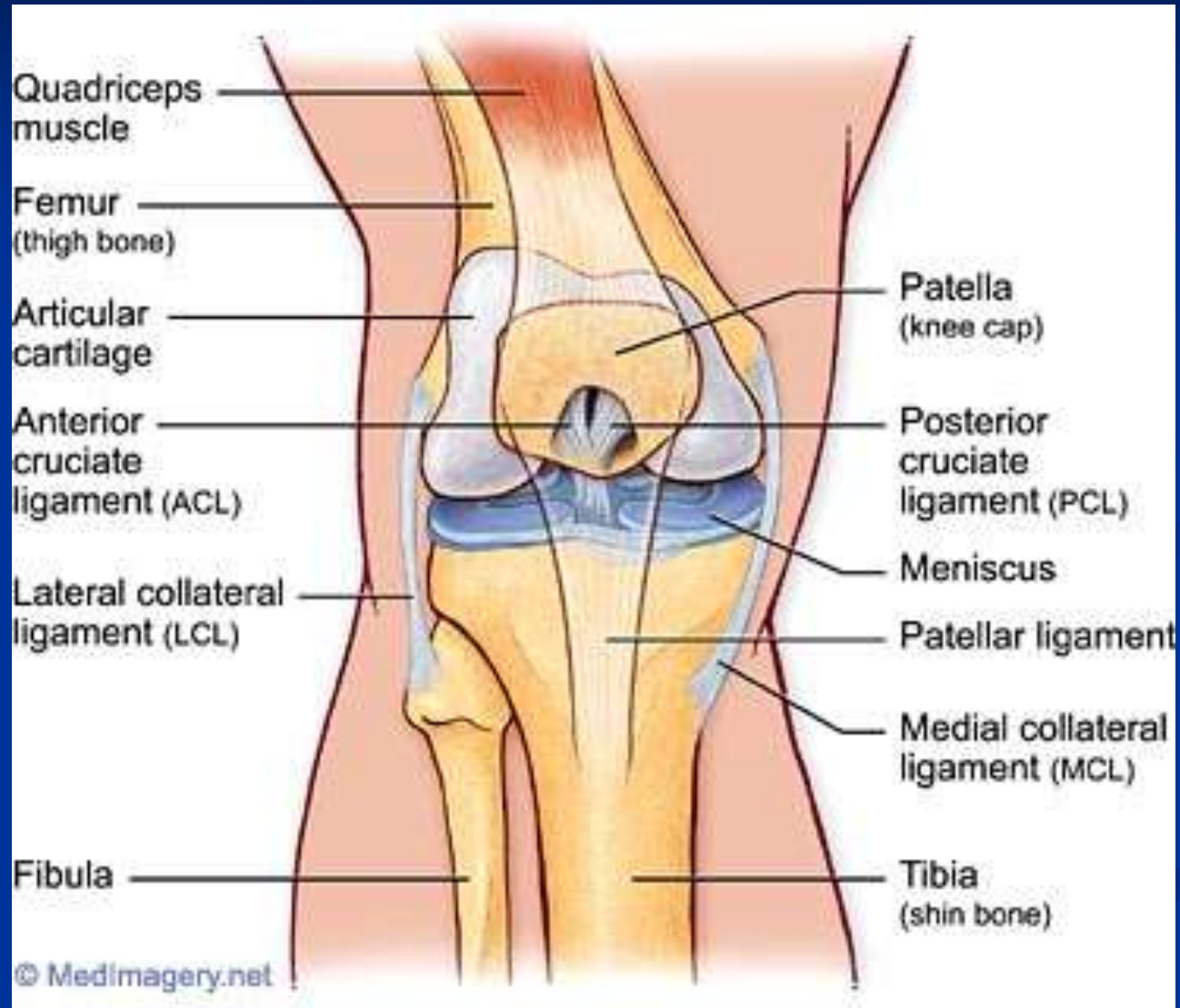
# What is it not?

- It is not a normal consequence of aging
- It is not “Wear and tear”
  - Running does not increase progression
  - Staying off the joints (being sedentary) may actually increase progression; it definitely increases symptoms

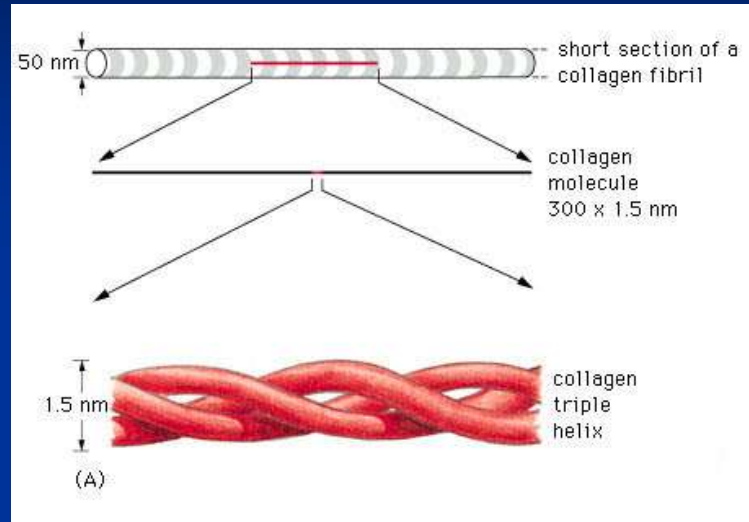


**Fig. 6.** In normal cartilage, catabolic and anabolic processes balance out on average. However, in osteoarthritic cartilage, catabolism of matrix components exceeds the synthetic capacity of the cell to replace them.

Why?



# Synthesis



Collagen has an unusual amino acid composition and sequence:

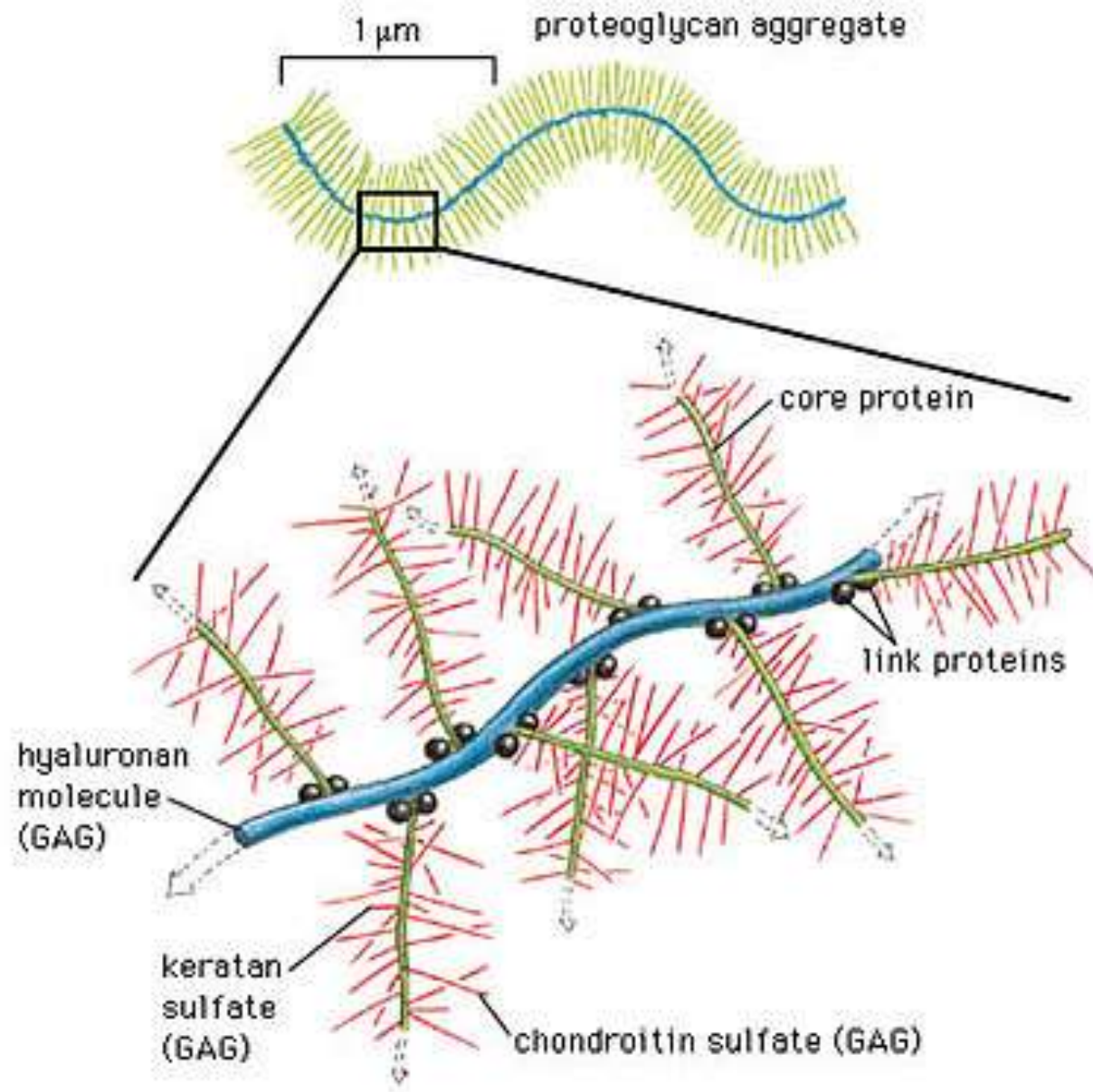
**Glycine (Gly)** is found at almost every third residue

**Proline (Pro)** makes up about 9% of collagen

**Hydroxyproline (Hyp)**, derived from proline

**Hydroxylysine** derived from lysine.

Production of both requires **vitamin C** as a cofactor



Hyaluronate

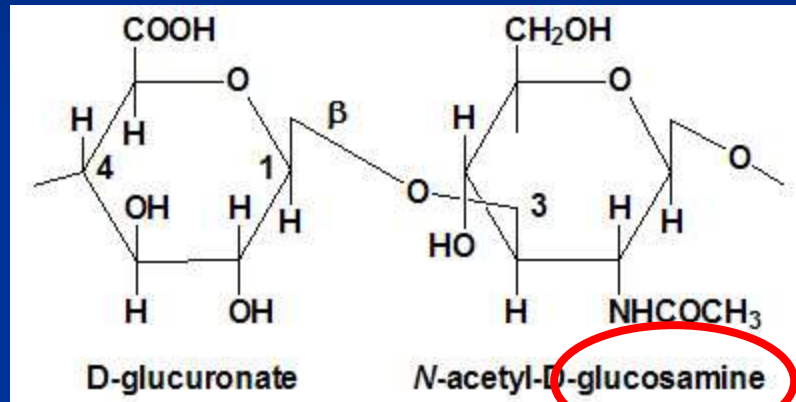
synovial fluid,  
ECM of loose connective  
tissue

large polymers, shock  
absorbing

Chondroitin sulfate

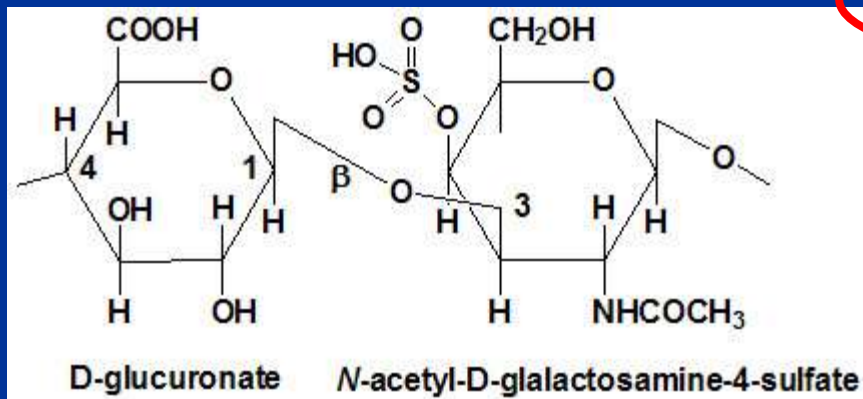
cartilage, bone, heart valves

most abundant GAG



### Hyaluronates:

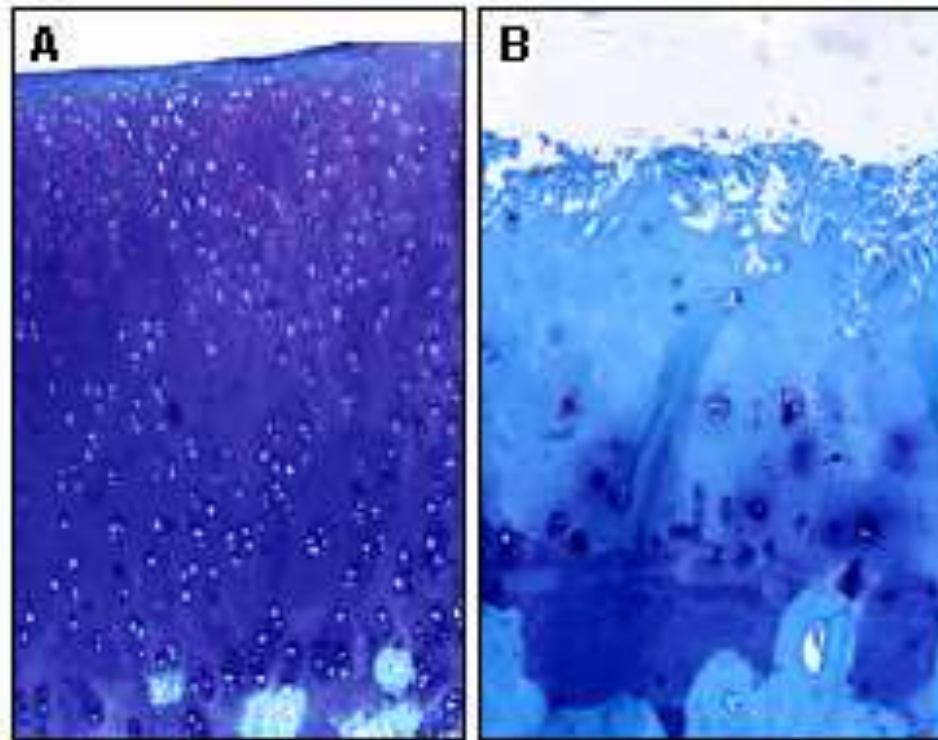
composed of D-glucuronate +  
GlcNAc  
linkage is  $\beta(1,3)$



### Chondroitin 4- and 6-sulfates

composed of D-glucuronate  
and GalNAc-4- or 6-sulfate  
linkage is  $\beta(1,3)$   
(the figure contains GalNAc 4-  
sulfate)

# Degradation



**Fig. 4.** Photomicrograph of alcian blue-stained sections of femoral condylar articular cartilage from (a) normal joints and (b) osteoarthritic joints. Note the surface fibrillation, loss of staining for proteoglycans and chondrocyte nesting (chondrons) in osteoarthritic cartilage. *Magnification: x 100.*

# Pathophysiology of Joint Degradation

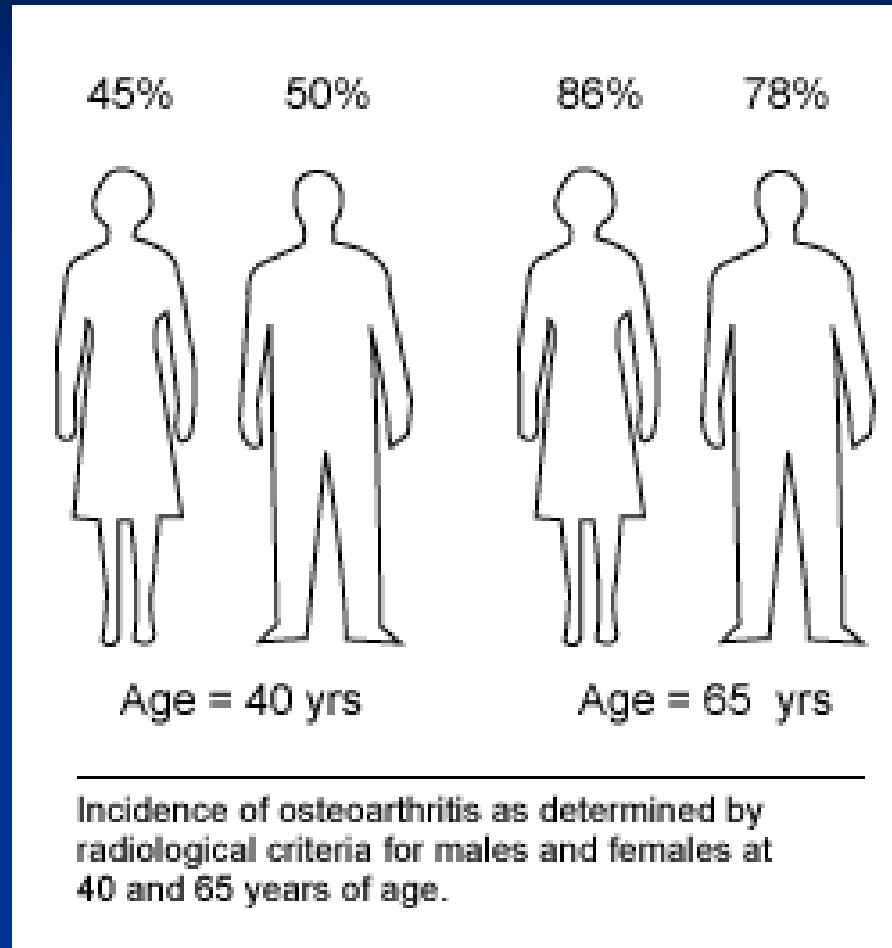
- Trauma → Release of arachidonic acid
- AA → Prostaglandins, leukotrienes (inflammation)\*
- PG, LT - chondrocytes → proteolytic enzymes
- Enzymes → destroy proteoglycans, collagen
- Breakdown products antigenic → immune-mediated inflammation\*
- Bony changes related to atherosclerotic changes in subchondral bone vessels\*

\* Note many of these processes have things in common with CV disease

# Overview

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  - Treating symptoms

# Xray Prevalence of DJD



Number seeking care for it: 20%

Prevalence is expected to double by 2020

# Disability

- Arthritis is the leading cause of disability in the US
- 21.6% of the adult U.S. population (46.4 million persons) had doctor-diagnosed arthritis in 2005
- 8.3% (17.4 million) had arthritis-attributable activity limitations
  - Women, older adults, persons with little education, or those who are obese, overweight, or physically inactive are more likely affected *MMWR* 2006 55(40);1089-1092

## Predictors of functional impairment of the lower body assessed by stepwise multiple regression model

Dependent: Symptom

Unadjusted  $R^2 = 0.502$

Adjusted  $R^2 = 0.478$

$F = 18.02$ ;  $p < 0.0001$

	B	SE	T	P
PHQ-9 score	0.446	0.117	3.960	<0.0009
Symptom*	0.412	0.114	3.064	0.001
Educational level	-0.279	0.149	-2.092	0.029
BMI	0.332	0.072	2.022	0.005
Social*	0.201	0.098	2.034	0.042
Age	0.178	0.102	1.998	0.001

\* AIMS2-SF scale

# Financial Burden



- Estimated cost in medical care of \$15.5 billion.
- Up to \$65 billion if we add days of work lost.

# Overview

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- What is the impact of OA?
- Treatment
  - Slowing progression
  - Treating symptoms

# Goals in Treatment

- Limit progression of the disease (“Disease-modifying therapies”, DMOADs)
  - Removing tacks
  - Disease-modifying treatments
- Decrease pain and disability – i.e. symptomatic management

# The Rules of Tacks

1. If you are sitting on a tack, it takes a lot of aspirin to make the pain go away.
2. If you are sitting on 2 tacks, removing one does not result in a 50% improvement in symptoms.  
(It still hurts to sit down.)

# “Tacks”/Risk Factors for OA

- Aging
- Heredity
- Severe or recurrent injury, heavy exercise
- Skeletal/postural deformity
- Sedentary lifestyle
- Obesity: risk is 50-350% higher in men for knee
  - Risk is higher even in hand *Lancet* **350** (1997), pp. 503–508; Ann Rheum Dis. 2009 May 31
- Nutritional deficiency: Vitamin C, vitamin D, Vitamin K, calcium, magnesium, manganese, protein, EFA's, sulfates
- A local issue: Lyme

# Diet as a “tack”

- Dietary Excess – Obesity
- Dietary Deficiency
- Dietary Sensitivity

# Obesity and Inflammation

- Adipose tissue (fat) makes inflammatory mediators – this may be part of why it is associated with diabetes and heart attacks as well as chronic pain
- People who are obese have more joint pain, in the hands as well as weight-bearing joints.
- J Clin Invest. 2003 December 15; 112(12): 1821–1830. **Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance.** Haiyan Xu, Glenn T.
- **Elevated Levels of Interleukin 6 Are Reduced in Serum and Subcutaneous Adipose Tissue of Obese Women after Weight Loss** The Journal of Clinical Endocrinology & Metabolism Vol. 85, No. 9 3338-3342
- Food restriction slows the development of osteoarthritis and increases the lifespan of Labrador retrievers by 2 years Proc Nutr Soc. 2009 Feb;68(1):98-102

# Weight Management

- 6-week weight-control program in 22 OA patients
  - Decreasing body fat and increasing physical activity were more important than body-weight loss for symptomatic relief of knee OA

*The Journal of Rheumatology* 1998, **25**: 2181–2186.

# Weight Loss Intervention in Knee OA

- 9.4% (4.8 to 13.9%) improvement in WOMAC for each percent of body fat reduced ( $P = 0.0005$ ).
- Weight reduction of 10% improved function by 28%
- The 'Number Needed to Treat (NNT)' to ensure an improvement in WOMAC  $\geq 50\%$  was 3.4 (2.1 to 8.8) patients.

# Diet as a “tack”

- Dietary Excess – Obesity
- Dietary Deficiency
- Dietary Sensitivity

# What to eat more of. . . .

- Fruits, vitamin C –

- Associated with a reduction in bone size and the number of bone marrow lesions *Arthritis Res Ther.* 2007;9(4):R66.
- 3X ↓risk of OA progression, reduced risk of cartilage loss, for both the middle and the highest tertile of vitamin C intake *Arthritis and Rheumatism* 39 (1996), pp. 648–656, *Annals of the Rheumatic Diseases* 1997;56:397–402

- Possibly hydrolyzed collagen (more later)

- Probably curries – ginger, curcumin

# Not Indicated:

## ■ Vitamin E supplements

- Vitamin E supplement had no effect on cartilage loss J Rheumatol. 2002 Dec;29(12):2585-91
- Vitamin E had no effect on symptoms Vasc Med 1997; 2:296-301.

## ■ Vitamin K supplements

- Ann Rheum Dis. 2008 Nov;67(11):1570-3. Epub 2008 Jul 14

# Diet as a “tack”

- Dietary Excess – Obesity
- Dietary Deficiency
- Dietary Sensitivity

# What to eat less of. . .

## ■ Dietary irritants

- Maybe Nightshades – no clear data, tons of anecdotes
  - Potatoes, tomatoes, peppers, eggplant
  - Solanine is hypothesized irritant – acute poisoning produces vomiting, , confusion

## ■ Possibly some starches –

- London diet in AS Clin Rheumatol 1996 Jan;15 Suppl 1:61-65, 62-66

# What to eat less of. . .

## ■ Dietary allergens

- Gluten - Celiac – 26% (or more) have arthritis, some RA, some AS, some look like OA – blood test!
- Others (idiosyncratic)

## ■ Elimination diet is worthwhile.

- Most studied for RA, fibromyalgia, where 40+% of people respond
- Consider a trial of a “live foods diet” as reintroducing foods

# What to eat less of. . .

## ■ Meat - Odds Ratio of degenerative arthritis

Meat Consumption	Women	Men
0	1	1
< 1/week	1.31(1.21-1.43)	1.19 (1.05-1.34)
≥ 1/week	1.49 (1.31- 1.70)	1.43(1.20-1.70)

Protective associations with nut and salad consumption

J Nutr Health Aging. 2006 Jan-Feb;10(1):7-14

# The “Live Foods Diet”

- Significant reductions in serum peroxides, plasma fibrinogen, apolipoproteins A and B, and serum total cholesterol
- In FM patients: significant improvement in pain scores, quality of sleep, morning stiffness, health assessment questionnaire scores, and general health questionnaire

- BMC Complement Altern Med. 2001; 1: 7
- Plant Foods Hum Nutr. 1993 Jan;43(1):55-61.
- Scandinavian Journal of Rheumatology Volume 29, Number 5 / October 27, 2000
- Bangladesh Med Res Counc Bull. 2000 Aug;26(2):41-7.
- Toxicology. 2000 Nov 30;155(1-3):45-53.

# The “Live Foods Diet”

- Foods to eat : fresh fruits, salads, raw vegetables, carrot juice, nuts, seeds, whole grain products, tubers, flax oil, extra virgin olive oil
- Foods to avoid: alcohol, caffeine, foods containing refined sugar, corn syrup, refined and/or hydrogenated oil, refined flour, dairy, eggs, and all meat

# Goals in Treatment

- Limit progression of the disease (“Disease-modifying therapies”)
  - Removing tacks
  - Disease-modifying treatments
- Decrease pain and disability – i.e. symptomatic management

# DMOADs - An area of great interest, but persistent controversy

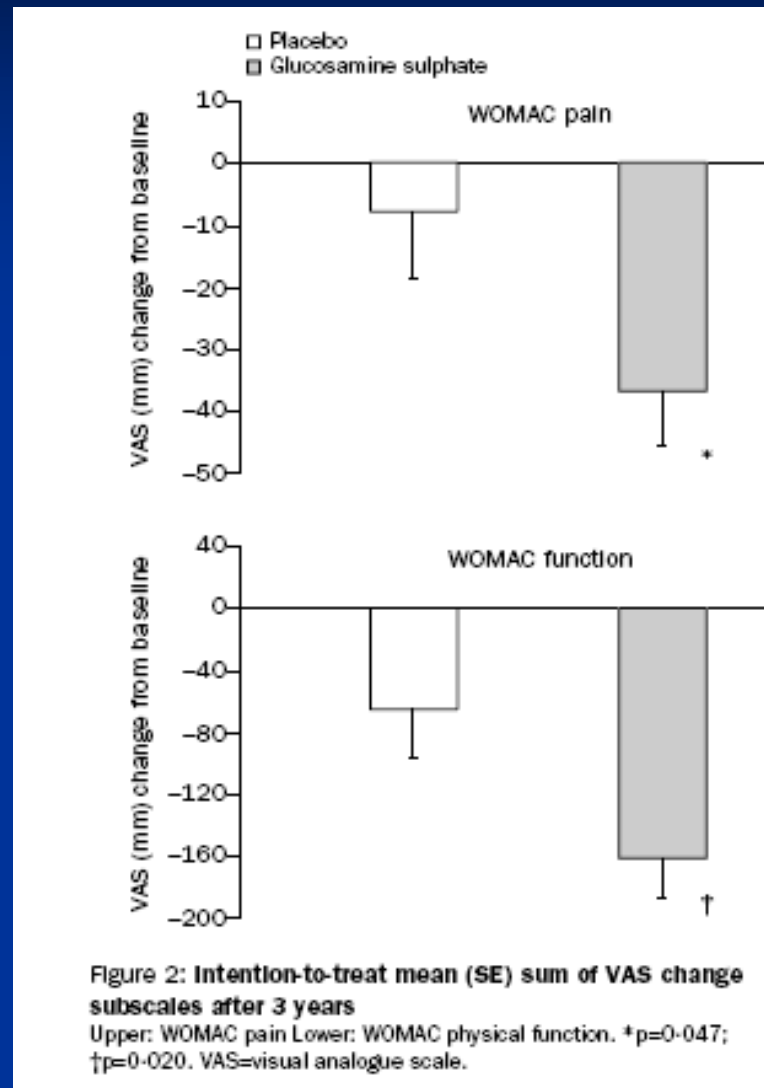
- Glucosamine sulfate
- Chondroitin sulfate
- Doxycycline
- Diacerein
- Others? - Vitamin D?

# Glucosamine Sulfate:

Over 300 studies – >20 are double-blind, placebo controlled

- Building block of proteoglycans that make up cartilage
- Proven to:
  - Regenerate cartilage
  - Reduce cartilage-degrading enzymes
  - Relieve joint pain – better than LT ibuprofen
  - Increase joint mobility

# Glucosamine Sulfate x 3 years



# Joint-Space Narrowing

	Patients assessed for 3 years			
	Placebo (n=71)	Glucosamine sulphate (n=68)	Difference (95% CI)	p
Mean joint-space narrowing (mm)	-0.31 (-0.57 to -0.04)	0.07 (-0.17 to 0.32)	0.38 (0.02 to 0.73)	0.038
Minimum joint-space narrowing (mm)	-0.40 (-0.64 to -0.17)	0.11 (-0.10 to 0.33)	0.51 (0.20 to 0.83)	0.002

**Table 2: Average (95% CI) joint-space narrowing after 3 years**

*Lancet* 2001; 357: 251–56

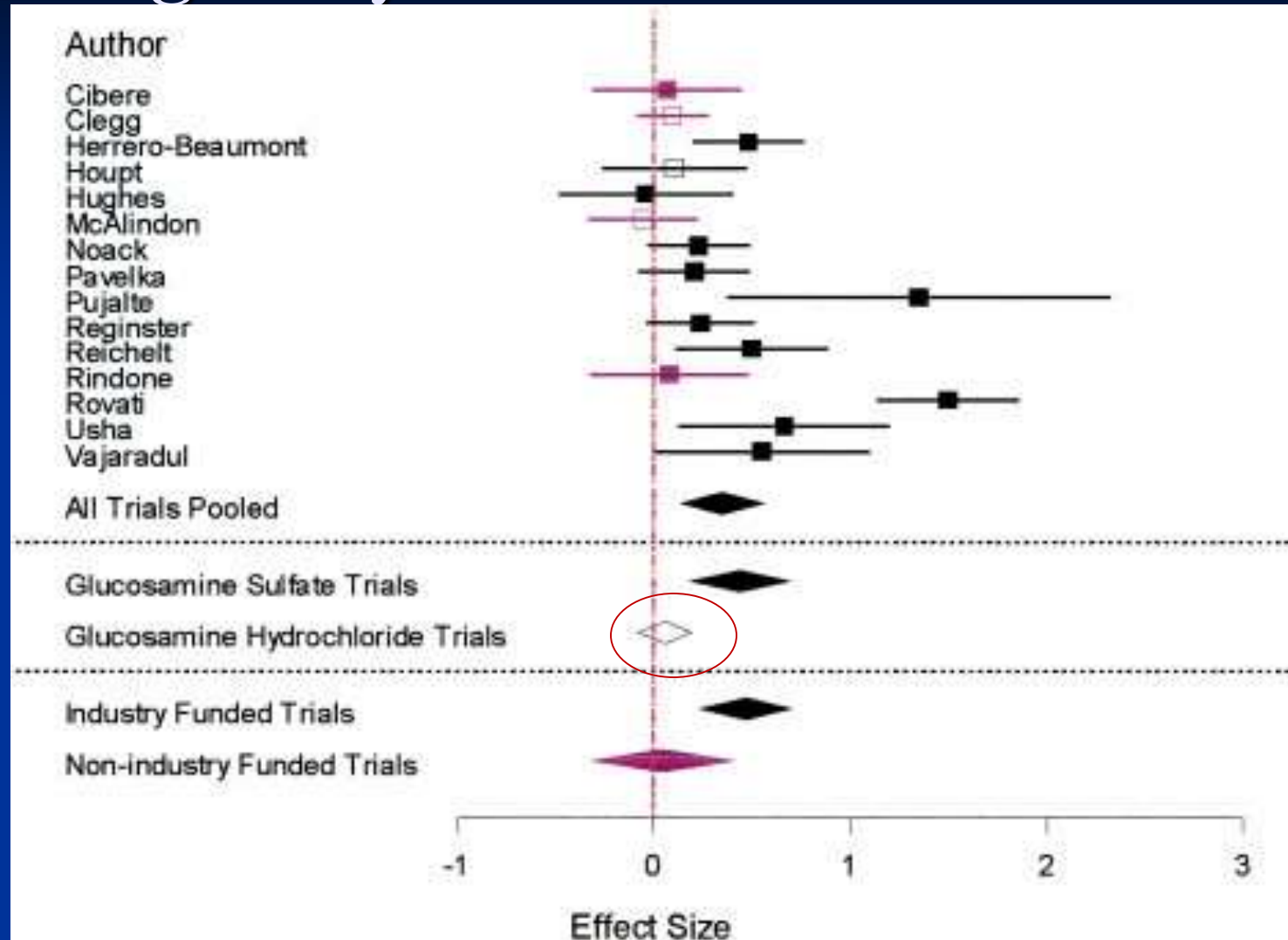
# 1-year vs. 3-year Effect on Joint Space Narrowing

- Minimum JSN - Glucosamine sulfate vs. controls
  - First year of treatment no effect (SMD 0.078, 95% CI -0.116 to -0.273,  $P = 0.429$ ).
  - After 3 years of treatment, small to moderate protective effect on minimum JSN (SMD 0.432, 95% CI 0.235-0.628,  $P < 0.001$ ).
- Chondroitin sulfate: small but significant protective effect on minimum JSN after 2 years (SMD 0.261, 95% CI 0.131-0.392,  $P < 0.001$ ).

# Another Study on Progression

- Glucosamine sulfate vs. placebo
    - Risk of disease progression was reduced by 54% (pooled RR 0.46; 95% CI 0.28 to 0.73;  $p = 0.0011$ ).
    - The number-needed-to-treat was 9 (95% CI 6 to 20).
- Ann Pharmacother. 2005 Jun;39(6):1080-7. Epub 2005 Apr 26

# Heterogeneity of Trials with Glucosamine



Arthritis Rheum Vol.56, 7 Pages: 2267-2277

See also Rheum Dis Clin N Am 29 (2003) 789-801

# Glucosamine Sulfate (not Hydrochloride)

## ■ Dose

- Up to 3,000mg for 1st 12 weeks

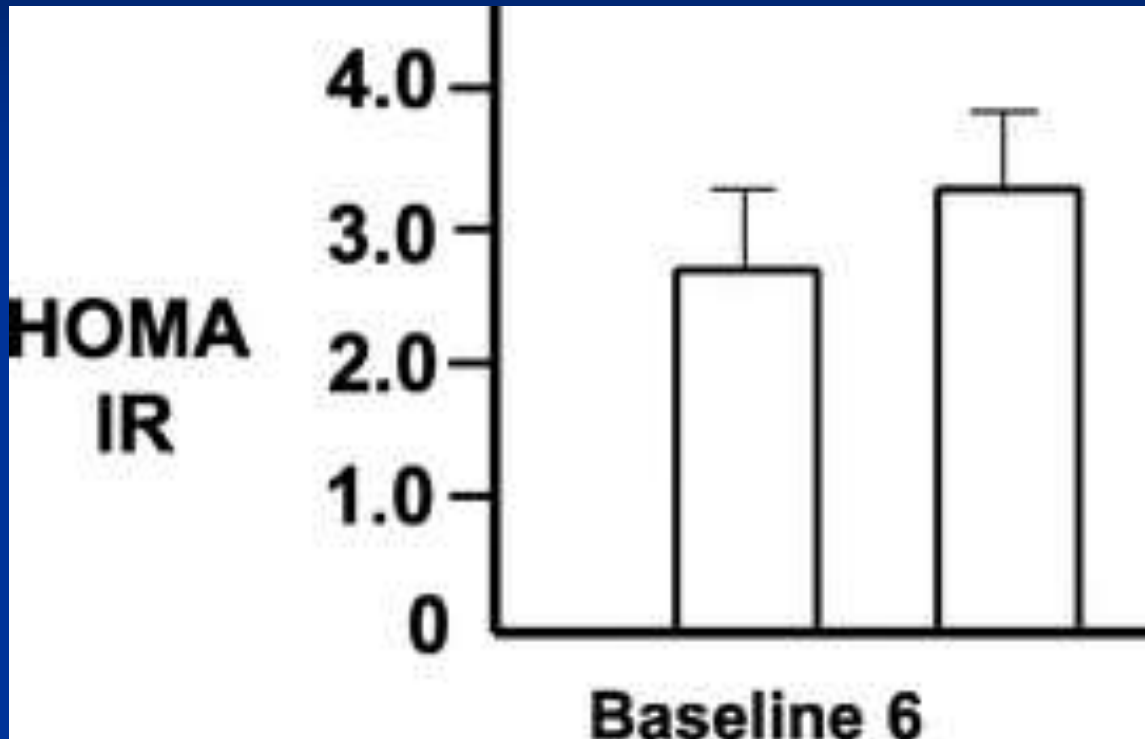
## ■ Maintenance dose

- 1,500mg daily of sulfate form

## ■ Side effects

- Effect on insulin resistance – measurable, probably not clinically significant.

# Glucosamine and Insulin Resistance



Baseline HOMA and HOMA after 6 weeks of 1500 mg glucosamine PO every day in the 35 subjects. The average at baseline was statistically different from that after 6 weeks of glucosamine ( $P = 0.04$  by Student's *t* test). Pham, T et al. American Journal of the Medical Sciences. 333(6):333-339, June 2007

Homeostasis model assisted estimate of insulin resistance

# Glucosamine and clinically significant glucose changes

- No change in hgbA1C after 90 days of usual treatment dose Daren A. Scroggie, MD; Allison Albright, MD; Mark D. Harris, MD *Arch Intern Med.* 2003;163:1587-1590
- Fasting glucose actually decreased after 3 years on glucosamine sulfate

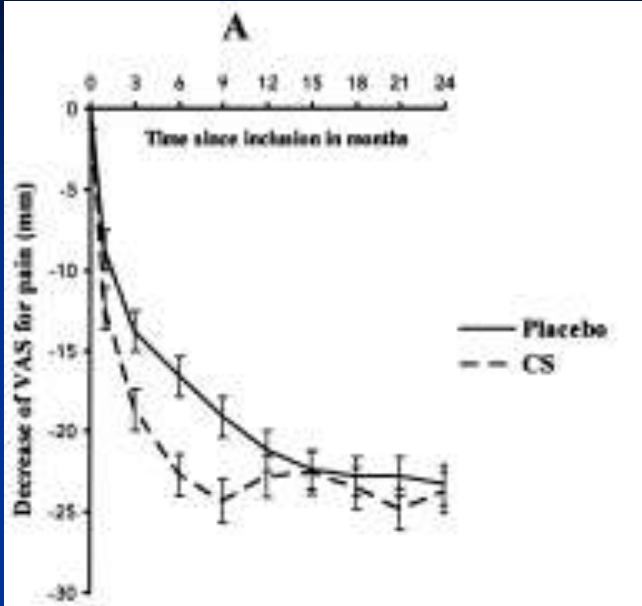
Reginster JY et al Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial *Lancet* 2001; 357: 251–56

# Effects on cancer risk

- Any use of glucosamine and chondroitin over the previous 10 years
  - significantly lower lung cancer risk: HR 0.74 [95% confidence interval (95% CI), 0.58-0.94] and HR 0.72 (95% CI, 0.54-0.96)
  - Lower colorectal cancer risk: HR 0.73 (95% CI, 0.54-0.98) and HR 0.65 (95% CI, 0.45-0.93), respectively. *Cancer Epidemiology Biomarkers & Prevention* 18, 1419, May 1, 2009.
- Potentially biased (observational)

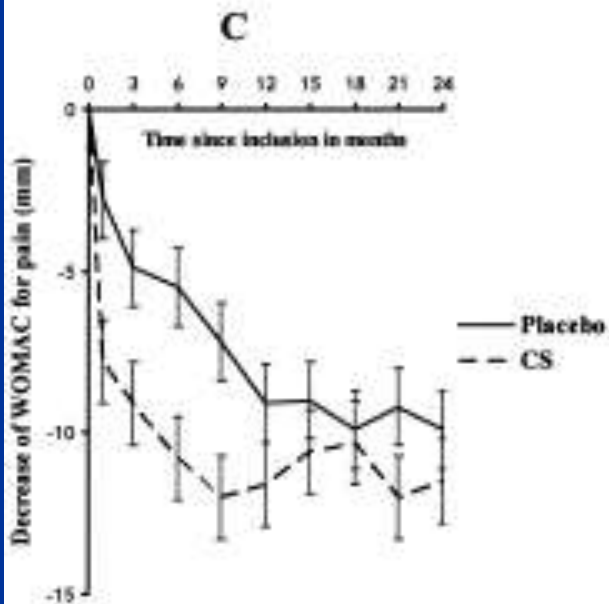
# Chondroitin Sulfate

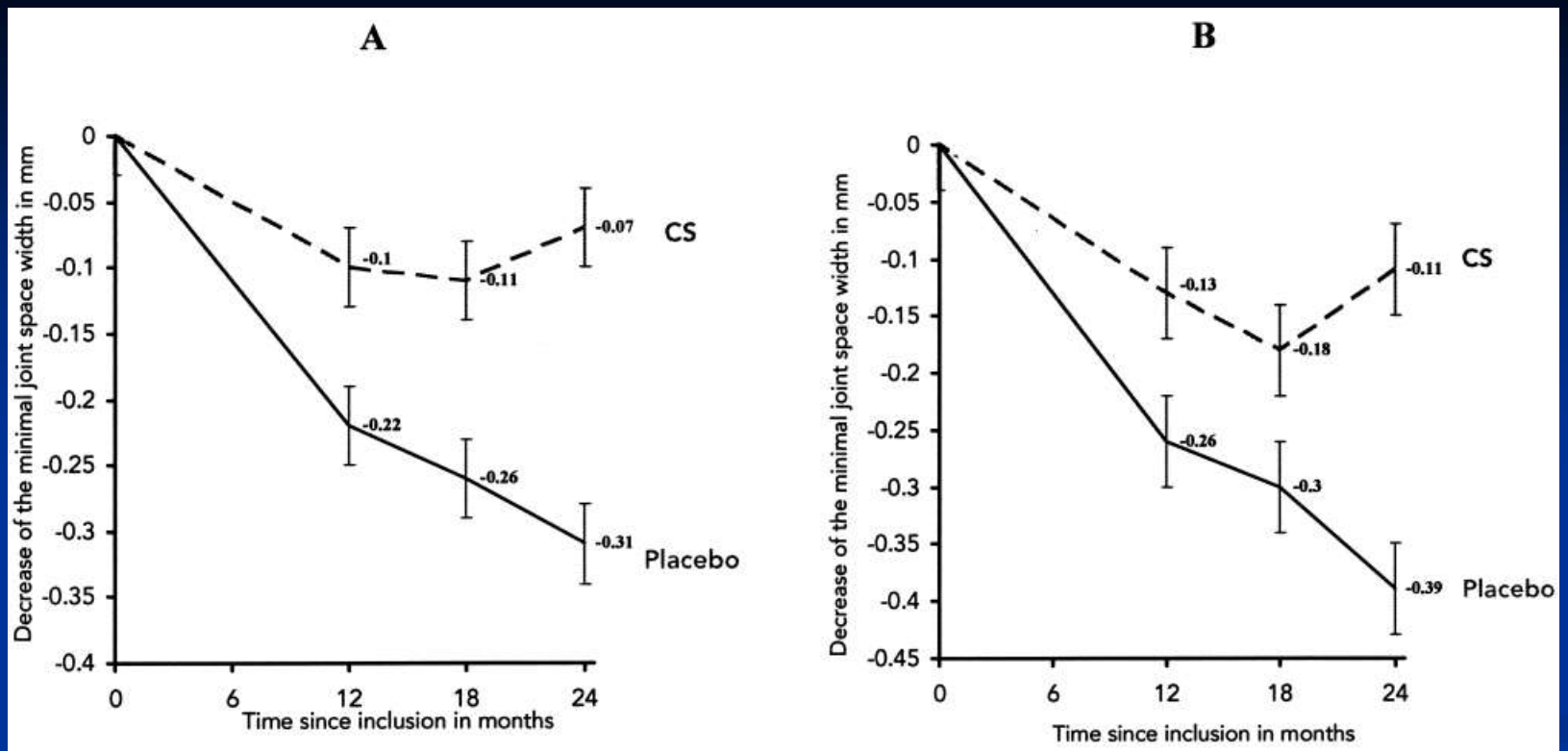
- Dose: 400mg. 2 – 3 x daily
- Side effects: Rare GI disturbance



Chondroitin sulfate (pharmaceutical grade from Europe) 800 mg daily vs. placebo x 2 years.

Change in pain over time.

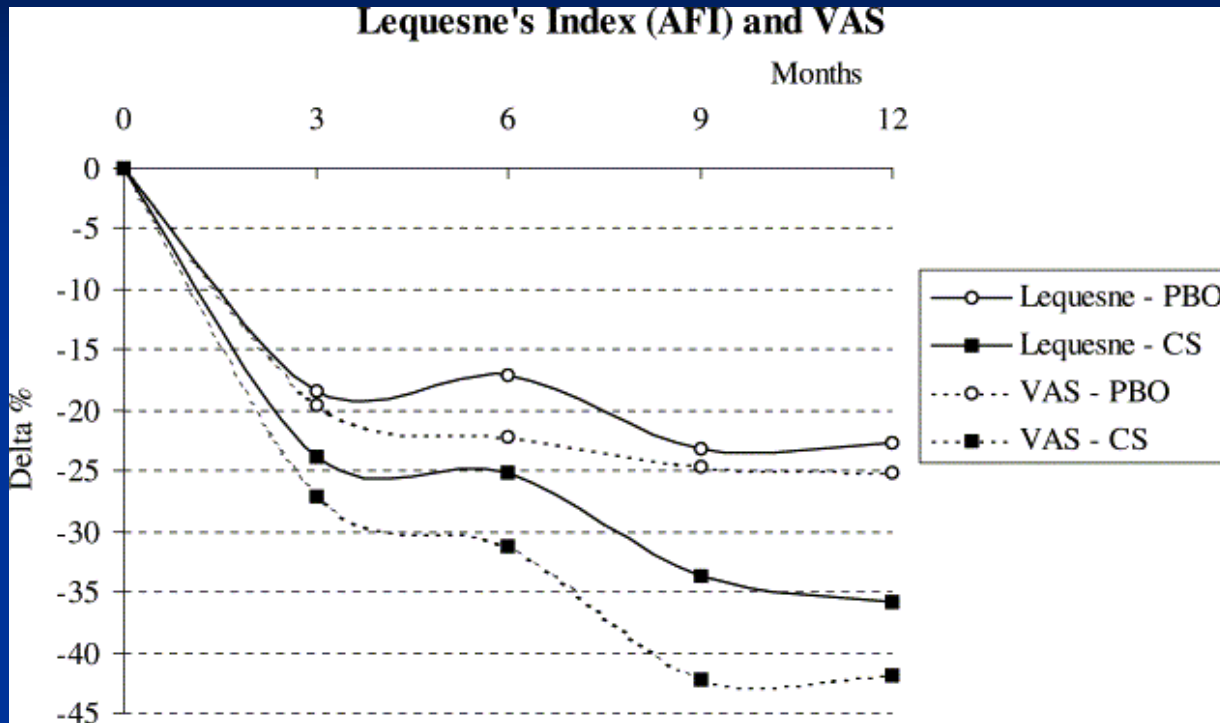




**Figure 2.** Change in minimum joint space width over time. **A**, Intent-to-treat analysis. **B**, Per-protocol analysis. Values are the mean  $\pm$  SEM. CS = chondroitin sulfate. **Arthritis Rheum** Vol.60, 2 Pages: 524-533 2009

Effect of the treatment more important in patients with a higher body mass index ( $P = 0.03$ ).

# Intermittent CS



	CS (n=77)	PBO (n=76)	Difference (95% CI)	P (t-test)
JSSA (mm <sup>2</sup> )	0.19 (-3.56 to 3.17)	4.55 (-8.61 to -0.49)	4.36 (-0.19 to 8.91)	0.060
MiJSW (mm)	-0.04 (-0.23 to 0.14)	-0.32 (-0.57 to -0.07)	0.27 (0.004 to 0.55)	0.047
MeJSW (mm)	-0.006 (-0.20 to 0.18)	-0.29 (-0.53 to -0.04)	0.28 (0.01 to 0.55)	0.039

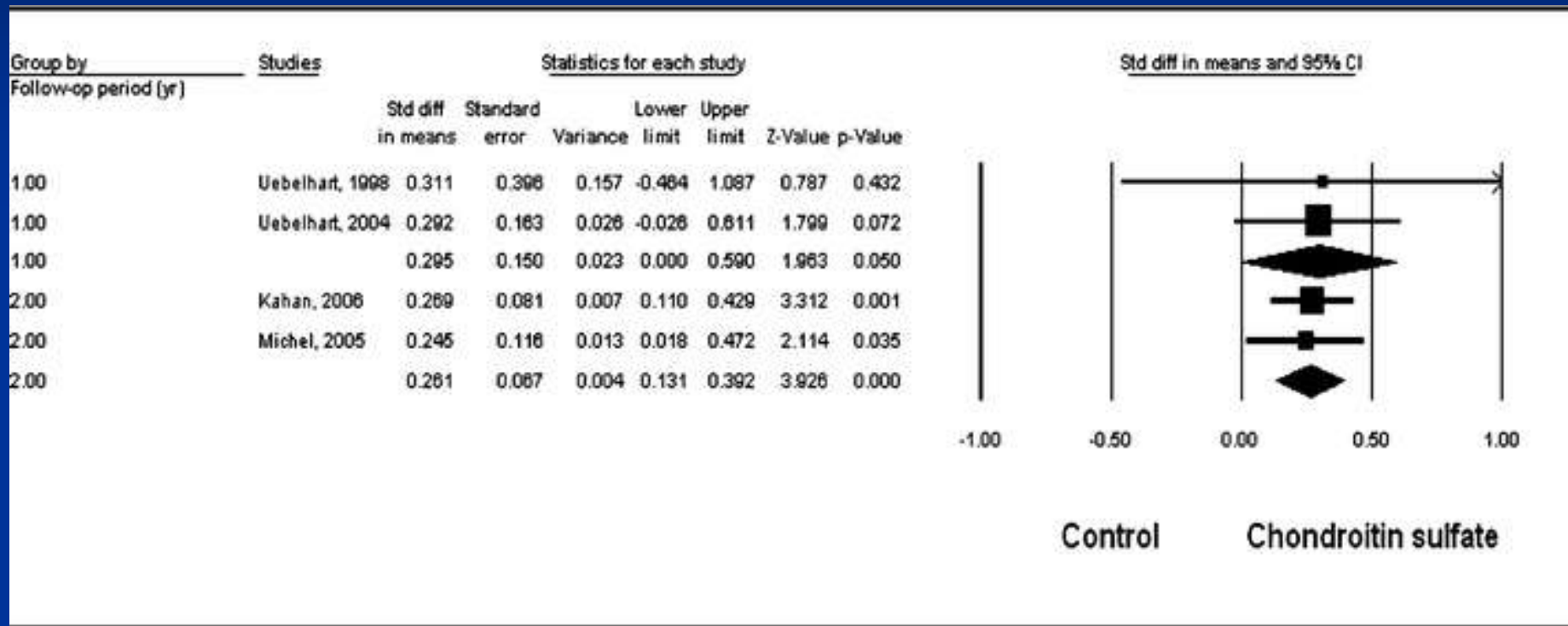
CS 800 mg per day for 3 month intervals twice a year Uebelhart D et al [Osteoarthritis and Cartilage](#)

[Volume 12, Issue 4](#), April 2004, Pages 269-276

# Chondroitin Sulfate

- Recent meta-analyses call effectiveness into question, however note there are methodological questions about the trials they included
- Reichenbach S et al **Meta-analysis: Chondroitin for Osteoarthritis of the Knee or Hip** *Ann Intern Med.* 2007;146:580-590.
  - GAIT trial showed no effect of CS but also no effect of celecoxib; note a 60% placebo response may have limited ability to detect response to active treatment

# Chondroitin and JSN



Rheumatol Int. 2009 Jun 21. [Epub ahead of print] PMID: 19544061

# Caution:

- In 2007, ConsumerLab.com reported that 73% of all products tested that contained chondroitin failed potency testing. In 2009, 26% failed.
- Some glucosamine supplements from shellfish contained excessive lead.

# Doxycycline

**Table 2. Radiographic outcomes shown as quantitative changes in JSW<sup>a</sup>**

	Doxycycline		Placebo		
	n	Mean ± SD	n	Mean ± SD	P <sup>b</sup>
Baseline JSW, mm	218	3.64 ± 1.15	211	3.61 ± 1.19	0.740
16-month change in JSW, mm	188	0.15 ± 0.42	191	0.24 ± 0.54	0.027
30-month change in JSW, mm	181	0.30 ± 0.60	180	0.45 ± 0.70	0.017

20% increase in WOMAC pain score after 6 months:

Placebo 30.2 ± 21.1%

Doxycycline 23.8 ± 22.7%

*P* = 0.004

**Arthritis & Rheumatism** 52(7): 2015-25, 2005.

# Diacerein

- Blocks interleukin-1
- Slowed the progress in OA of the hip more than a placebo; did not slow OA of the knee
- Pain decreased by about 5 more points on a 0-100 scale for people who took diacerein than a placebo
- Diarrhea in 42%
- Not available in US

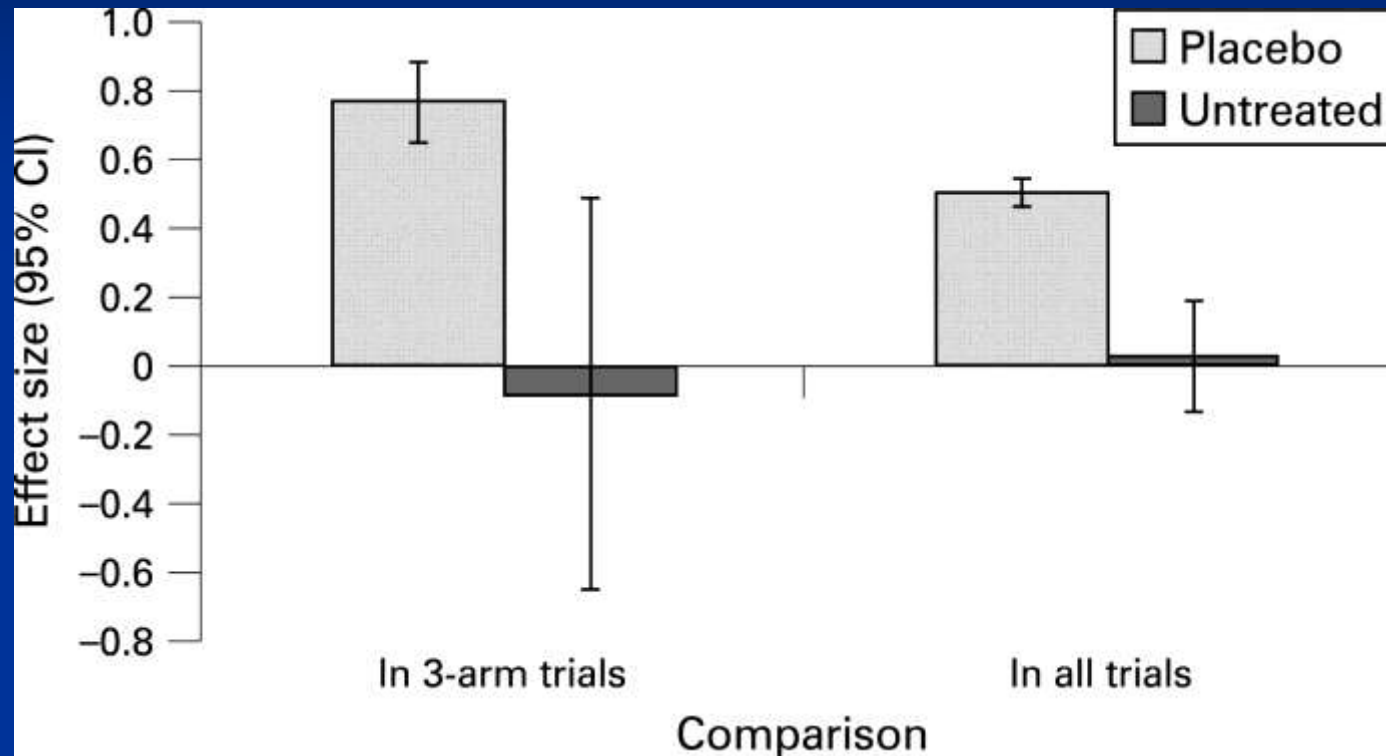
# Goals in Treatment

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# Placebo

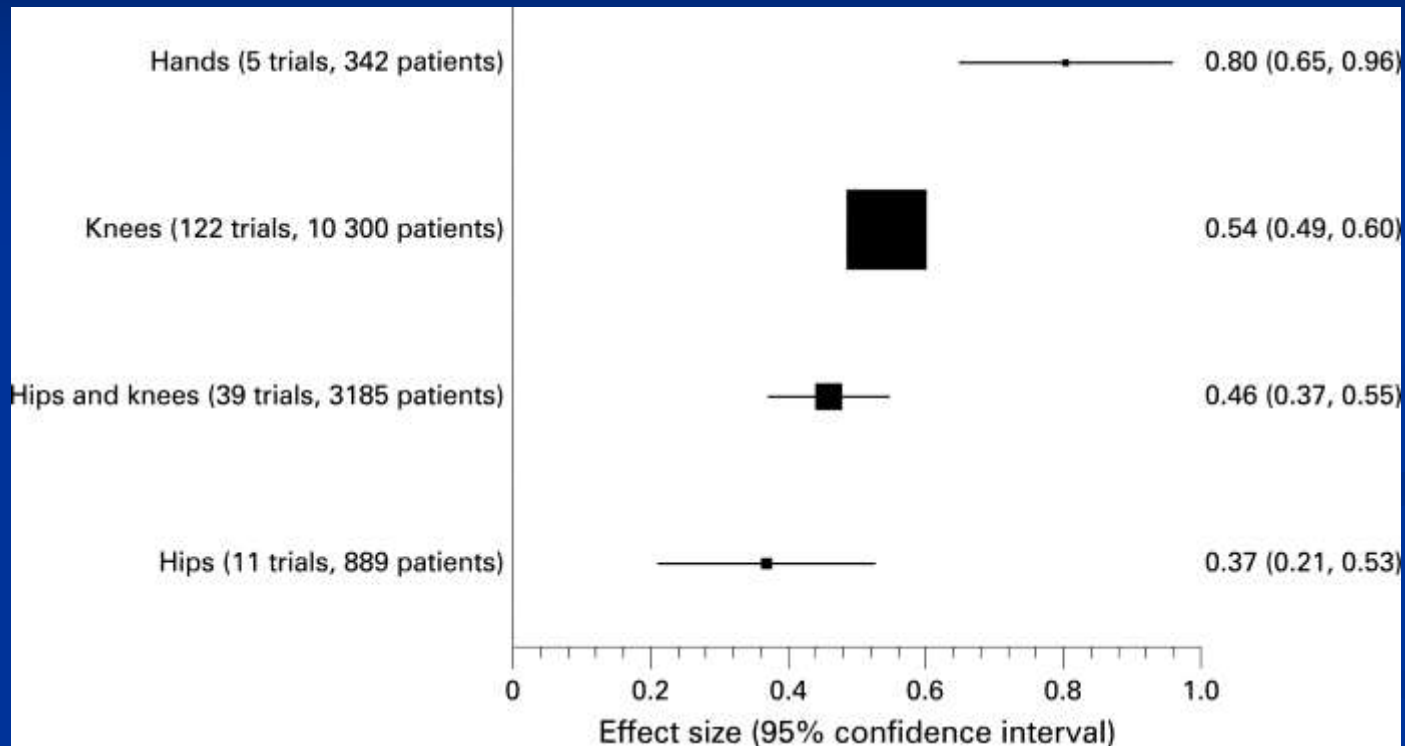
- Placebos are effective at decreasing pain in OA, as well as improving stiffness and function
- ES (Effect Size) 0.51 for the placebo group vs. 0.03 for untreated control
- More effective for those with higher baseline severity, increased expected strength of the treatment, invasive route of delivery.

**Figure 3 Effect size between placebo and untreated control. In three-arm trials: direct comparison between placebo and untreated control within the three trials that included placebo and untreated control, In all trials: indirect comparison between all placebo (n = 193) and all untreated control (n = 14) from different trials.**



Zhang, W et al. Ann Rheum Dis 2008;67:1716-1723

**Figure 5 Placebo effect for pain for different sites of osteoarthritis (OA).**



Zhang, W et al. Ann Rheum Dis 2008;67:1716-1723

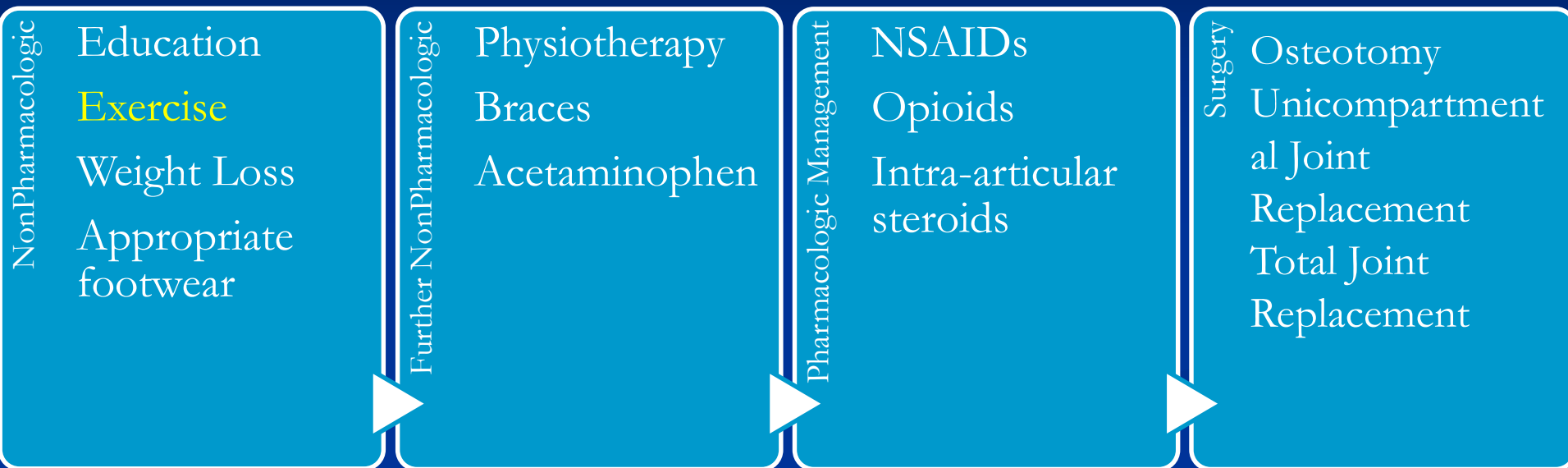
# Predictors of Placebo Response

Variables	$\beta$ (95% CI)	p Value
ES <sub>treatment</sub>	0.3802 (0.2545 to 0.5059)	<0.001
Percentage baseline pain (0–100) (either high or low baseline pain may decrease response)	0.0055 (0.0012 to 0.0099)	0.014
Sample size	0.0007 (0.0003 to 0.0012)	0.004
Invasive treatment (yes = 1, no = 0)*	0.1436 (0.0247 to 0.2625)	0.020

Not predictive: age, gender , BMI (kg/m<sup>2</sup>), intention-to-treat analysis, blindness, community trial , trials funded by industry, trial conducted in the US , and topical therapy..  $\beta$  is the partial regression coefficient.

\*Invasive treatment included acupuncture, intra-articular, intramuscular, intravenous injections and surgical therapies.

# Step Treatment



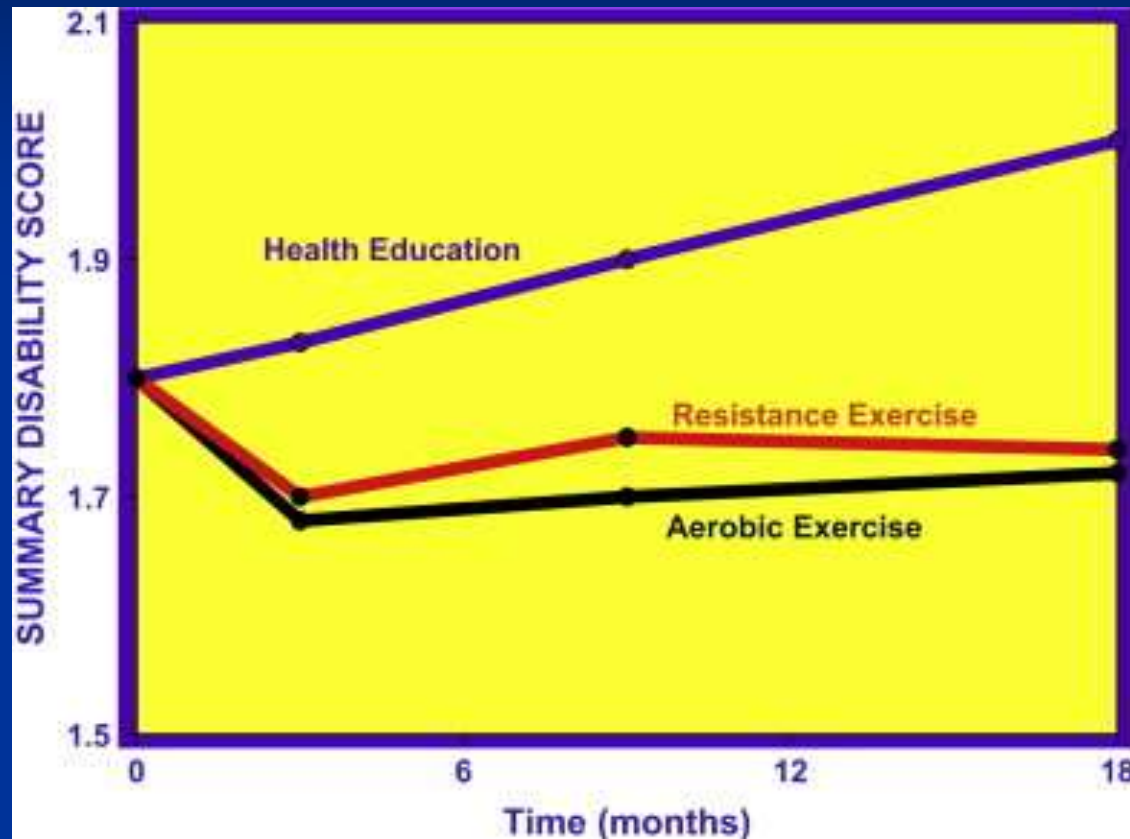
Mild

Symptom Severity

Severe

Osteoarthritis. BMJ 2006;332(7542):641

# Exercise in the Elderly



The Fitness Arthritis and Seniors Trial  
(FAST). JAMA 1997;277(1):29

# Walking Programs. . .

- Functional status improved 39% (CI, 15.6% to 60.4%) with an 8-week walking program. (P=0.001)
- Pain decreased 27% (CI, 9.6% to 41.4%) (P = 0.003). *Ann Intern Med* - 1992; 116(7): 529-34
- At 24 months, highly significant reductions in knee pain in exercise groups.
- The reduction in pain was greater the closer patients adhered to the exercise plan. *BMJ*. 2002 October 5; 325(7367): 752

# Exercise: Land vs. Water

**Table 4.**

Visual Analog Scale (VAS) Scores for Pain Before and After the 50-foot (15.24-m) Walk Test (50FWT) in Participants With Osteoarthritis of the Knee at 0 Weeks (T0), 9 Weeks (T9), and 18 Weeks (T18) After Intervention

	<b>Water-Based Exercise Group (n=32)</b>	<b>Land-Based Exercise Group (n=32)</b>	<b>P (Intergroup)</b>
	<b>Mean±SD (95% CI)<sup>a</sup></b>	<b>Mean±SD (95% CI)</b>	
VAS for pain before 50FWT (mm)			
T0	39.6±23.4 (31.0–48.1)	53.0±24.4 (43.6–62.4)	.045 <sup>b</sup>
T9	21.7±20.7 (13.0–30.5)	26.5±28.1 (16.9–36.1)	
T18	14.8±21.4 (5.4–24.2)	28.8±30.8 (18.5–39.1)	
P (intragroup)	<.001 <sup>b</sup>	<.001 <sup>b</sup>	
VAS for pain after 50FWT (mm)			
T0	48.2±25.6 (39.9–56.5)	61.1±19.6 (52.0–70.2)	.028 <sup>b</sup>
T9	25.4±22.3 (16.3–34.6)	30.3±28.4 (20.4–40.3)	
T18	15.1±19.8 (5.8–24.4)	33.4±31.7 (23.2–43.6)	
P (intragroup)	<.001 <sup>b</sup>	<.001 <sup>b</sup>	

<sup>a</sup> CI=confidence interval.

<sup>b</sup> P value statistically significant.

PHYS THER 88(1), January 2008, pp. 12-21

Recommendation is to use water exercise to start, but transition to land-based exercise, which has been studied more long-term. Cochrane Database Syst Rev. 2007 Oct 17;(4):CD005523

# Exercise Modalities with Grade A Evidence for improving pain and functional status

- Lower-extremity (LE) strengthening (isometric)
- Concentric resistance training
- General LE exercise program (including muscle force, flexibility, and mobility/coordination)
- Whole-body functional exercise
- Walking program
- Jogging in water
- Yoga

# Other Exercise

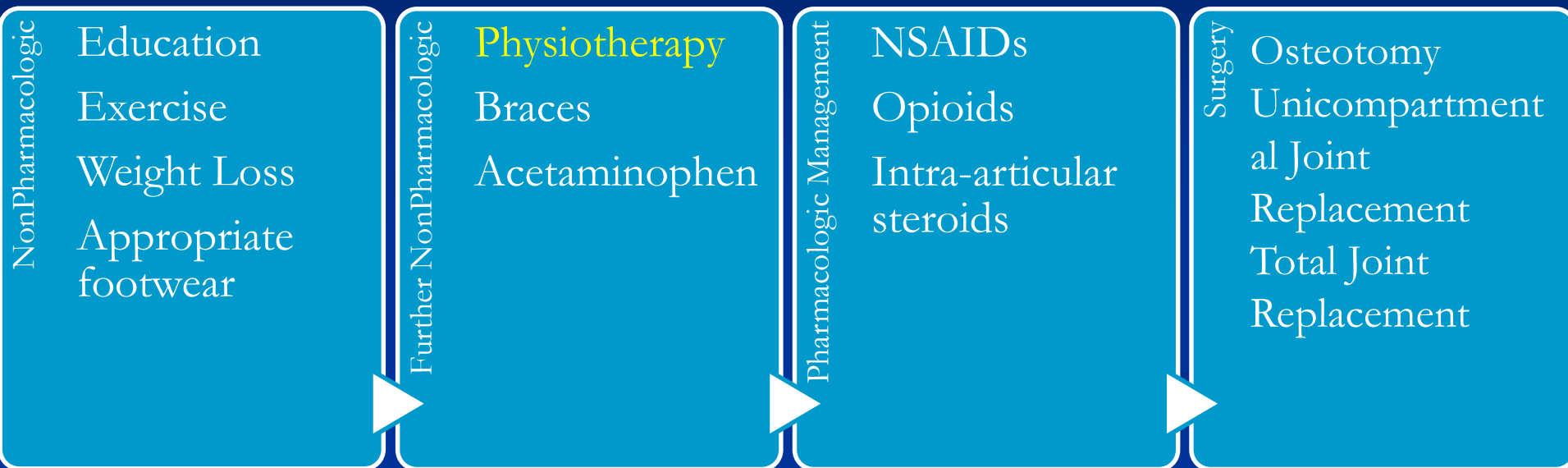
## ■ Tai chi

- Reduction in pain and stiffness in joints,
- Decreased difficulties in physical function
- Improved self-efficacy for arthritis symptoms
- Improved health behaviors in diet and stress reduction

Song R *et al.* (2003) *J Rheumatol* **30**: 2039–2044, Hartman CA *et al.* (2000) *J Am Geriatr Soc* **48**: 1553–1559, Taehan Kanho Hakhoe Chi. 2007 Mar;37(2):249-56

***Separate research shows decrease in hip fractures with Tai chi***

# Step Treatment



Mild

Symptom Severity

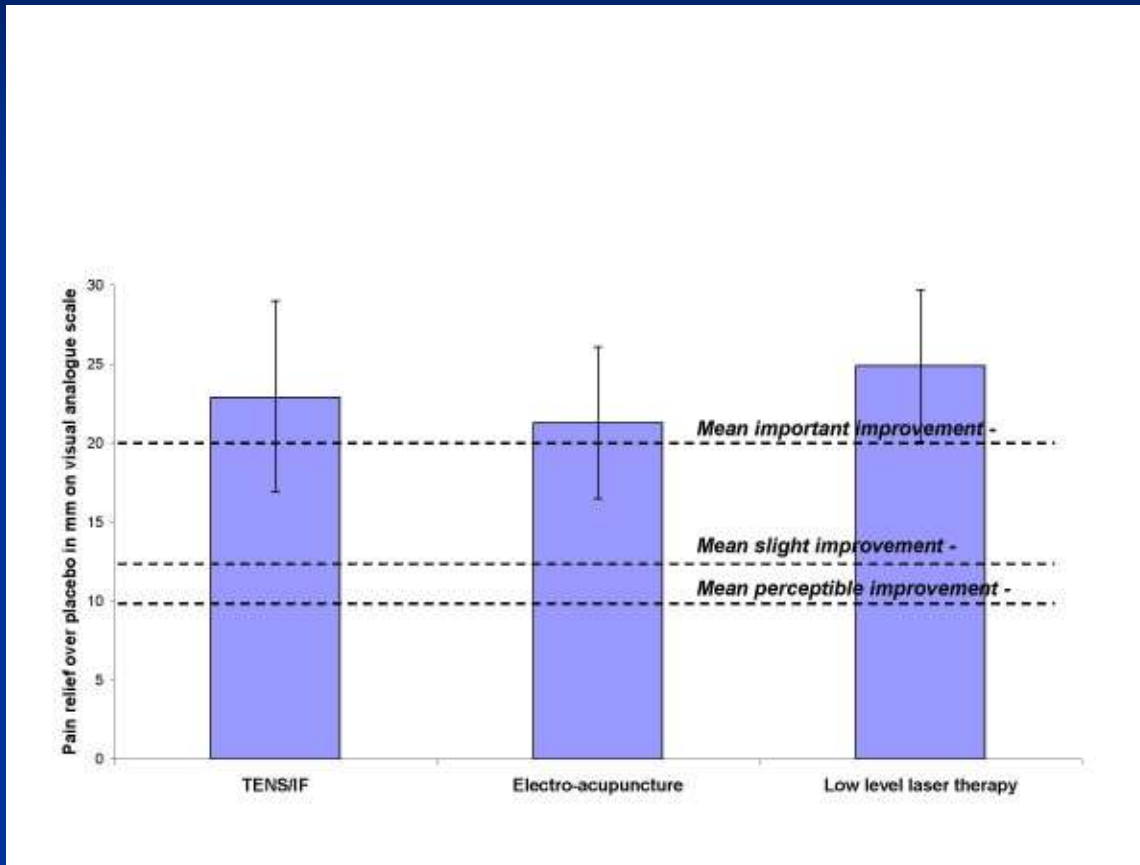
Severe

Osteoarthritis. BMJ 2006;332(7542):641

# Balneotherapy

- Beneficial effects on pain, quality of life and analgesic intake of mineral baths compared to no treatment
- *Cochrane Database of Systematic Reviews* 2007, Issue 4. Art. No.: CD006864

# Other PT Interventions



TENS      Electro-Acupuncture      Laser

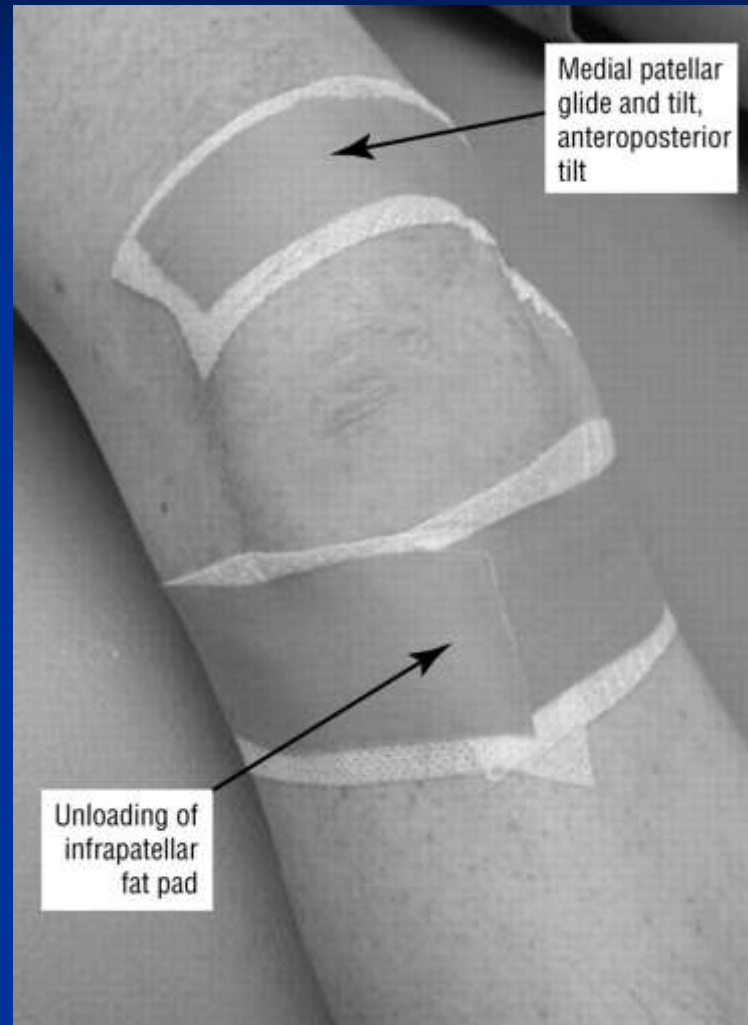
Bjordal JM et al BMC Musculoskelet Disord. 2007; 8: 51.

Note 2009 Cochrane says TENS of no benefit for OA

# Footwear and Braces



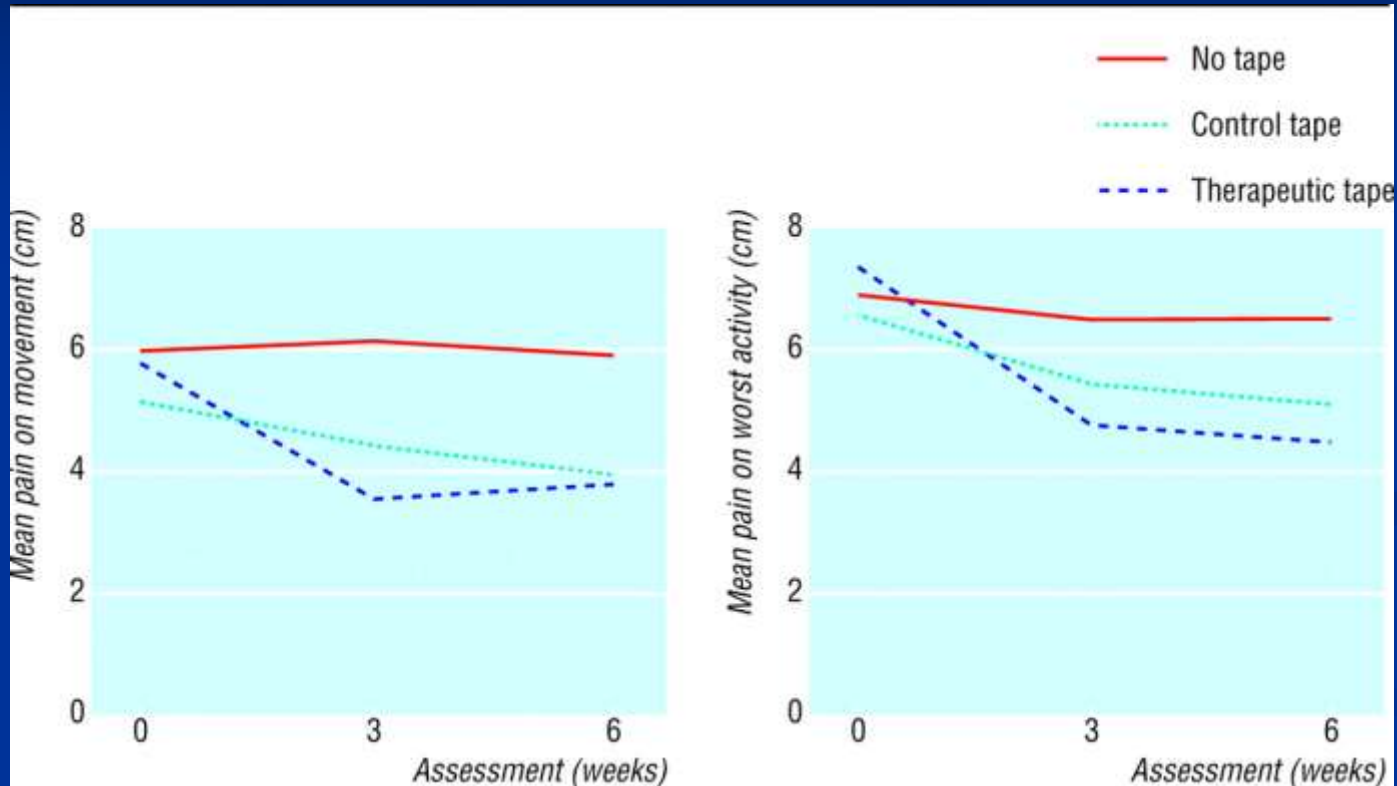
# Knee Taping



Hinman, R. S et al. BMJ 2003;327:135

BMJ

# Fig 3 Pain scores on primary outcomes over time by intervention group



Hinman, R. S et al. BMJ 2003;327:135

# Splint for Base-of-Thumb Osteoarthritis



# After nighttime splint

**Table 2. Estimates of Mean Change in Outcomes From Baseline to 1 or 12 Months and Estimates of Slope With Intervention and Control Treatment**

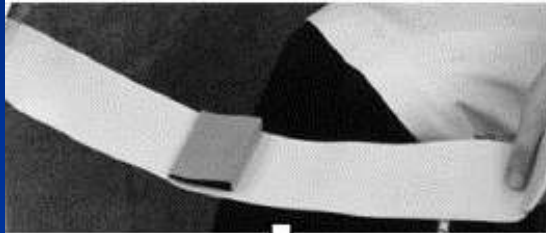
Outcome	Intervention Group	Patients Available, n	Control Group	Patients Available, n	Difference (95% CI)*	P Value
<b>Pain level (VAS score [range, 0–100 mm])</b>						
Mean at baseline (SD)	45.5 (19.9)	57	47.7 (19.8)	54	–	–
Mean change from baseline to 1 mo (±SE)†	–10.1 ± 3.6	55	–10.7 ± 3.3	46	0.6 (–7.9 to 9.1)	0.89
Mean change from baseline to 12 mo (±SE)†	–22.2 ± 3.2	52	–7.9 ± 3.5	45	–14.3 (–23.4 to –5.2)	0.002
Estimate of slope at 12 mo (±SE)‡	–19.2 ± 3.1	–	–4.2 ± 3.3	–	–15.0 (–24.0 to –5.9)	0.001
<b>CHFS score (range, 0–90)</b>						
Mean at baseline (SD)	19.4 (12.2)	56	17.7 (12.9)	55	–	–
Mean change from baseline to 1 mo (±SE)†	1.3 ± 1.4	54	–0.3 ± 1.5	47	1.6 (–2.3 to 5.5)	0.42
Mean change from baseline to 12 mo (±SE)†	–1.9 ± 1.6	49	4.3 ± 1.7	46	–6.3 (–10.9 to –1.7)	0.008
Estimate of slope at 12 mo (±SE)‡	–2.3 ± 1.5	–	3.8 ± 1.6	–	–6.1 (–10.4 to –1.8)	0.006
<b>Patient-perceived disability (VAS score [range, 0–100 mm])</b>						
Mean at baseline (SD)	38.2 (25.2)	57	38.6 (21.5)	55	–	–
Mean change from baseline to 1 mo (±SE)†	0.2 ± 3.4	56	–0.7 ± 3.8	47	0.9 (–8.7 to 10.6)	0.85
Mean change from baseline to 12 mo (±SE)†	–11.6 ± 3.1	51	1.5 ± 3.4	46	–13.1 (–21.8 to –4.4)	0.003
Estimate of slope at 12 mo (±SE)‡	–13.6 ± 2.7	–	1.5 ± 2.8	–	–15.1 (–22.8 to –7.4)	0.001

CHFS Cochin Hand Function Scale;

*Note 1 yr improvements*

*Ann Intern Med.* 2009;150:661-669.

A. Strapped insole



B. Inserted insole



# A 2-year follow-up of a study to compare the efficacy of lateral wedged insoles with subtalar strapping and in-shoe lateral wedged insoles in patients with varus deformity osteoarthritis of the knee

	Lequesne index of disease severity			Femorotibial angle		
	Baseline	6 months	2 years	Baseline	6 months	2 years
Strapped insole group						
Mean $\pm$ SD	9.7 $\pm$ 5	7.5 $\pm$ 5.8	7.3 $\pm$ 5.6	183.4 $\pm$ 6	180.7 $\pm$ 5.7	179.7 $\pm$ 3.2
Median	10	8	8	184	180	179
95% CI	7.7–11.6	5.3–9.6	4.8–9.9	181.1–185.8	178.5–182.9	178.2–181.1
	P=0.031			P=0.015		
Inserted insole group						
Mean $\pm$ SD	9.9 $\pm$ 5	9 $\pm$ 5	9.6 $\pm$ 4.8	184.1 $\pm$ 5.1	184.1 $\pm$ 5.1	182.4 $\pm$ 4.7
Median	9	10	10	184	183	183
95% CI	7.9–11.8	7.9–11.6	7.4–11.8	182.2–186.1	181.7–185.7	180.3–184.5
	P=0.79			P=0.27		

*Osteoarthritis and Cartilage*, Volume 14, Issue 3, Pages 231-237

Y. Toda, N. Tsukimura

However more popliteal, low back, and foot pain as well.

# Unloader Brace/Valgus Brace

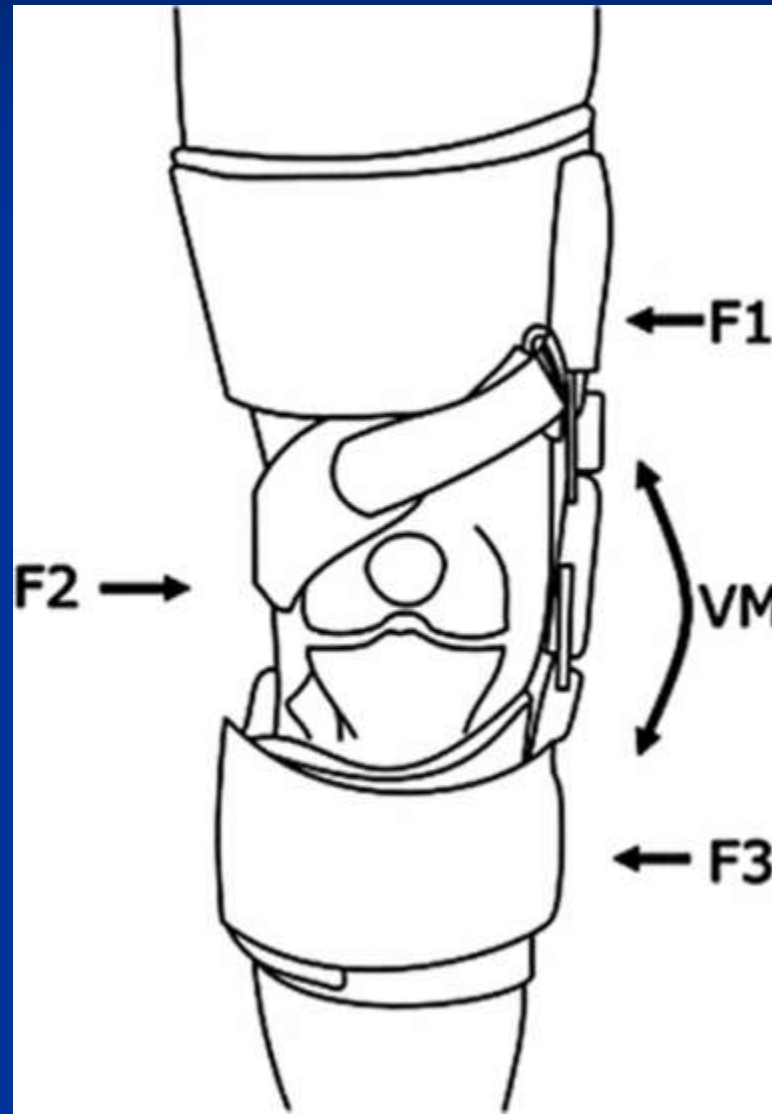
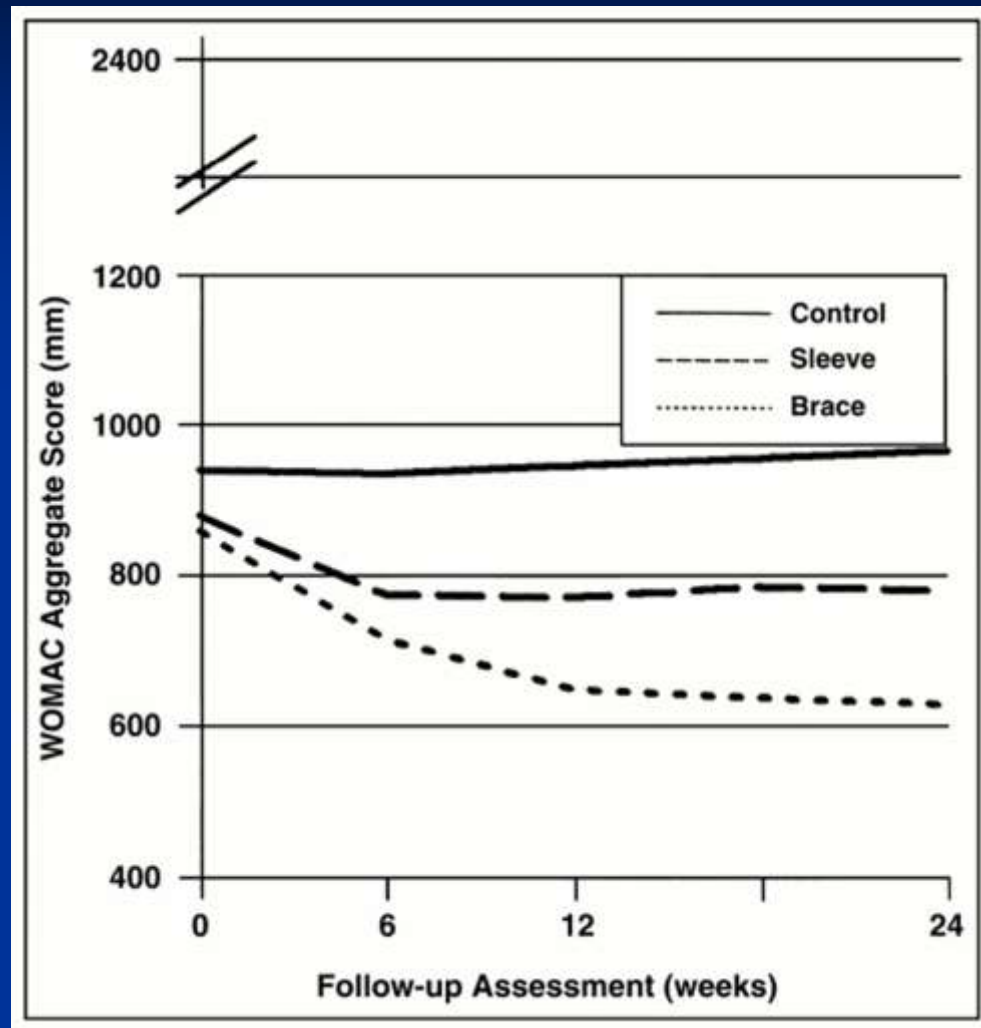


Fig. 1 Graph showing the mean aggregate absolute scores on the WOMAC (Western Ontario and McMaster University Osteoarthritis Index)



KIRKLEY A. et.al. J Bone Joint Surg 1999;81:539-48

# Brace Plus. . . .



OActive™ Brace with BioniCare®  
System  
Available August 2009

## **SIGNAL GENERATOR**

Four ounce, battery-powered device generates the proprietary electrical signal.

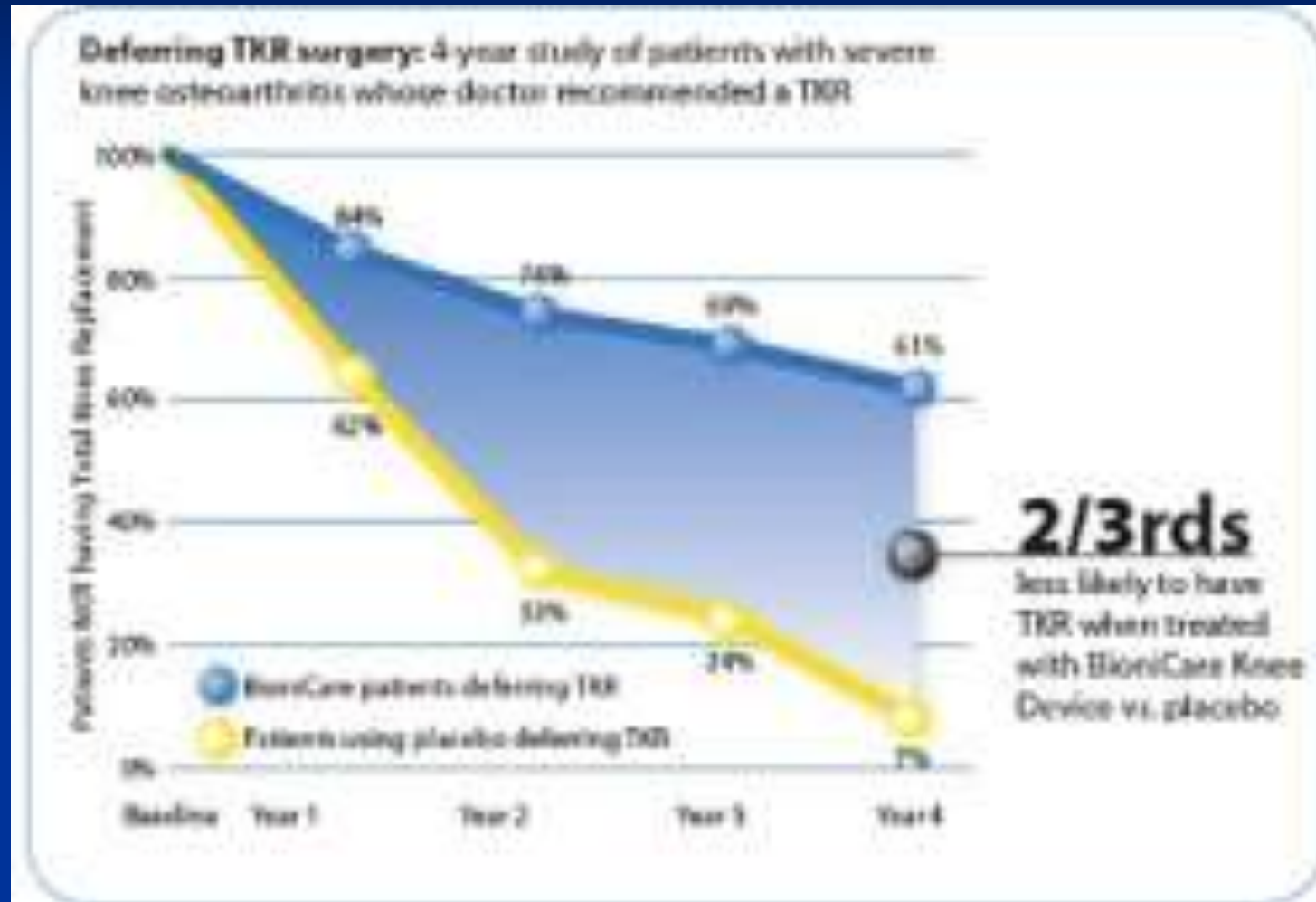
## **OACTIVE KNEE BRACE:**

Low profile, light weight brace provides 3 points of leverage to reduce pressure inside the knee joint.

## **TWO PADS:**

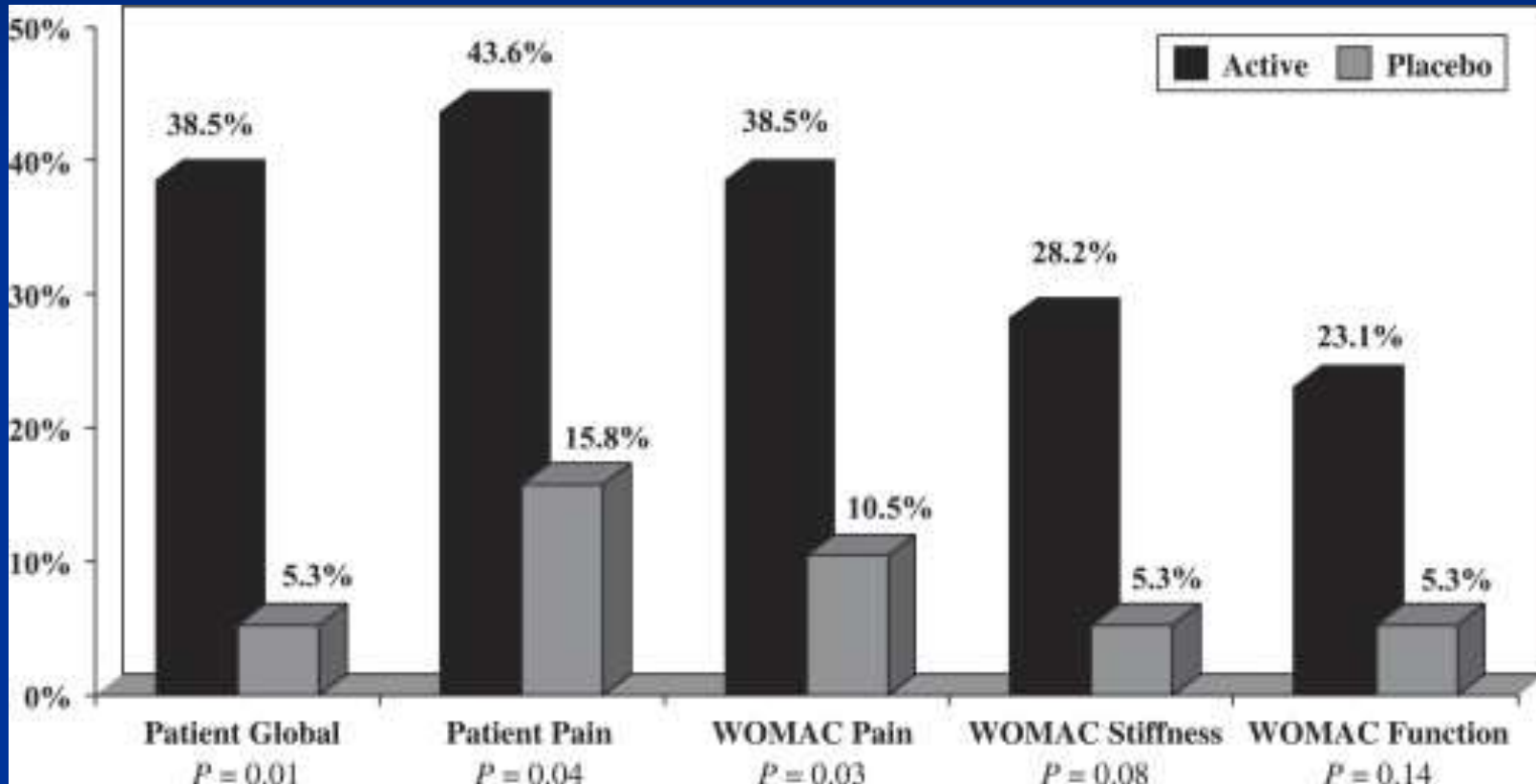
One covers the knee and the other one rests on the thigh to deliver the signal carried via wires from the Signal Generator.

# Open-label trial



There was a “matched group,” not placebo, but surgery could be delayed.

And actually did perform better than placebo short-term. . .



Percentage of patients improving 50% or greater in each of the primary outcome measures.

**Osteoarthritis and Cartilage** Volume 15, Issue 6, June 2007, Pages 630-637

# Magnets

- Improved self-rated pain and physical function ( $P=.002$  and  $.001$ , respectively) more than changes in gait speed ( $P=.042$ ) Hinman et al. *Altern Ther Health Med.* 2002 Jul-Aug;8(4):50-5
- Improved VAS pain scores at 4 hours (0-500) decreased  $79 \pm 18$  mm in the active group and  $10 \pm 21$  mm in the placebo group ( $P < 0.05$ ). Wolsko et al *Altern Ther Health Med.* 2004 Mar-Apr;10(2):36-43

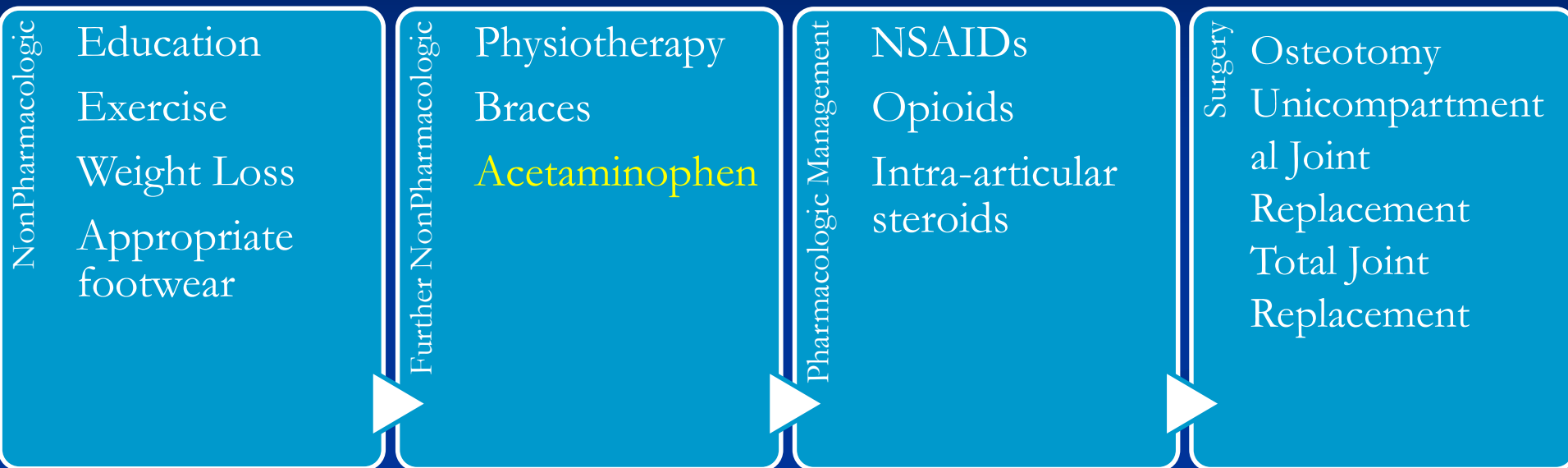
# Magnetic Bracelet

- Visual analogue scale for pain<sup>†</sup>:

	Active Bracelet	Weak Bracelet	Dummy Bracelet
High level of improvement	20%	14%	9%
Moderate improvement	37%	42%	22%

- significant difference for change in WOMAC A score ( $P = 0.026$ )
- Magnet strength for effect: (47 to 180 mTesla),
- BMJ. 2004 December 18; 329(7480): 1450–1454

# Step Treatment



Mild

Symptom Severity

Severe

Osteoarthritis. BMJ 2006;332(7542):641

# Pharmacotherapy

- Acetaminophen as first-line
- I might add Devil's Claw in here as an analgesic
  - ↓ iNOS, ↓ activity and translocation of NF- $\kappa$ B
  - Antioxidant
  - Peripheral Analgesic

# Harpagophytum

- Moderate evidence:

- *Harpagophytum* powder at 60 mg harpagoside in the treatment of osteoarthritis of the spine, hip and knee;

- Strong evidence:

- Aqueous *Harpagophytum* extract, 50–100 mg harpagoside/d in acute exacerbations of chronic NSLBP; equivalent to or better than viox

Gagnier JJ et al BMC Complement Altern Med. 2004; 4: 13.

# An Argument Against NSAIDs

- Toxicity
- An anti-DMOAD

# Adverse effects of NSAIDs:

- Gastrointestinal
  - bleeding and gastric ulceration
  - Increased intestinal permeability
- Renal
  - Renal Failure
  - Hypertension, exacerbation CHF
- Cardiovascular
- Joint Effects (more later)
- Hepatic Effects
- Death

# GI toxicity

- 107,000 Hospitalizations Annually for NSAID-related GI complications
- **“At least 16,500 NSAID-related deaths occur each year among arthritis patients alone”**

*Am J Med.* 1998 Jul 27; 105(1B): 31S-38S

# The “safer” anti-inflammatories?

## **Merck to Withdraw Vioxx Because of Heart Risks**

Sept. 30 (Bloomberg) -- Merck & Co. withdrew its Vioxx painkiller, which generated \$2.5 billion in sales last year, because of a link to heart attacks and strokes. The company's shares slid as much as 28 percent, wiping out \$28 billion in market value.

New three-year data from Merck suggested that patients taking Vioxx for more than 18 months faced twice the risk of a heart attack compared with those taking a placebo.

Celecoxib use associated with increased risk CHD in Tennessee Medicaid population  
Pharmacoepidemiol Drug Saf. 2009 Jul 27.

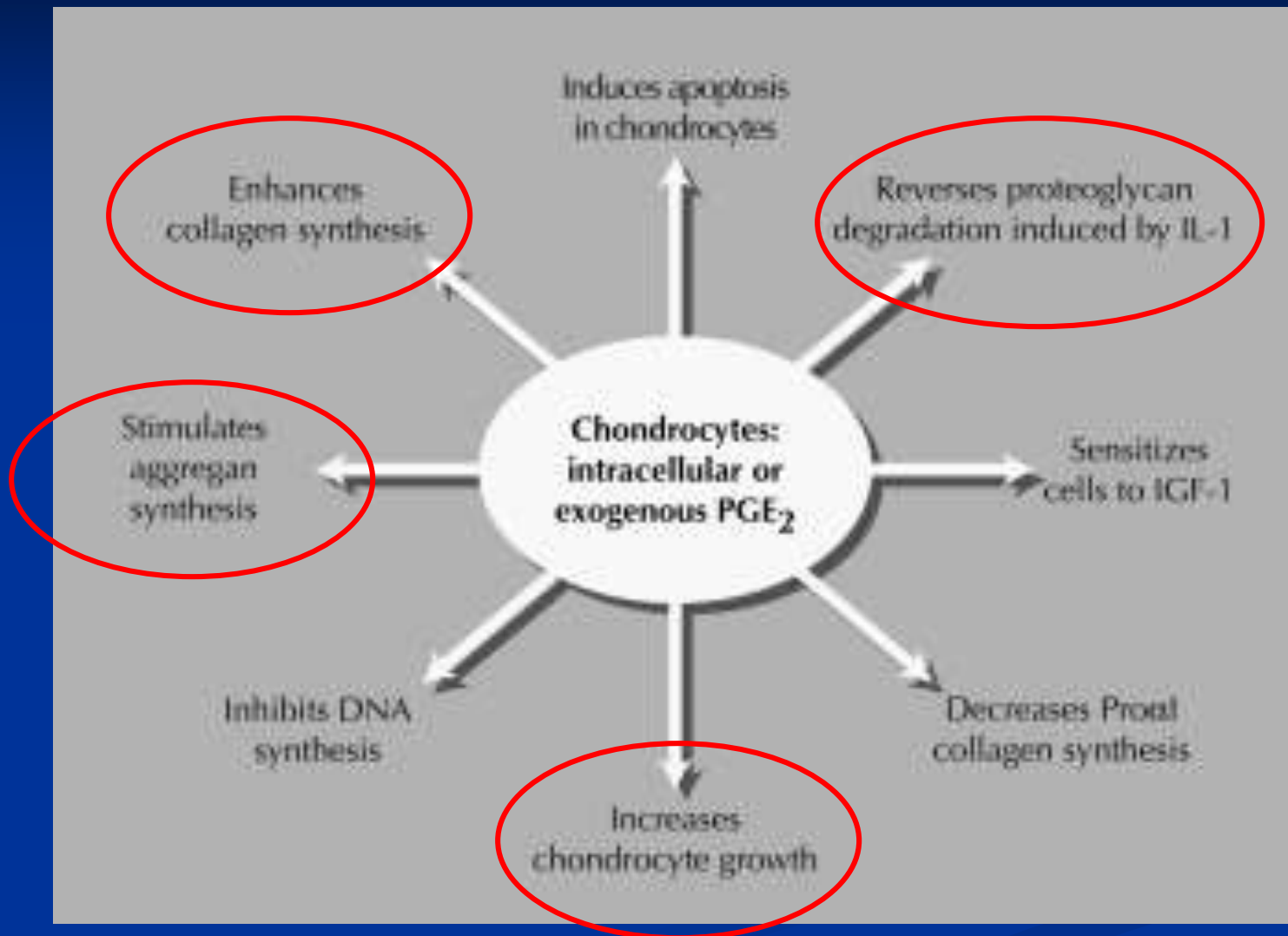
Celecoxib associated with stroke and GI hemorrhage Drug Saf. 2009;32(4):335-43.

# Cardiovascular Risk with Nonselective NSAIDs

Drug and time of last prescription	Adjusted odds ratio <sup>*</sup> (95% CI)	P value
<b>Celecoxib</b>		
Within 3 months of index date	1.21 (0.96 to 1.54)	0.11
<b>Rofecoxib</b>		
Within 3 months of index date	1.32 (1.09 to 1.61)	0.005
<b>Ibuprofen</b>		
Within 3 months of index date	1.24 (1.11 to 1.39)	<0.001
<b>Diclofenac</b>		
Within 3 months of index date	1.55 (1.39 to 1.72)	<0.001
<b>Naproxen</b>		
Within 3 months of index date	1.27 (1.01 to 1.60)	0.04

■ BMJ. 2005 Jun 11;330(7504):1366 Looks like a class effect

# Mixed Effects of PG in Chondrocytes



Current Rheumatology Reports 2000, 2:447–453

Some effects of prostaglandin are anabolic

# NSAIDs Impair Joint Repair

*In vivo* studies with NSAIDs at physiologic concentrations have shown that several NSAIDs reduce glycosaminoglycan synthesis.

- Salicylate
- Acetylsalicylic acid
- Fenoprofen
- Isoxicam
- Tolmetin
- Ibuprofen

- “...femoral head collapse and **acceleration of osteoarthritis** have **been well documented in association with the NSAIDs...**” *Lancet*. 1985 Jul 6; 2(8445): 11-4

# NSAIDs

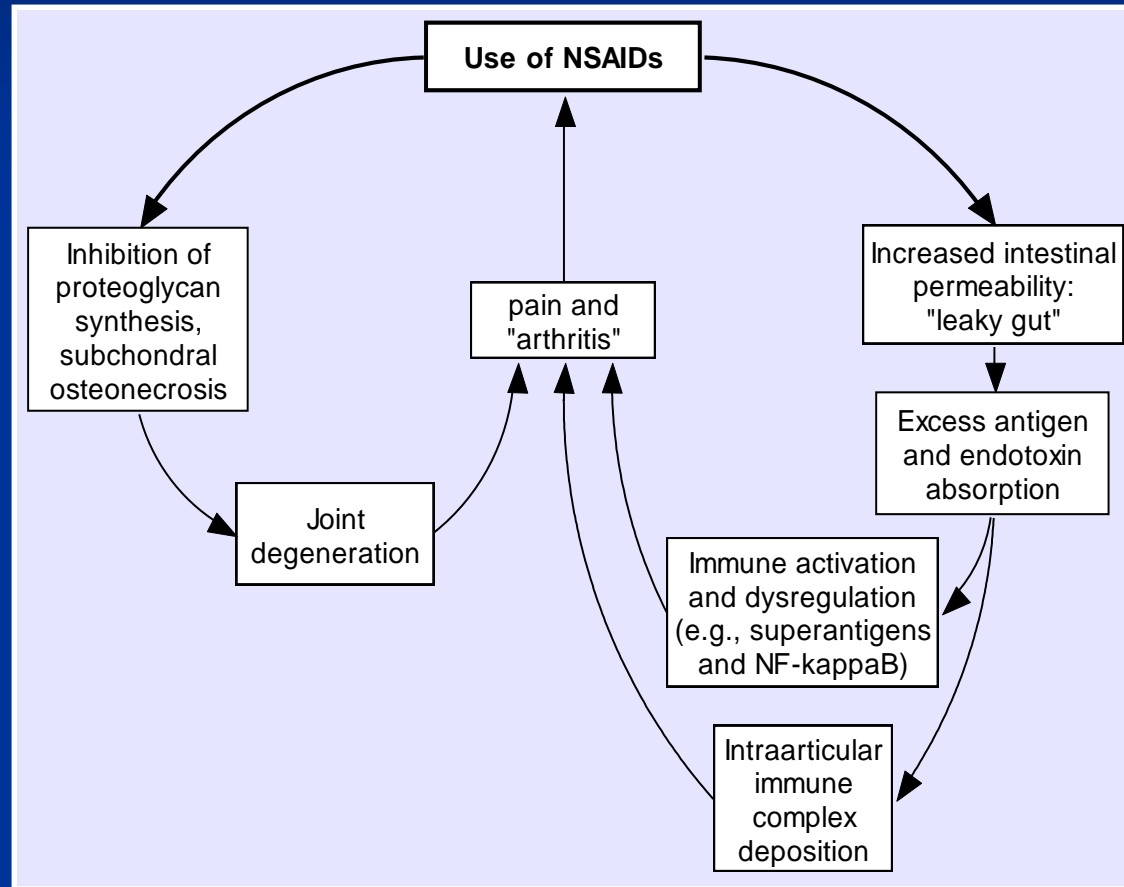
**Table 3** Associations between Use of NSAIDs, Increases in Knee Cartilage Defect, and Loss of Cartilage Volume Over 2.9 Years

	Increases in Defects* OR (95% CI)	Cartilage Loss pa* $\beta$ (95% CI)
Use of COX-2 inhibitors vs nonuse		
Medial tibiofemoral	0.4 (0.2-1.0)†	-0.03 (-1.8-1.8)
Lateral tibiofemoral	1.3 (0.6-2.9)	0.9 (-0.8-2.6)
Patellar	0.8 (0.3-2.1)	0.1 (-1.9-2.0)
Use of conventional NSAIDs vs nonuse		
Medial tibiofemoral	3.1 (1.0-9.1)†	-1.1 (-3.4-1.2)
Lateral tibiofemoral	2.6 (1.0-6.7)†	-1.1 (-3.1-0.8)
Patellar	0.2 (0.1-1.1)	-1.0 (-3.3-1.3)

■ A DMOAD in the wrong direction

*The American Journal of Medicine* (2009) 122, 836-842

# Vicious Cycle of NSAID Use: Chondrolysis and Intestinal Injury



# But if you must. . . .

## ■ Topical NSAIDs

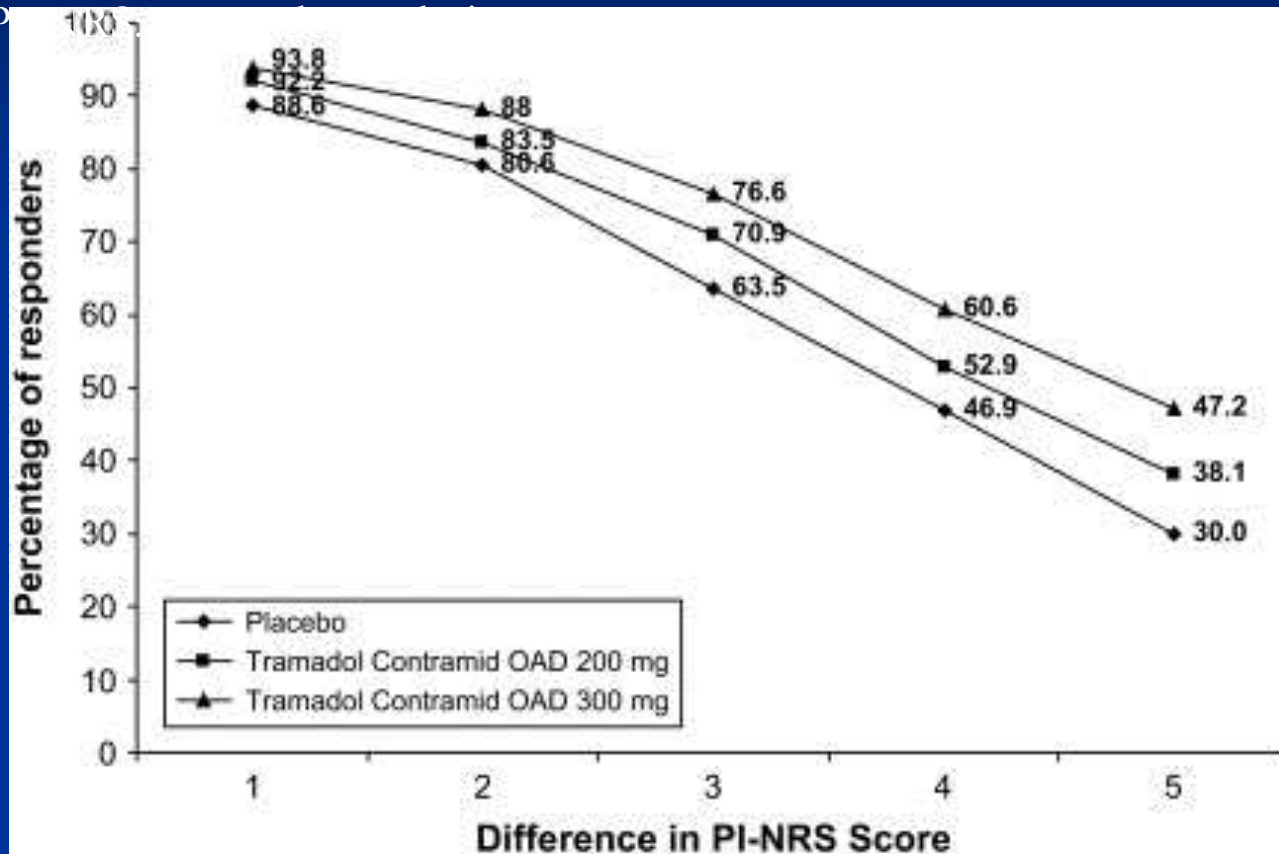
- Efficacy somewhat in question (many trials of limited quality, effect decreases with increasing sample size, etc.) however efficacy does appear equivalent to oral NSAIDs
- BMJ 2008;336:105-106 (19 January),  
BMJ 2008;336:344 (16 February)
- “The randomised controlled trial was powered for equivalence, and it found no significant difference in the WOMAC osteoarthritis index or major and minor adverse effects at one year between people who used the topical preparation or the oral drug. **Cynics might conclude that both interventions are useless.**”

# If Not NSAIDs, Then What?

- Tramadol
- Opioids
- Natural Products

# Tramadol

Fig. 3. P

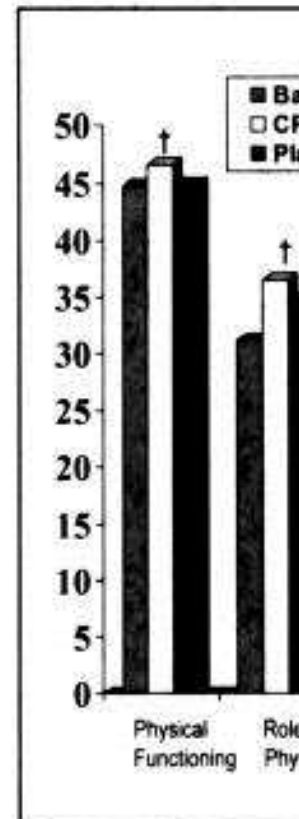


J Pain Symptom Manage. 2007 Sep;34(3):328-38.

# Tramadol

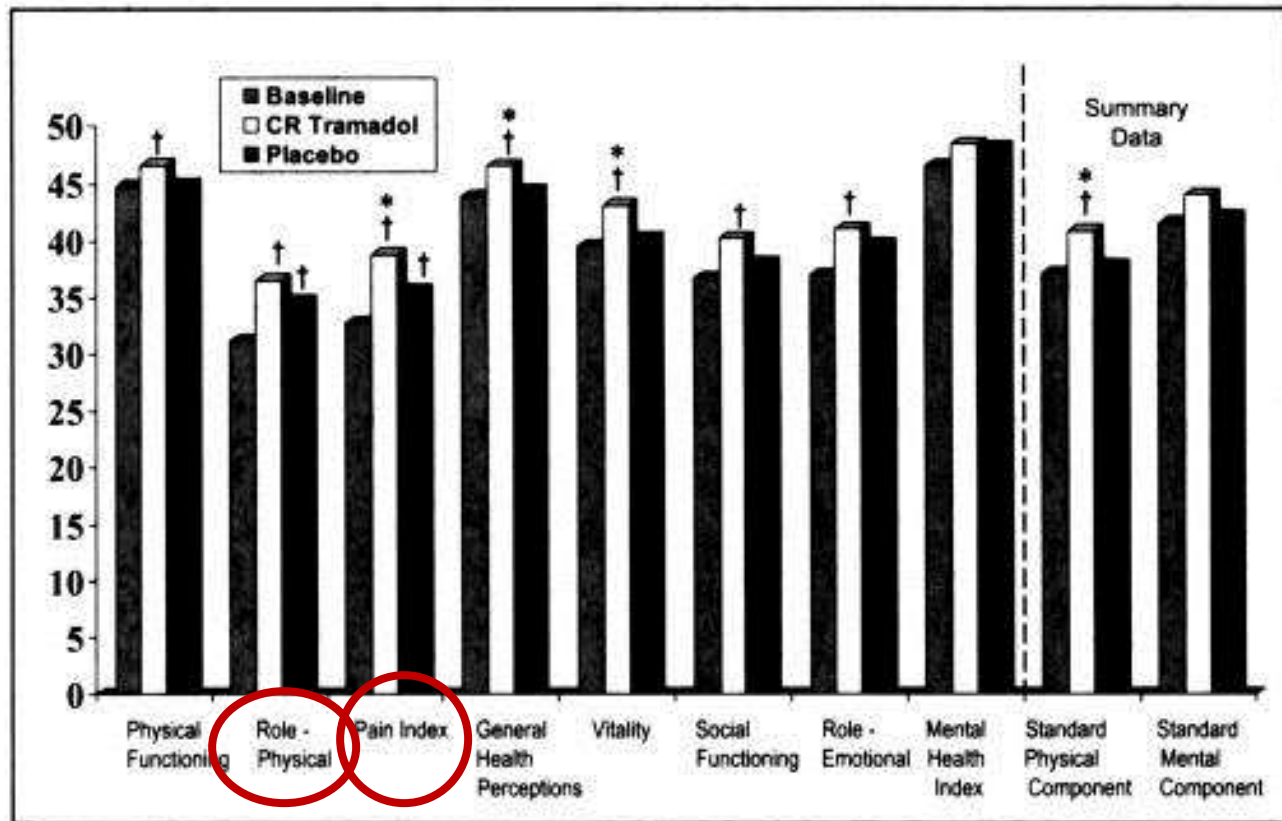
**TABLE 2**  
**Pain and Sleep Questionnaire during the last week of treatment**

	Baseline	Controlled-release tramadol	Placebo	P*
Trouble falling asleep	41.0±26.7	24.2±21.6 <sup>†</sup>	31.6±24.9 <sup>‡</sup>	0.0067
Needed pain medication to sleep	33.0±33.2	20.2±28.5 <sup>†</sup>	29.4±30.9	0.0027
Needed sleeping medication to sleep	16.9±29.7	8.4±21.1 <sup>†</sup>	13.6±25.9	0.0074
Awakened by pain at night	45.8±31.3	27.2±25.8 <sup>†</sup>	33.2±27.4 <sup>‡</sup>	0.0515
Awakened by pain in morning	45.6±33.6	24.7±24.7 <sup>†</sup>	33.5±27.8 <sup>‡</sup>	0.0020
Partner awakened	28.7±29.6	16.6±19.5 <sup>†</sup>	22.6±23.6	0.0632
Hours of sleep	6.0±1.6	6.5±1.2 <sup>†</sup>	6.2±1.4 <sup>‡</sup>	0.0096



**Figure 4)** Shown  
ment (per proto  
state. Data ne  
between treatm

# Tramadol



**Figure 4)** Short-form 36 Health Survey during the last week of treatment (per protocol population). Higher scores indicate a better health state. Data normalized to the Canadian population. \* $P \leq 0.0262$  between treatments; † $P \leq 0.0357$  change from baseline. CR Controlled-release

# Tramadol

**TABLE 3**  
**Incidence of most common adverse events (double-blind phase)\***

	Controlled-release tramadol, n (%)	Mean maximum severity	Placebo, n (%)	Mean maximum severity	P*
Nausea	40 (42.6)	1.8	22 (25.0)	1.5	0.0326
Somnolence	35 (37.2)	1.6	19 (21.6)	1.5	0.0833
Constipation	22 (23.4)	1.3	5 (5.7)	1.6	0.0011
Anorexia	6 (6.4)	1.0	1 (1.1)	1.0	0.1025
Vomiting	6 (6.4)	1.8	2 (2.3)	2.0	0.3173
Dizziness	5 (5.3)	1.4	3 (3.4)	1.0	0.4142
Sweating	5 (5.3)	1.6	0 (0.0)	0	0.0253
Asthenia	3 (3.2)	1.7	3 (3.4)	1.3	0.6547
Pruritus	3 (3.2)	1.0	0 (0.0)	0	0.0833
Headache	2 (2.1)	1.5	6 (6.8)	1.3	0.1573
Nervousness	2 (2.1)	1.5	0 (0.0)	0	0.1573
Insomnia	0 (0.0)	0	4 (4.5)	1.8	0.0455
Overall	75 (79.8)	1.7	58 (65.9)	1.5	0.0833

\*Based on 94 patients who received controlled-release tramadol and 88 patients who received placebo

# Bottom-line Tramadol

- (1) less pain [-8.5 units on a 0-100 scale; (95% CI -12.0 to -5.0)]
- (2) higher degree of global improvement: one of every 6 at least moderate global improvement
- (3) improvement in stiffness and function, an 8.5% improvement in WOMAC score
- Adverse events: minor in 1/5 participants
- Discontinuation in 1/8

# Tramadol and Seizure Risk

- Avoid combination with SSRIs and TCAs

# Opioids in Management of Chronic Nonmalignant Pain

- Benefits and Risks
- Side effects:
  - ◇ Constipation
  - ◇ Nausea
  - ◇ Sleep disruption
  - ◇ Respiratory depression
  - ◇ Altered mental status
  - ◇ Itching
- Hyperalgesia
- Addiction vs. Dependence – Physical dependence is nearly universal; addiction develops in 3-18%

# General Guidelines

- Lowest Doses Effective
- Informed Consent/”Contract”
  - Reasonable expectations of degree of pain relief, functional goals
  - Medication storage/security
- Monthly Visits – documentation functional outcome as well as pain relief
- Long-acting medications where possible
  - Avoid “peaks and troughs”
  - Sleep

# Natural Products Supported By At Least One Clinical Trial

- Pycnogenol
- Avocado-Soybean Unsaponifiables
- Collagen
- MSM
- Capsaicin - topical
- Boswellia
- SAMe
- Niacinamide
- Cat's Claw (*uncaria tomentosa*)
- Rose Hips
- Ginger
- Phytodolor *Populus tremula, Fraxinus excelsior and Solidago virgaurea*
- SKI306X *Clematis mandshurica, Trichosanthes kirilowii, Prunella vulgaris*)
- Willow Bark
- Duhuo Jisheng Wan
- Stinging Nettle
- Gitadyl (*feverfew, American aspen and milfoil*)
- Etc.

# Pycnogenol

- Concentrate of polyphenols: phenolic acids, catechin, taxifolin and procyanidins
  - Inhibit MMPs, elastase, collagenase
  - inhibits the activation of NF- $\kappa$ B
  - Cross-link collagen and elastin

*Phytother. Res. 22, 1087–1092 (2008)*

*Note Grape Seed Extract may be a cheaper alternative*

- WOMAC Pain scores after 3 months on pycnogenol ( $p < 0.05$ )

Pycnogenol		Placebo	
Inclusion	3 months	Inclusion	3 months
17.3	7.7	17.1	15.2

- Exercise test – distance achieved on treadmill at 8 km/h, inclination 10%

	Pycnogenol	Placebo	Significance level
Inclusion	68 m (0–133)	65 m (12–98)	n.s.
3 months	198 m (55–374)	88 m (25–102)	< 0.05

The use of NSAIDs dropped by 58% during treatment with Pycnogenol, whereas under placebo NSAID use was reduced by only 1%.

**Table 2. Analgesics consumption in Pycnogenol/placebo group during the time of the treatment**

	Pycnogenol group	Placebo group
Same level	62%	82%
Increased dosage	0%	10%
Decreased dosage	38%	8%

## ■ Percentage Reduction of costs

Costs	Pycnogenol	Placebo	Significance level
Drugs and treatments besides NSAIDs	54%	11%	$p < 0.05$
Hospital admissions	55%	5%	$p < 0.05$
Days hospitalized	60%	11%	$p < 0.05$

# Other effects of Pycnogenol in RCTs

- ↓LDL cholesterol, ↑HDL cholesterol
- ↓systolic blood pressure, ↓serum thromboxane
- ↓serum reactive oxygen species, ↓lymphocyte apoptosis
- ↓edema and pain, leg heaviness
- ↓platelet aggregation, ↑diameter of microvessels

Am J Clin Nutr 81(1):243S-255S, 2005

## ■ Effective in:

◇ Asthma

◇ Athletic performance

◇ Venous insufficiency

◇ Hypertension

◇ Retinopathy

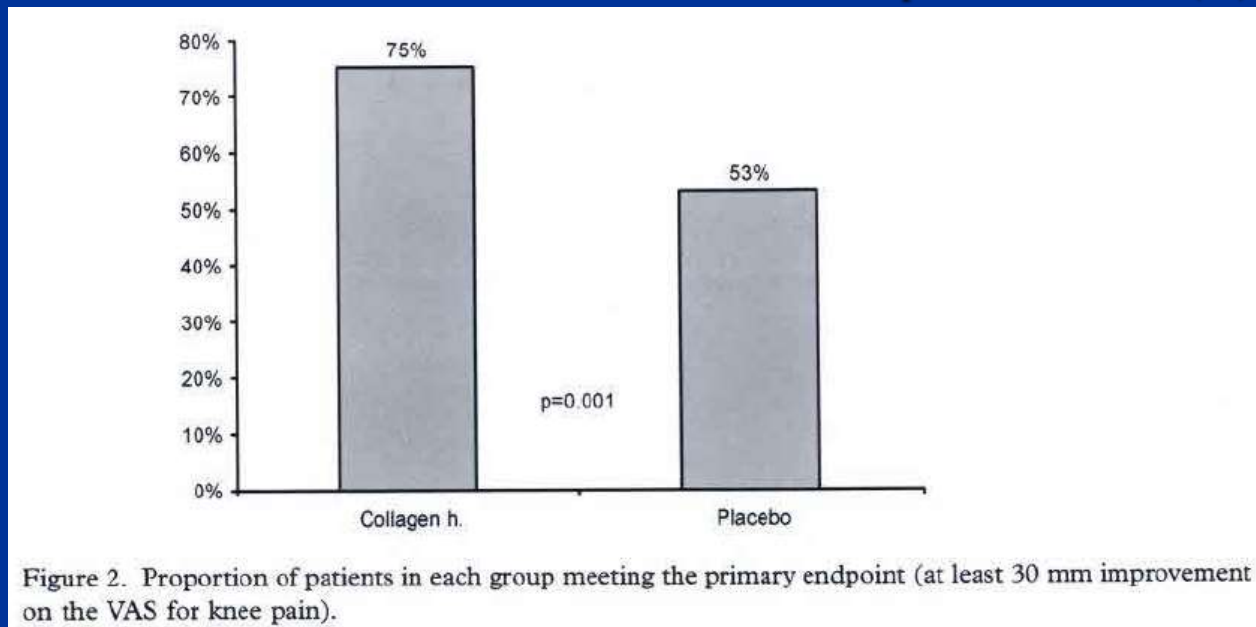
Natural Medicines Comprehensive Database

- And a new study on hot flashes!

# Collagen Hydrolysate

- 4 open-label, 3 double-blind studies
- Improvement in measures of pain and function.
  - Looks more effective in those more severely affected

Semin Arthritis Rheum 30:87-99. 2000. Curr Med Res Opin. 2006 Nov;22(11):2221-32



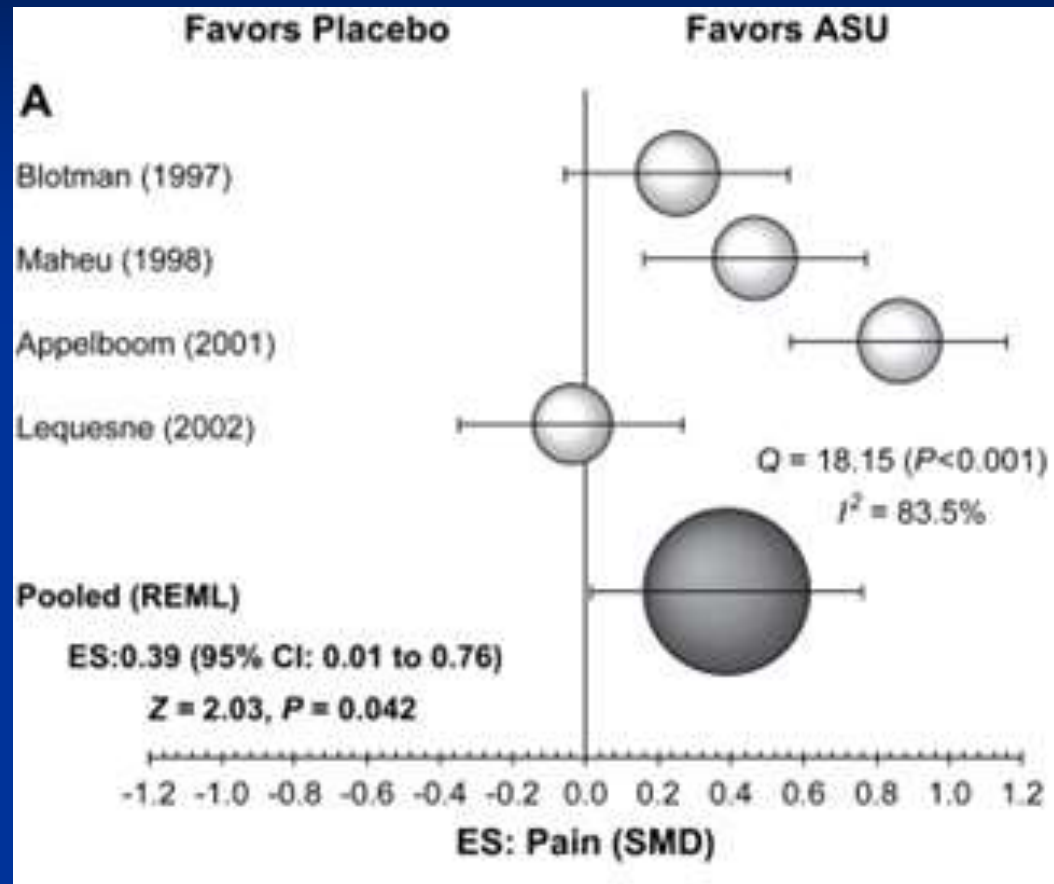
Works best in those eating  $<1.549$  g meat per week ( $<\sim 8$  oz meat per day) Int J Food Sci Nutr. 2009;60 Suppl 2:99-113. Epub 2009 Feb 11.

# Collagen

"He who has stabbing pains in his limbs and bones, as well as stomach and intestinal pain, should frequently eat plenty of well cooked beef trotters including fat and calluses. That soon gets rid of the pain. " St. Hildegard, 12<sup>th</sup> Century

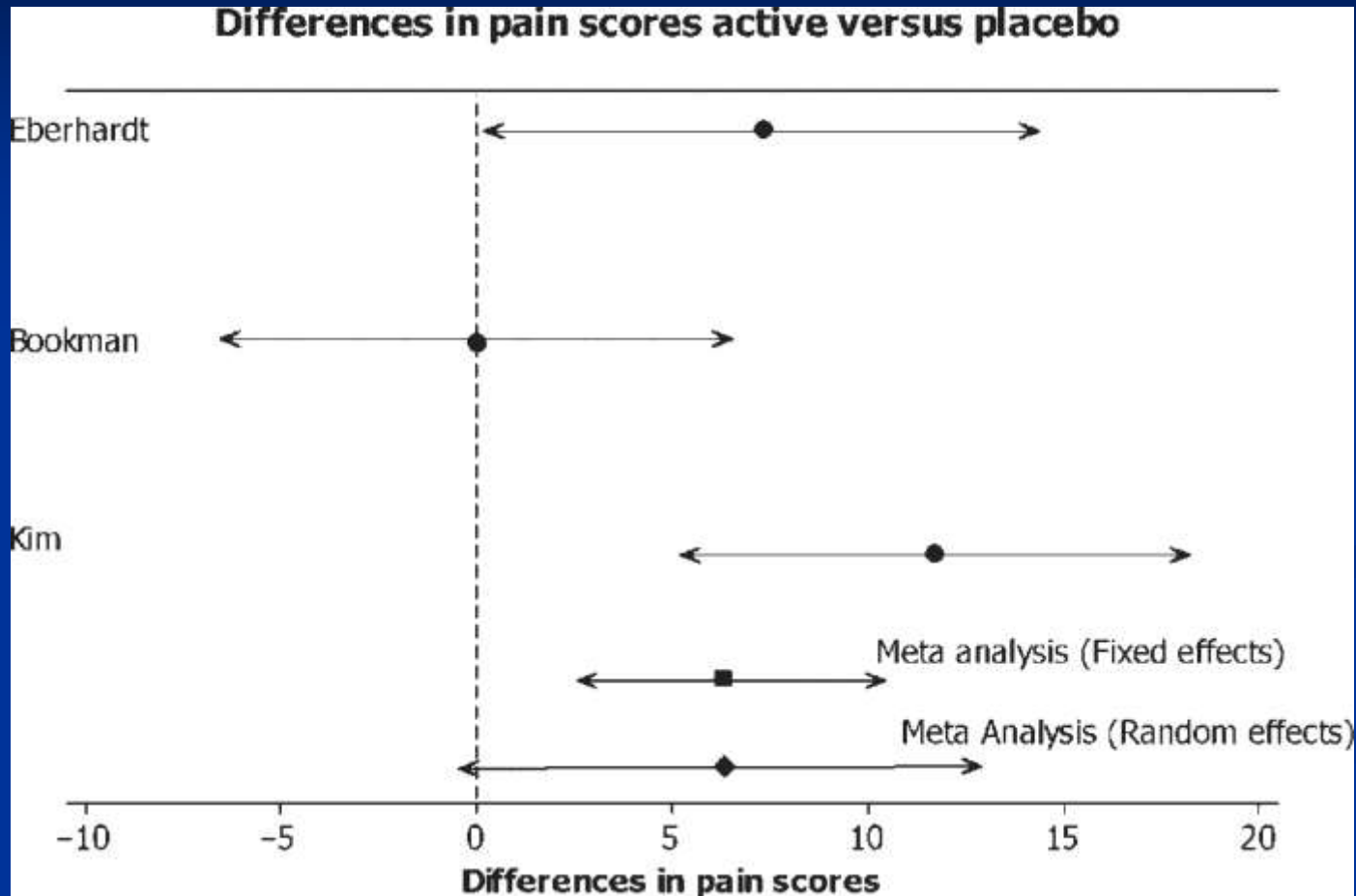
- Dose: 10 g daily
- The dietary equivalent is soup made from bones and gristle and boiled much of the day. May also have some benefit for prevention of osteoporosis.

# Avocado-Soybean Unsaponifiables



- Osteoarthritis and Cartilage 2008 16(4):399-408
- may promote OA cartilage repair by acting on subchondral bone osteoblasts

# Meta-analyses of randomized controlled trials of MSM



Brien, S. et al. eCAM 2009 0:nep045v1-45; doi:10.1093/ecam/nep045

# MSM with Glucosamine Sulfate

- Glu, MSM and combination significantly improved signs and symptoms of osteoarthritis compared with placebo.
- Combination more effective than either alone for pain, swelling, and improving functional ability
- Onset of analgesic and anti-inflammatory activity was found to be more rapid with the combination than with Glu
- Clin Drug Investig. 2004;24(6):353-63

# Capsaicin

- Knee – apply 0.025% qid vs. placebo x 4 wk
  - mean reductions in pain of 57% in RA and 33% in OA ( $P = 0.003$  and  $P = 0.033$ ).
  - 80% of the capsaicin-treated patients experienced a reduction in pain after two weeks of treatment according to the global evaluations Deal CL et al Clin Ther. 1991 May-Jun;13(3):383-95
- Hand – 0.075% qid
  - Capsaicin reduced tenderness ( $p < 0.02$ ) and pain ( $p < 0.02$ ) associated with OA McCarthy GM et al., J Rheumatol. 1992 Apr;19(4):604-7

# Capsaicin Continued

- Combination with Glyceril Trinitrate
- Reduction in pain scores:

■	<b>Glyceril trinitrate 1.33%</b>	<b>0.59</b>	<b>P&lt;0.05</b>
	Capsaicin 0.025%	0.5	P<0.05
	GTN and Capsaicin	1.1	P<0.05

# Botanical Medicine for OA

- Boswellia: Ayurvedic herb Researched in India to relieve inflammation, joint swelling, and promote joint circulation
  - boswellic acids in the tree resin counteract the effects of leukotrienes
  - Increases joint blood supply
- Dose: 500mg standardized to 70% boswellic acids 3-5x daily on empty stomach

# Botanical Therapy for OA

- In one study, Boswellia, Turmeric (Curcumin) were combined with Withania, Ginger and 70% of subjects had a significant decrease in pain and disability, double the relief of placebo ( $P < 0.05$ ) J Clin Rheumatol. 2004 Oct;10(5):236-245
- Similar study with Boswellia, Turmeric, Withania and Zinc J Ethnopharmacol. 1991 May-Jun;33(1-2):91-5
  - Note withania has chondroprotective properties *in vitro* J Biosci. 2007 Mar;32(2):299-307

# SAMe: S-adenosyl Methionine

- Used extensively in Europe for OA and depression
- Several double-blind and comparison studies showing it as effective as naproxen and piroxicam for pain relief in OA
- May be increased by using folic acid, B12, and folic acid

# SAMe

- Dose recommendation:
  - Recommended 400mg 3x daily for 3 weeks
  - Maintenance Dose: 200mg 3x daily
  - Tip: take with bromelain to improve oral absorption
- Drawback: Expensive! May provoke mania.
- Contraindications: High serum homocysteine.

# Niacinamide:

- 1996 - niacinamide (500mg 6x daily) significantly improved severity of arthritis and joint mobility .
  - Increases circulation into the joint
  - Reduces chemicals that accelerate cartilage damage
  - Decreases inflammation by reducing cytokines (TNFa)
- Dose: 500mg 2-6x daily

# Vitamin D - Epidemiology

Serum levels of vitamin D	#	OR Progression	P value
Lowest tertile (4.9-24.0 ng/mL)	33	2.89(1.01 to 8.25)	0.05
Middle tertile (27.0-33.0 ng/mL)	20	2.83 (1.02 to 7.85)	0.05
Highest tertile (36.0-79.0 ng/mL)	9	1	—

Low intake and low serum levels of vitamin D each appear to be associated with an increased risk for progression of osteoarthritis of the knee.

*Ann Intern Med.* 1996;125:353-359.

A DMOAD?

# Vitamin D

- 3-4X increase in risk of progression of radiographically determined OA was seen in the middle and low tertiles of vitamin D intake and serum concentration *of the Rheumatic Diseases* 56 (1997), pp. 397–402
- High serum concentrations of vitamin D protected against both incident and progressive hip OA *Arthritis and Rheumatism* 42 (1999), pp. 854–860

# Vitamin D Intervention



Mixed trials for diffuse musculoskeletal pain, but note vitamin D has been shown to prevent falls in the elderly\*, decrease the risk of colon cancer, and it looks to be helpful in metabolic syndrome as well

Recommend Cholecalciferol (D3) 2000-4000 IU /d

\*J Bone Miner Res. 2003 Feb;18(2):343-51

# With So Many Choices, How Do You Decide?



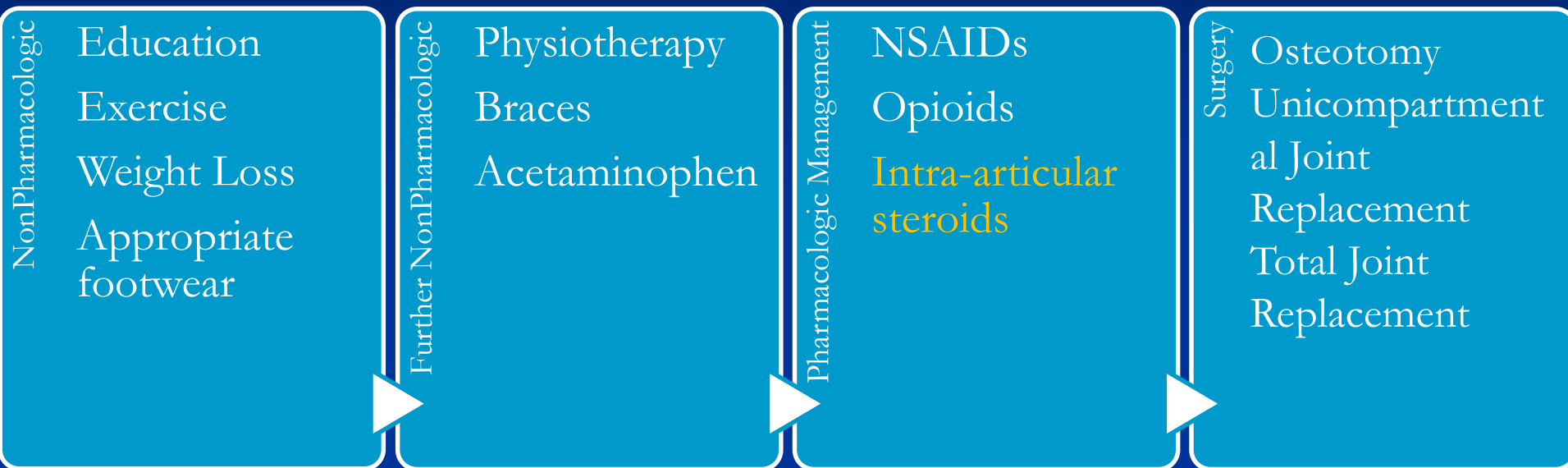
**Table 3**  
Recommendations taking into account the balance of benefit (pain reduction and function improvement) and harm (adverse event)

Product	Grade of Recommendation	Quality evidence	Balance benefit to harm
<i>Avocado/soybean unsaponifiables</i>	Strong	Moderate	Avocado/soybean unsaponifiables advantageous
<i>Chondroitin sulfate</i>	Strong	Moderate	Chondroitin sulfate advantageous
<i>Diacerein</i>	Strong	Moderate	Diacerein advantageous
<i>Glucosamine sulfate</i>	Strong	Moderate	Glucosamine sulfate advantageous
<i>Hyaluronic acid</i>	Strong	Moderate	Hyaluronic acid advantageous
<i>Oral calcitonin</i>	Weak	Low	Calcitonin not advantageous
<i>Risedronate</i>	Strong	High	Risedronate <u>not</u> helpful
<i>Strontium ranelate</i>	Weak	Very low	Strontium ranelate advantageous

# Or My Clinical Approach:

- Start with diet/exercise/etc. (incl. curries)
- Supplement glucosamine/chondroitin
- Vitamin D for all for other reasons. . . .
- Consider other remedies depending on comorbidities:
  - Pycnogenol with cardiovascular disease
  - Boswellia if there is inflammatory bowel disease
  - Collagen if there is neck or back pain
  - SAMe if there is depression (or B6, B12, folate)
  - Nettles for allergies, prostate trouble

# Step Treatment



Mild

Symptom Severity

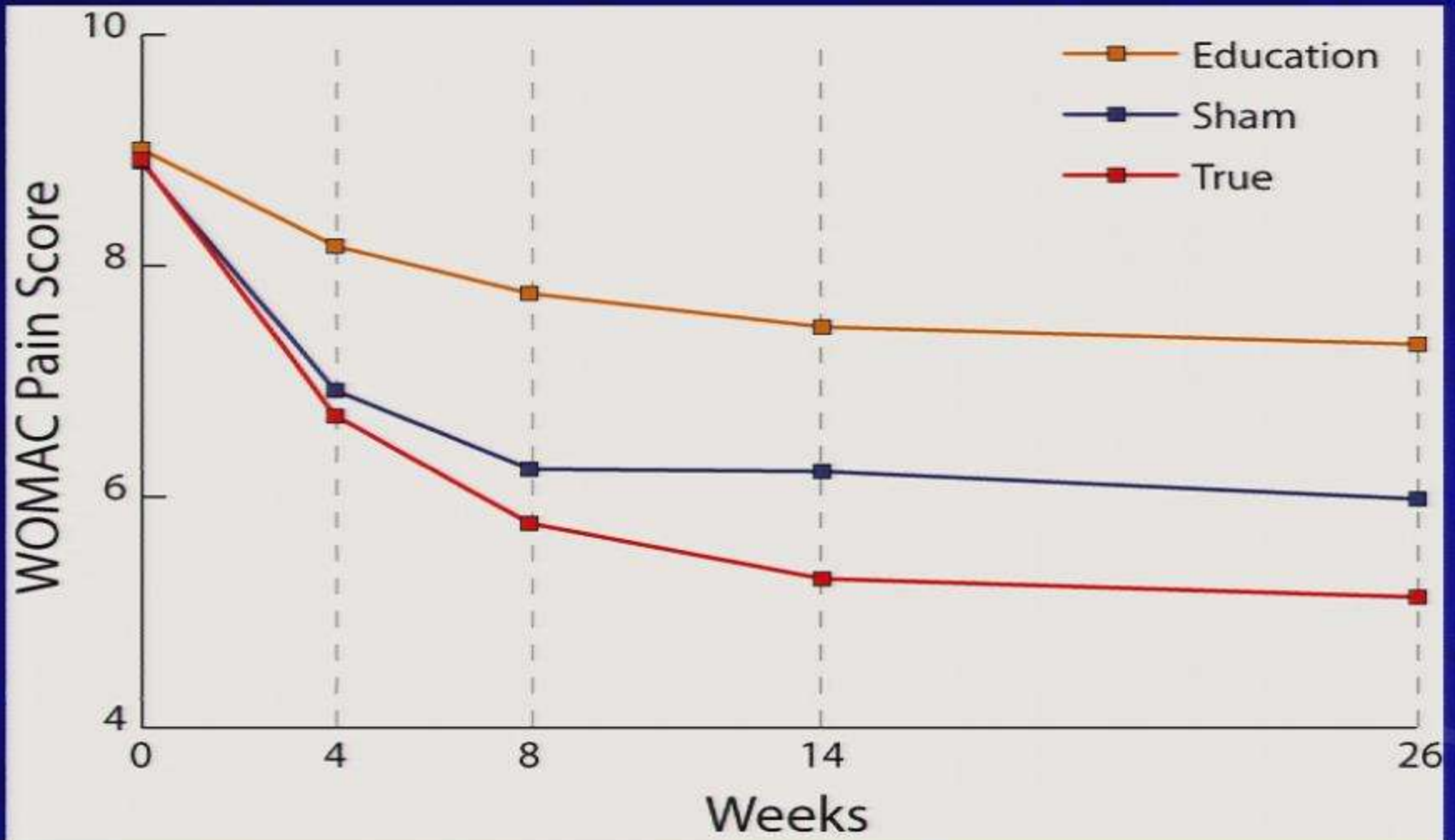
Severe

Osteoarthritis. BMJ 2006;332(7542):641

# Invasive Treatments

- Acupuncture
- Leeches
- Joint Injections
  - Synvisc
  - Corticosteroids

# Acupuncture

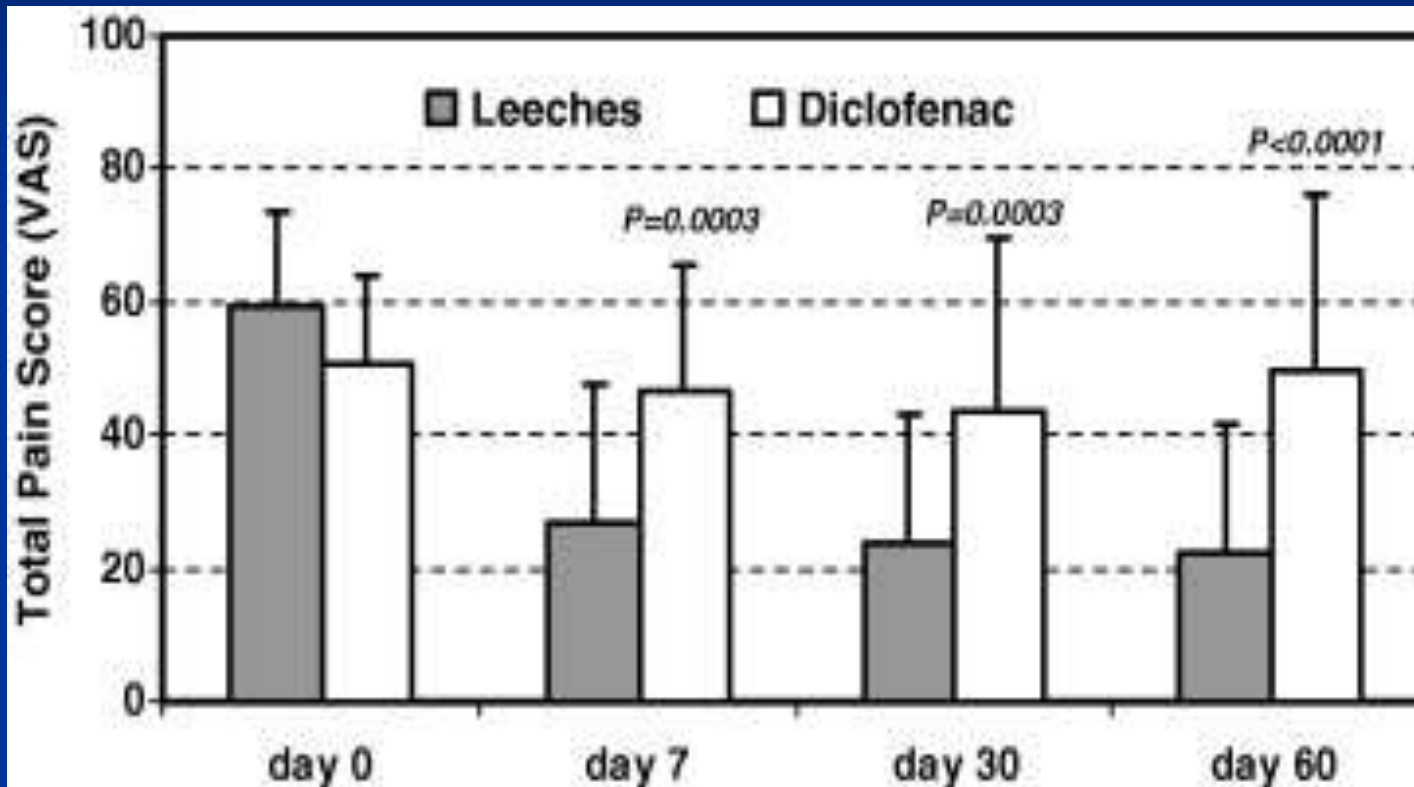


- **Meta-analysis: acupuncture for osteoarthritis of the knee.**
- Ann Intern Med. 2007; 146(12):868-77
- Compared to sham, acupuncture showed **clinically irrelevant** improvements in pain and function

# Unlikely Allies



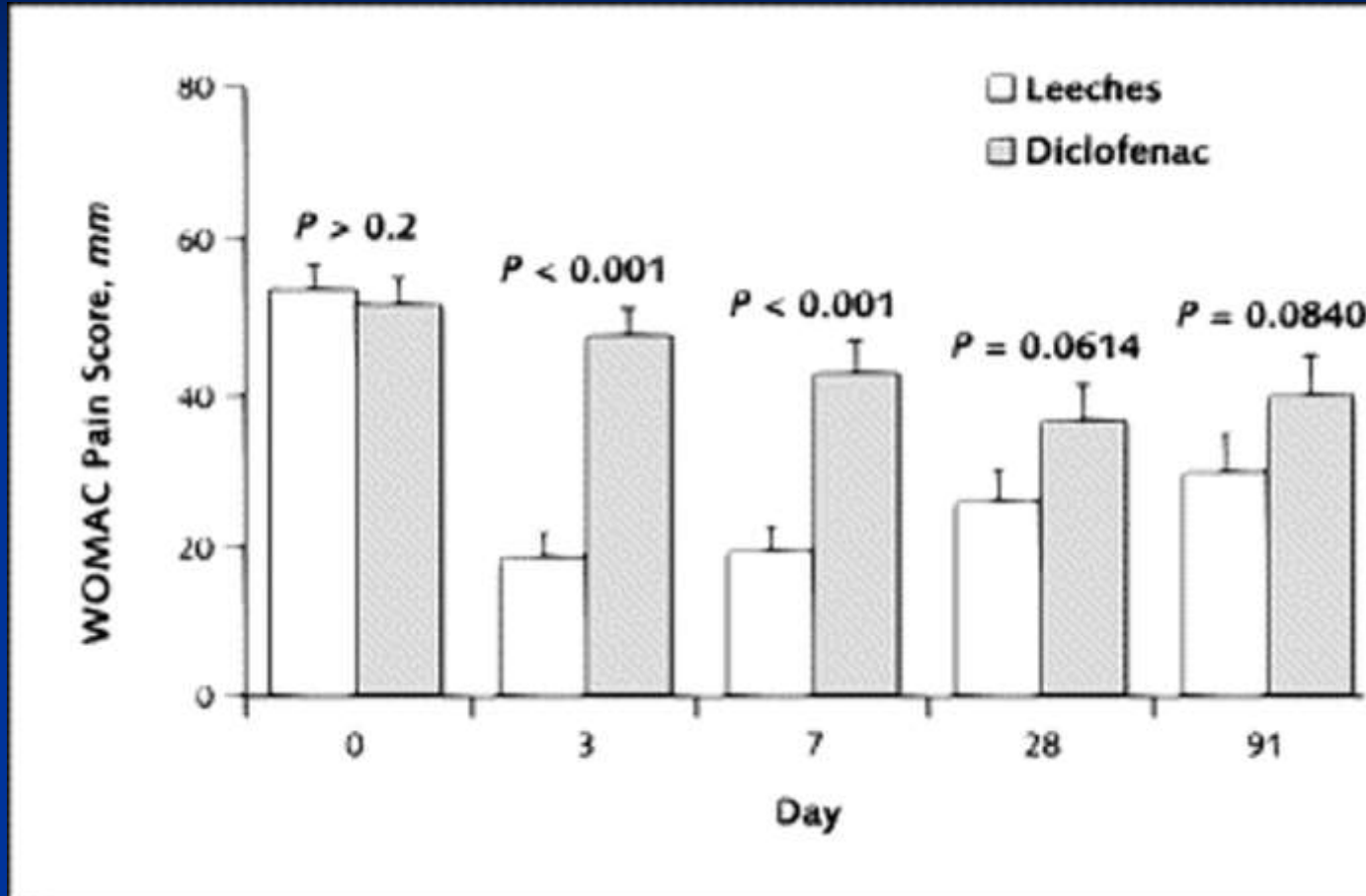
# Leeches and OA of the Thumb



disability in daily life as assessed by the DASH score improved rapidly with leech therapy. This effect was maintained at days 30 and 60 and resulted in significant group differences favoring leech therapy at all time points. [Pain](#) [Volume 137, Issue 2](#), 15 July 2008, Pages 452-459

# Leeches and OA of the Knee

## Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain score



Michalsen, A. et. al. Ann Intern Med 2003;139:724-730

# So if you are interested. . . .

- \$8 per leech and shipping,
- Can use every couple months, live a year
- (but each patient should have their own. . . .)

# Intra-articular Corticosteroids

- Significant benefit compared with placebo in most studies; however, the therapeutic effect is temporary at 1–4 weeks

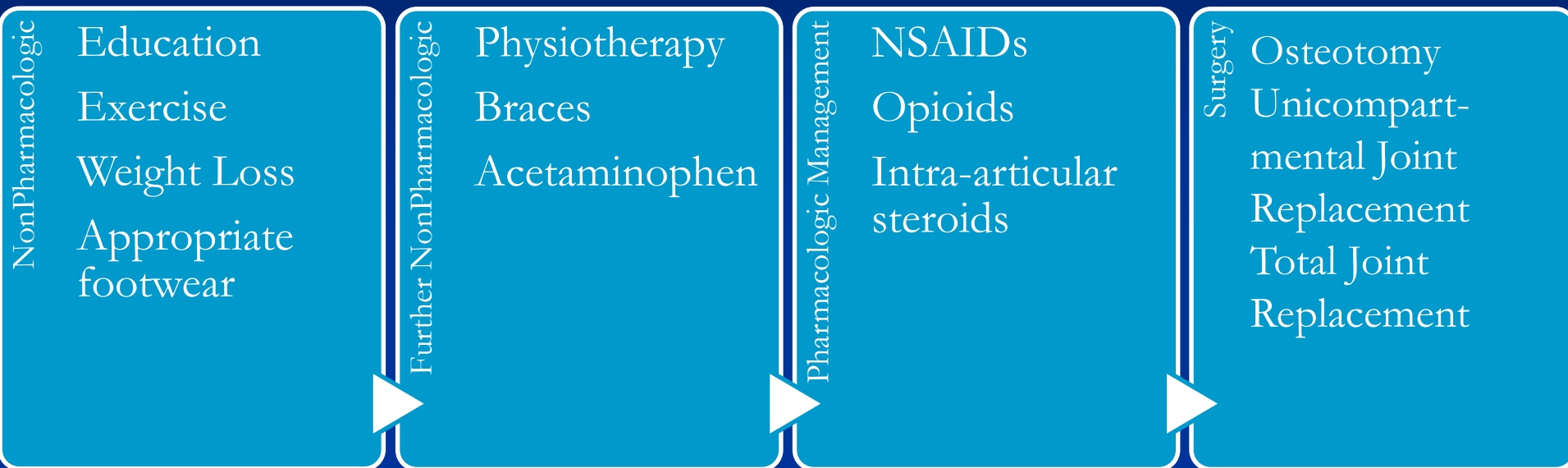
# Intra-articular Hyaluronic Acid

- 3-4 weekly injections of sodium hyaluronate provides significant pain relief in patients with OA of the knee for at least 60 days. A trend toward maintenance of therapeutic improvement is noted for up to a year in some patients
- benefit of a three-injection course of sodium hyaluronate appears to be equivalent to that of intra-articular steroids.

# Side Effects Intra-articular Steroids vs. Hyaluronic Acid

- Steroids are reported to cause:
  - Cystic lesions in cartilage, accelerated degeneration
  - Rare osteonecrosis, septic arthritis
- In most of the trials of hyaluronan and hyalin, rates of adverse reactions have been low (generally zero to 3%)
  - minor localized pain or effusion
  - Rare pseudogout; severe inflammation 1:500 (r/o infection, then inject steroid)

# Step Treatment



Mild

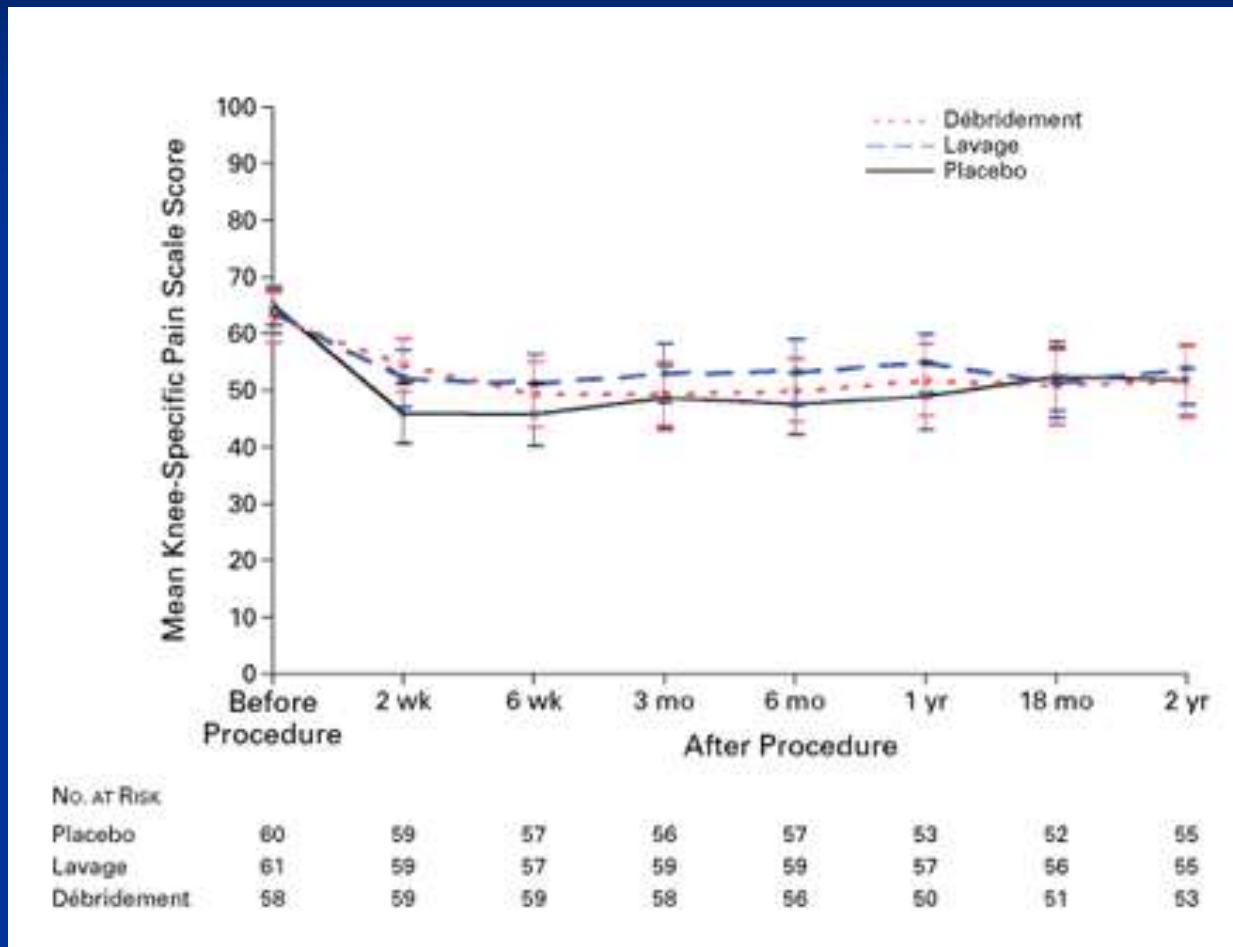
Symptom Severity

Severe

Why not arthroscopy?

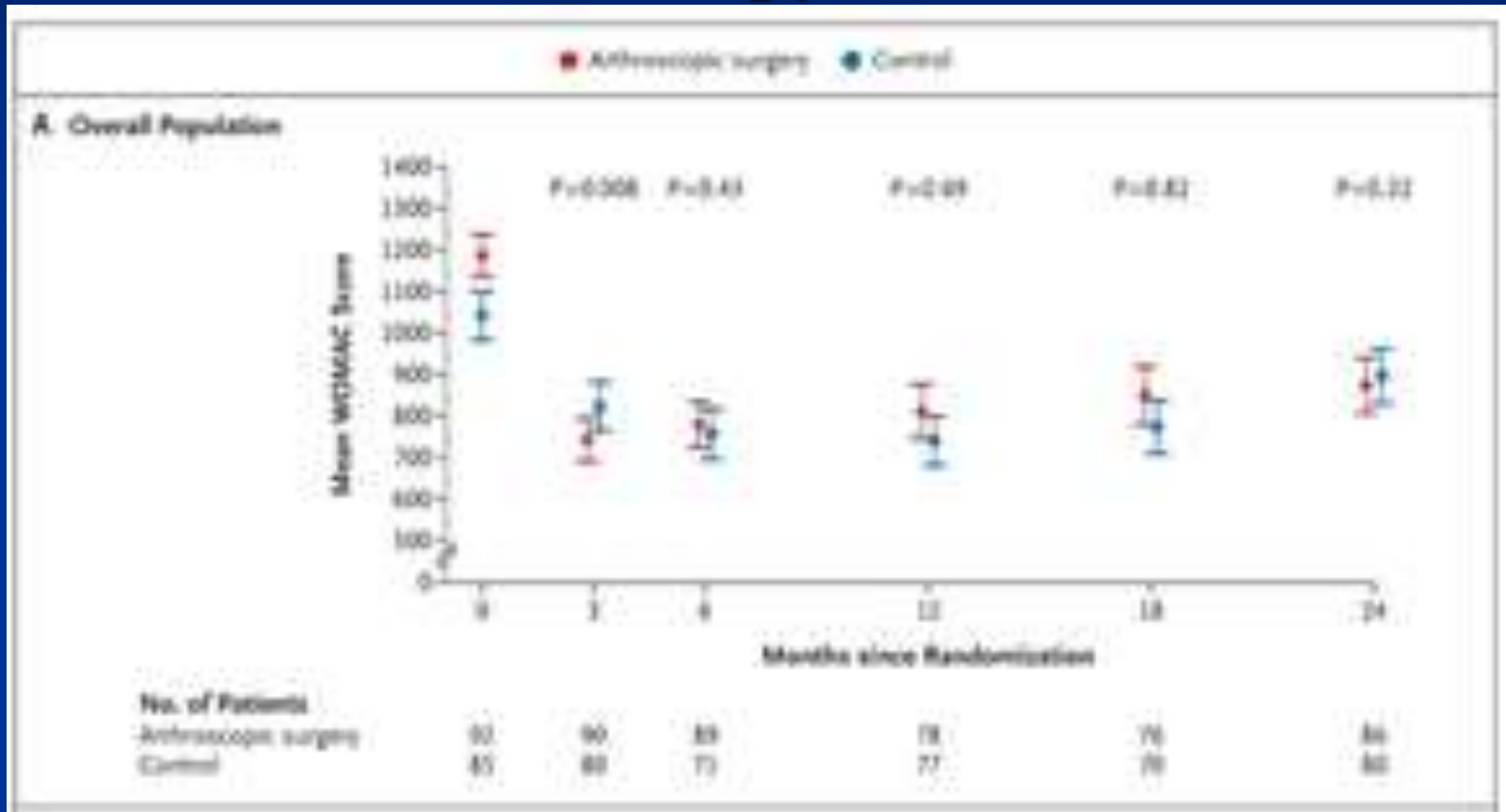
Osteoarthritis. BMJ 2006;332(7542):641

# Arthroscopy vs. Sham



NEJM Moseley et al. 347 (2): 81, Figure 1 July 11, 2002

# Arthroscopic Surgery and Optimized Physical and Medical Therapy vs. Latter 2 Alone



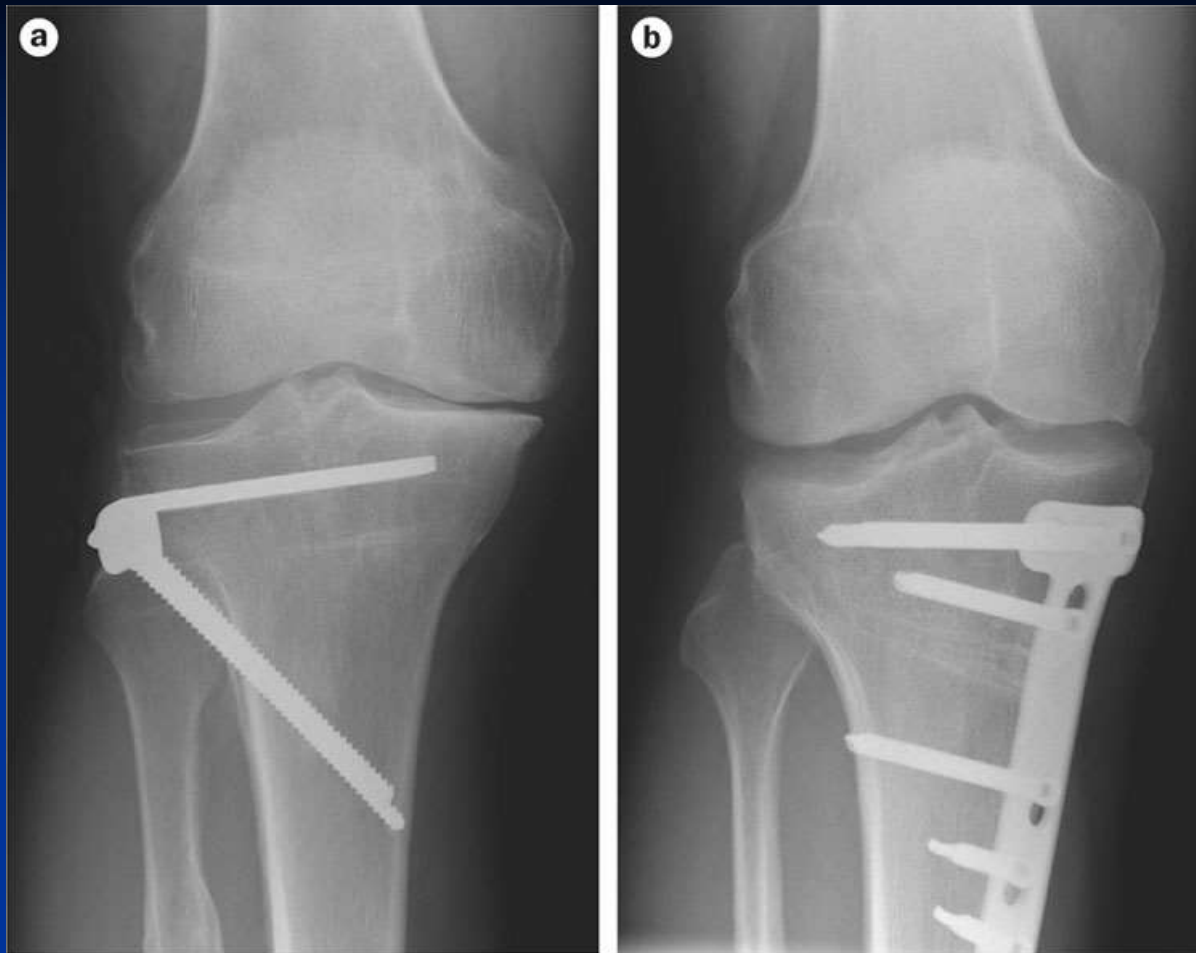
NEJM Volume 359:1097-1107 [September 11, 2008](#) Number 11

# Surgery

- 250,000 hips, 137,000 knees per year in US

# Osteotomy

- Cutting through the bone and fixing it in another position in order to change the alignment and, consequently, redistribute the weight load
- Recommended for younger, non-obese, high-functioning patients



Closing Wedge

Opening wedge

Overcorrect a varus malalignment and transfer the weight load to the intact lateral compartment

# Osteotomy outcomes

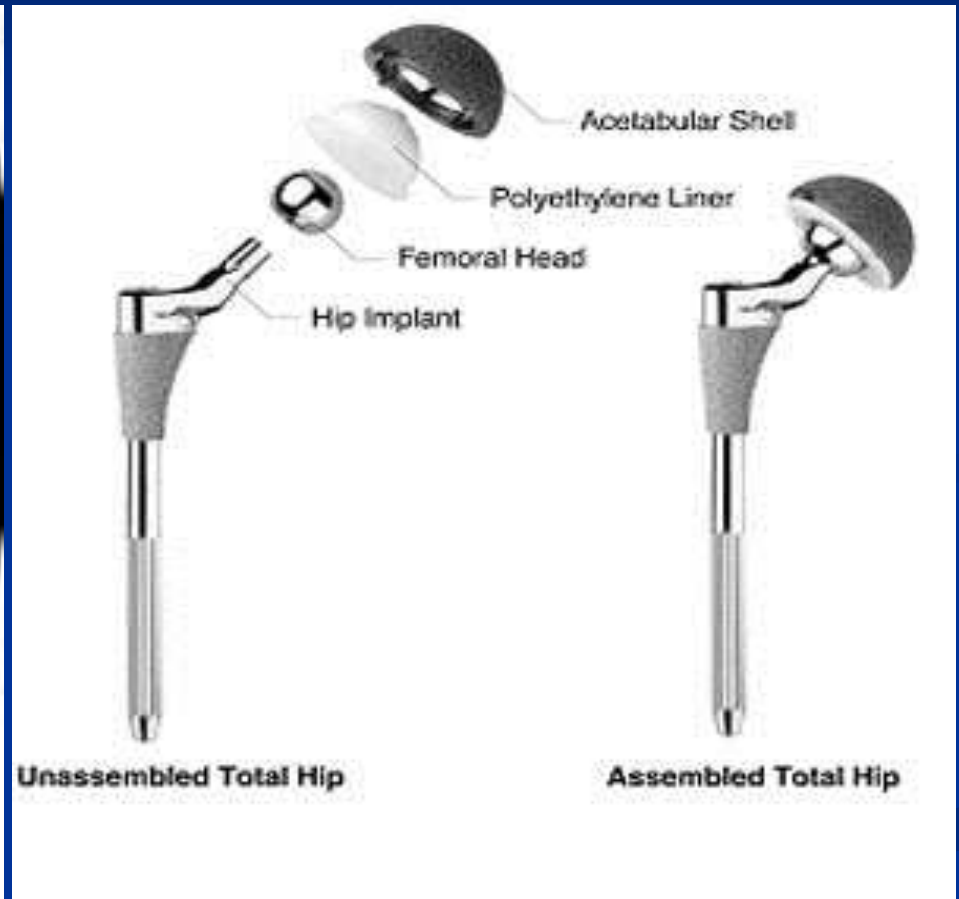
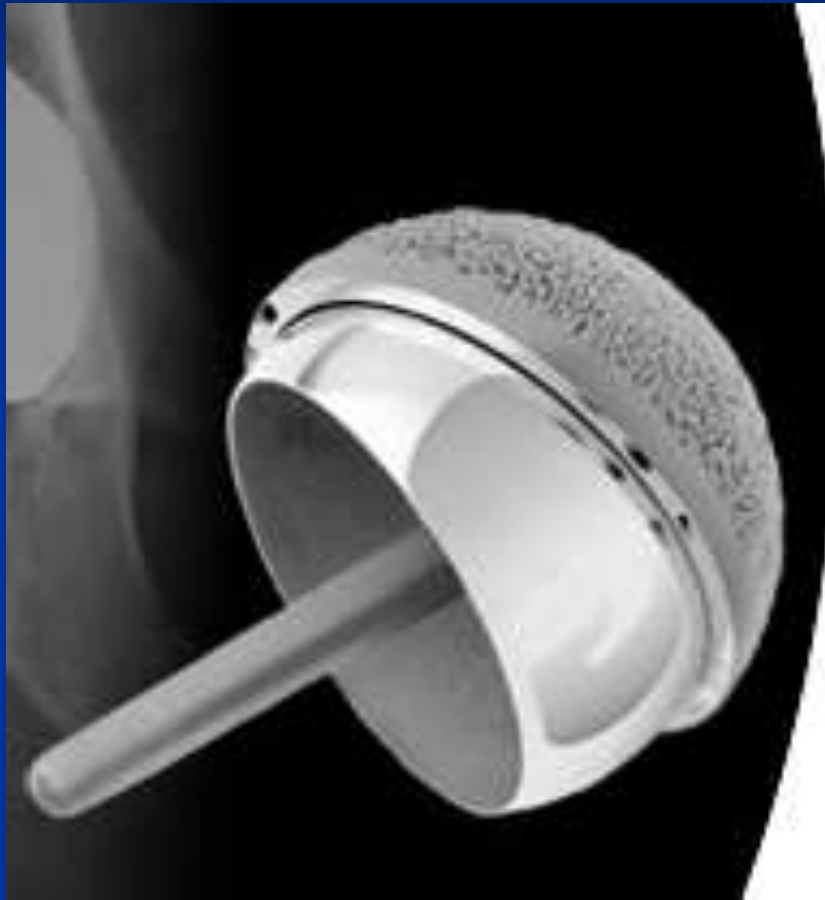
- Overall 10-year failure rate of 25%
- Average of 72 months btwn high tibial osteotomy and conversion to total knee arthroplasty.
- Probability of a 'good' or 'excellent' result:
  - 75% after 60 months
  - 60% after 100 months
- Arch. Orthop. Trauma Surg. 124, 258–261 (2004).

# Hip Resurfacing

- Complications led to revision surgery in 1.13% after 5 years (27 out of 2,385 hips.)

Effectiveness Measure*	5 years After Surgery
Survivorship: cases with device in place (not revised)	2,358 of 2,385 (98.5%)
OSHIP score: of patients with a good result (80 or better)	509 of 546 (93.2%)
Patient Satisfaction: patients who responded "Pleased" or "Extremely Pleased" with their results	543 of 546 (99.5%)

# Hip Resurfacing vs. THR

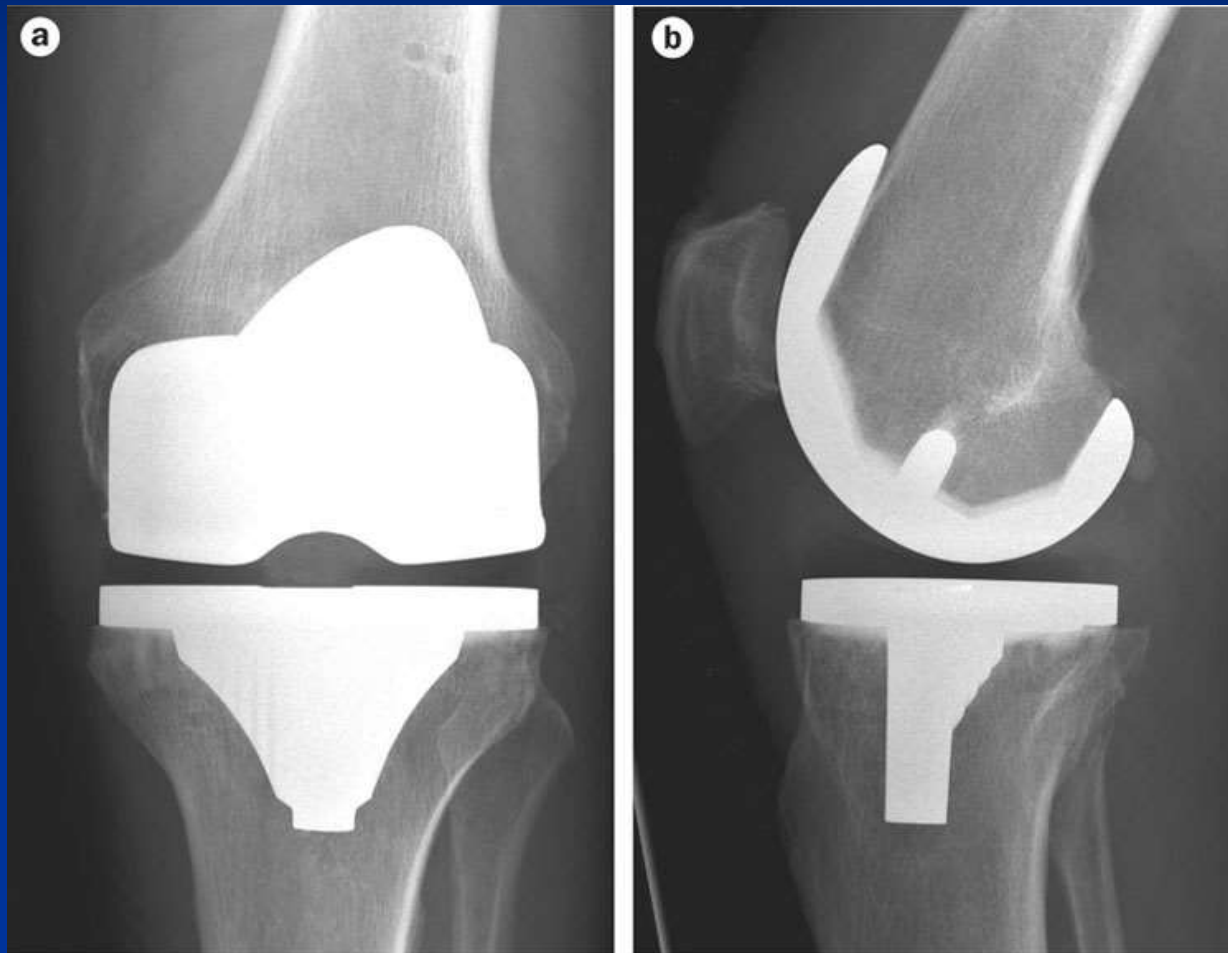


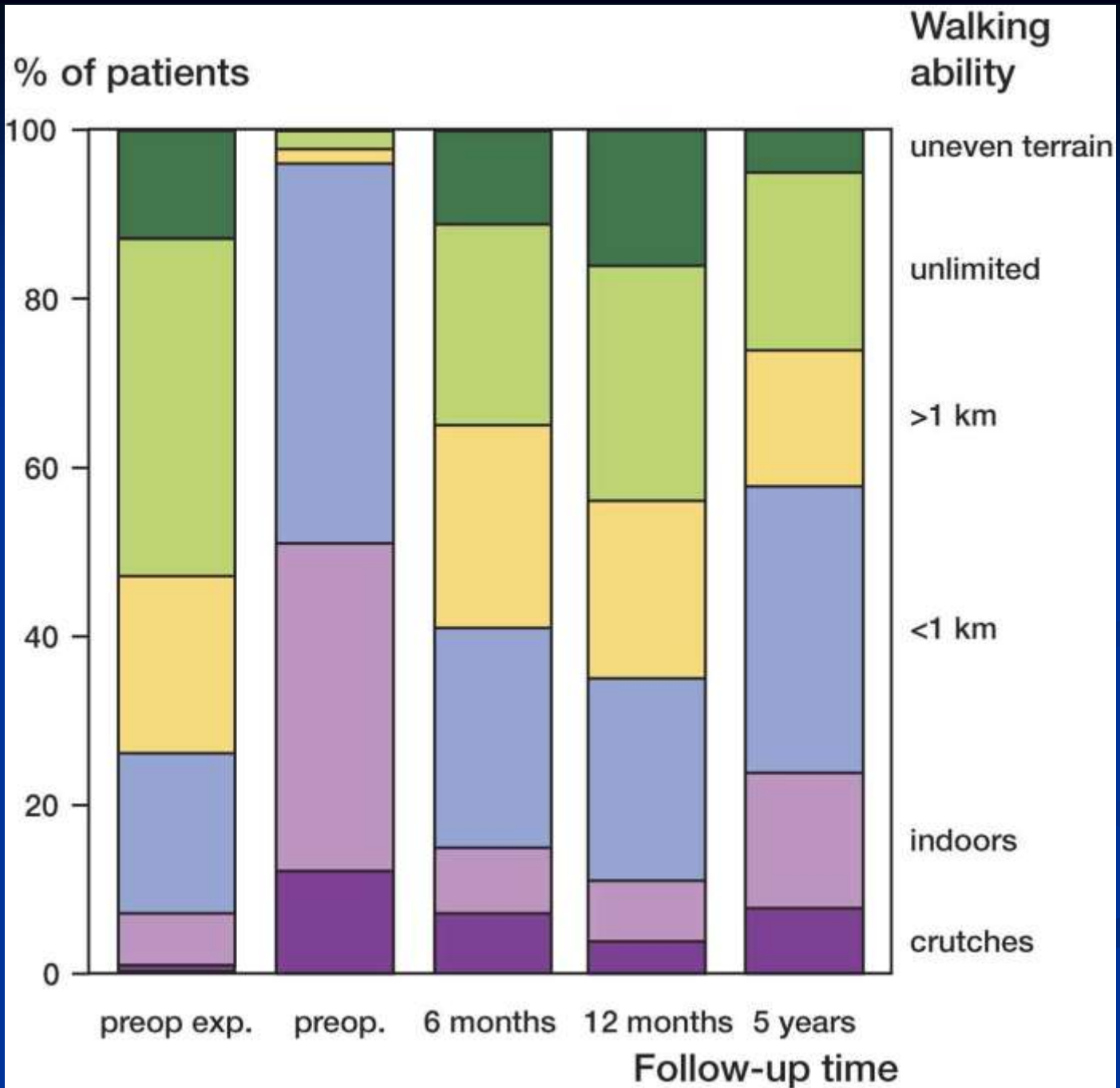
# Joint Replacement

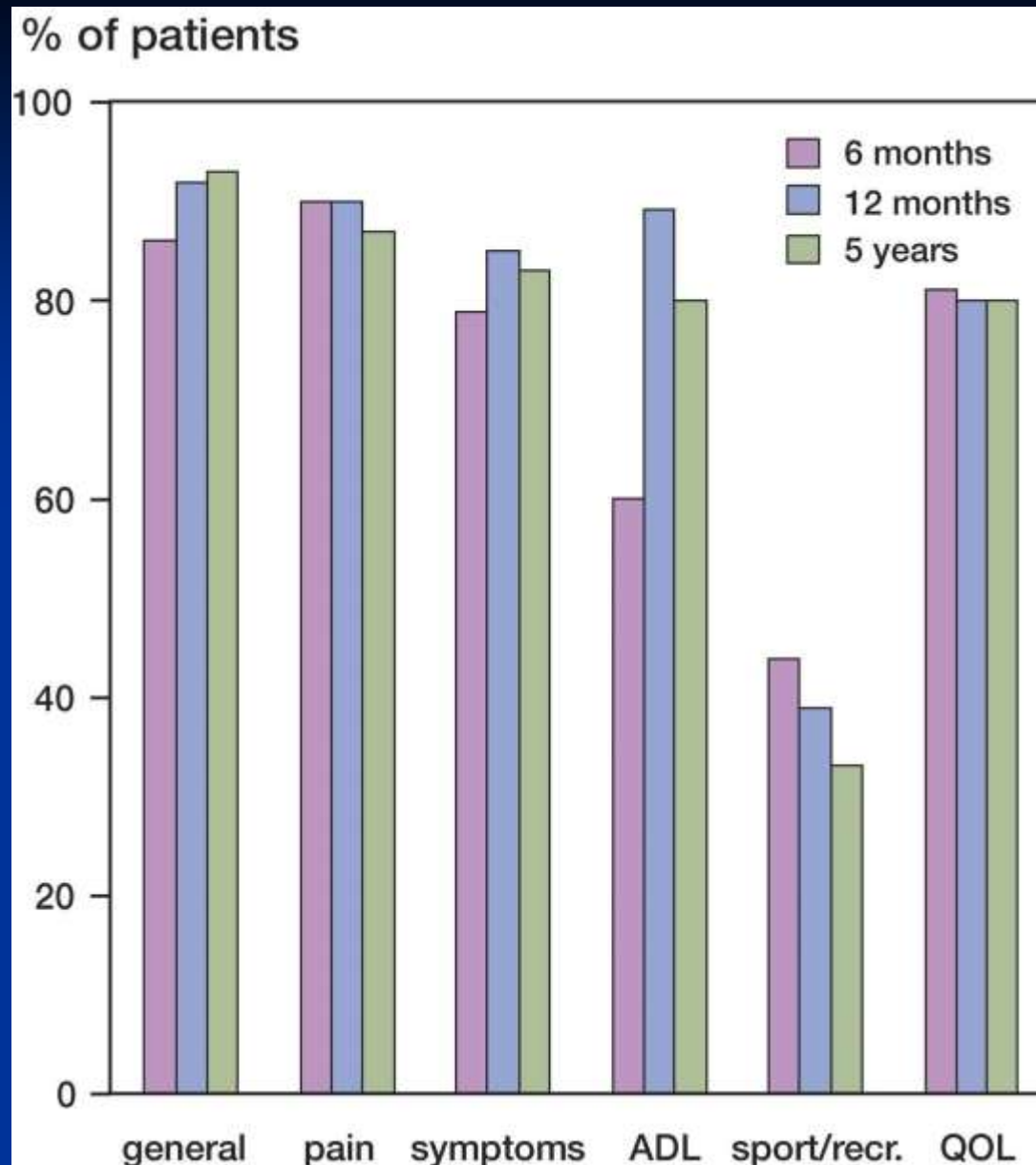
- Generally effective
- Generally safe
  - 90-day overall death rate was 0.31% (13 of 4253) J Bone Joint Surg Br. 2009 May;91(5):645-8
  - 222,684 patients in CA in the 90's
    - 1176 deaths (rate, 0.53%)
    - 1586 infections (0.71%)
    - 914 pulmonary emboli (0.41%) occurred within the first ninety days after discharge

*The Journal of Bone and Joint Surgery (American)*. 2006;88:480-485

# TKR







% Satisfied (extremely satisfied or very satisfied) at follow-up    Acta Orthopaedica,  
2009, 80( 1):55 - 61

# Joint Replacement Failures

- Remarkably higher risk of failure 10 years after implantation in patients aged 50 years and younger than in patients aged 70 years or older. Clin. Orthop. Relat. Res. 404, 102–107 (2002)

# The Mindbody Piece

- Severity on Xray has little correlation with symptoms
  - Knee OA: discordance of knee pain with radiographic OA
    - Stage 2-4 changes on xray: only 47% had knee pain
    - Knee pain – 15% had stage 2-4 changes on xray
- Journal of Rheumatology 2000; 27: 1513–1517
- Hip OA: similar Rheumatology 2005; 44: 337–341.

# Multidisciplinary Groups for Pain Management

- Improve pain management
  - Decrease depression
  - Decrease costs
  - May or may not increase functional level
- 
- Treatment Planning in Pain Medicine, Rollin M. Gallagher, MD, MPH, Medical Clinics of North America 83(3), May 1999
  - Caudill M, Schnable R, Zuttermeister P, et al: Decreased clinical utilization by chronic pain patients: Response to behavioral medicine intervention. Clin J Pain 7:305-310, 1991

# Program Materials

- <http://www.kcl.ac.uk/content/1/c6/04/79/67/escapeprogramme.pdf> - Escape programme, for self-management – handouts are there
- **Physiotherapy** Volume 95, Issue 2, June 2009, Pages 94-102
- <http://www.fullcircledmed.org/pain-management/>

# Patient Resources

- The Arthritis Foundation

Northern California Chapter 800-464-6240

<http://www.arthritis.org/>

- National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), Information Clearinghouse

877-22-NIAMS, <http://www.niams.nih.gov>