. «Συγκριτική εφαρμογή των θεραπειών της οστεοαρθρίτιδας»

Συντηρητική θεραπεία:
πότε, πώς, γιατί

Ευαγγελία Κασκάνη

Ρευματολόγος

Διδάκτωρ Πανεπιστημίου Αθηνών

Παθογένεια Οστεοαρθρίτιδας Συντηρητική θεραπεία

- Παρά την αυξημένη συχνότητα και βαριές επιπτώσεις της ΟΑ το ενδιαφέρον από ερευνητές και κλινικούς ιατρούς για την πάθηση αυτή ήταν περιορισμένο
- Βασικός παράγοντας η βασιζόμενη διαγνωστικά επιδημιολογική και κλινική προσέγγιση βάσει ακτινολογικής εικόνας που παρέπεμπε αναγκαστικά σε προχωρημένα στάδια της νόσου με απογοητευτικά αποτελέσματα θεραπευτικής παρέμβασης
- Σήμερα νέα δεδομένα για παράγοντες κινδύνου, παθογενετικούς μηχανισμούς, πρώιμη διάγνωση, δείκτες ενεργότητας νόσου οδηγούν σε πιο αποτελεσματικές θεραπευτικές παρεμβάσεις με αναπροσδιορισμό παλαιών θεραπευτικών μέτρων και στον σχεδιασμό και μελέτη εντελώς νέων θεραπευτικών στόχων

. «Συγκριτική εφαρμογή των θεραπειών της οστεοαρθρίτιδας»

Συντηρητική θεραπεία:

πότε;

EULAR evidence-based recommendations for the diagnosis of hand osteoarthritis: report of a task force of ESCISIT

W Zhang,[1] M Doherty,[1] B F Leeb,[2] L Alekseeva,[3] N K Arden,[4] J W Bijlsma,[5] F Dincer,[6] K Dziedzic,[7] H J Hauselmann,[8] P Kaklamanis,[9] M Kloppenburg,[10] L S Lohmander,[11] E Maheu,[12] E Martin-Mola,[13] K Pavelka,[14] L Punzi,[15] S Reiter,[16] J Smolen,[17] G Verbruggen,[18] I Watt,[19] I Zimmermann-Gorska[20]

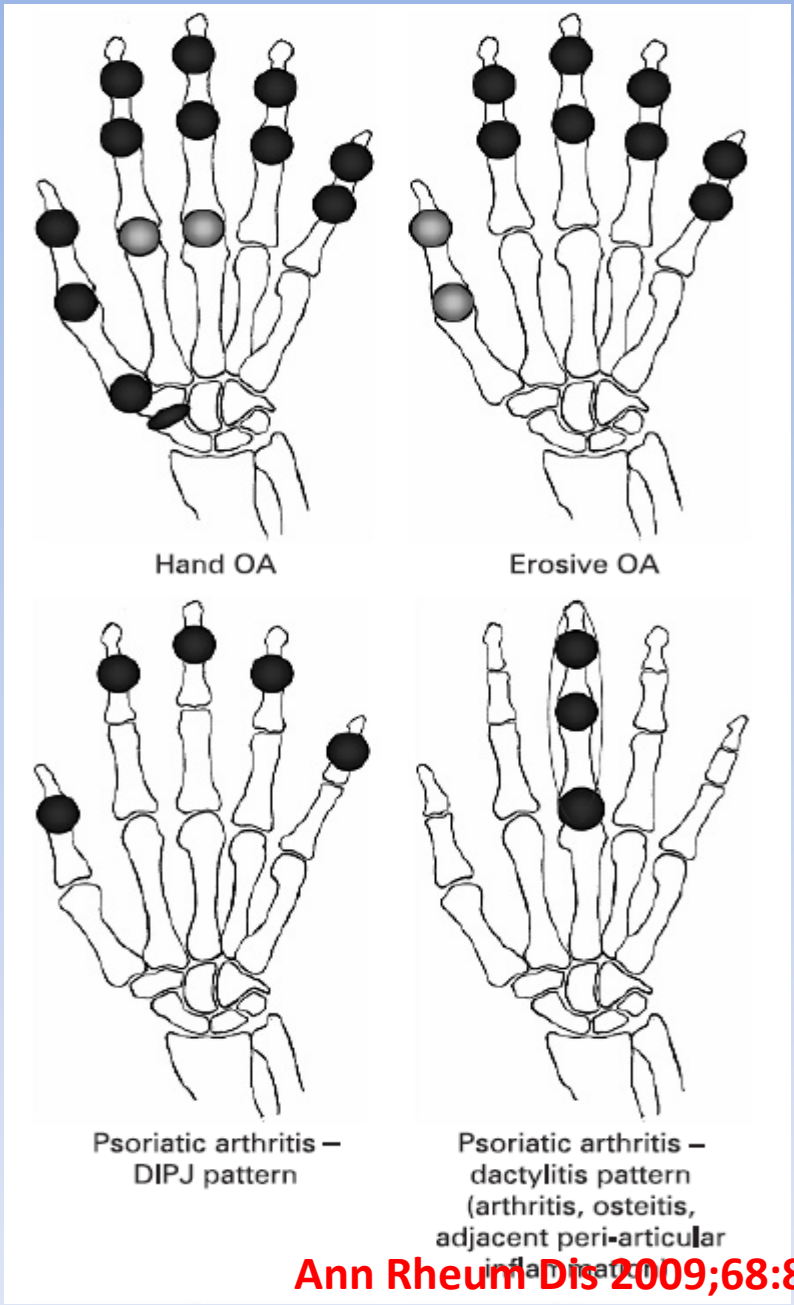
Ann Rheum Dis 2009;68:8–17. doi:10.1136/ard.2007.084772

Propositions and strength of recommendation (SOR) – order according to topic (risk factors, clinical, subsets, differential diagnosis, images and laboratory tests)

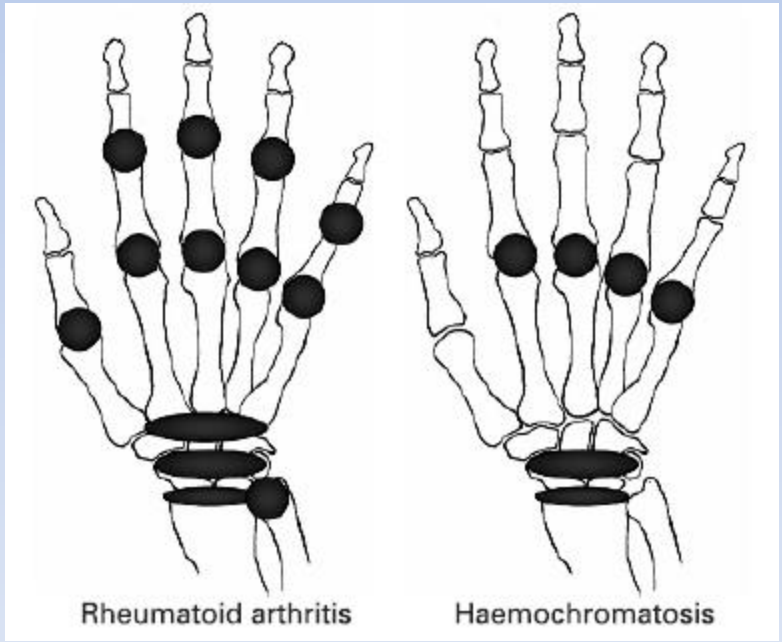
No.	Proposition	LoE	SOR (95% CI)
1	Risk factors for HOA include female sex, increasing age over 40, menopausal status, family history, obesity, higher bone density, greater forearm muscle strength, joint laxity, prior hand injury and occupation or recreation-related usage.	Ib–IIb	69 (54 to 84)
2	Typical symptoms of HOA are pain on usage and only mild morning or inactivity stiffness affecting just one or a few joints at any one time; symptoms are often intermittent and target characteristic sites (DIPJs, PIPJs, thumb base, index and middle MCPJs). With such typical features, a confident clinical diagnosis can be made in adults aged over 40.	IIb	85 (77 to 92)
3	Clinical hallmarks of HOA are Heberden and Bouchard nodes and/or bony enlargement with or without deformity (eg, lateral deviation of IPJs, subluxation and adduction of thumb base) affecting characteristic target joints (DIPJs, PIPJs, thumb base and index and middle MCPJs).	Ib–IV	80 (69 to 90)
4	Functional impairment in hand OA may be as severe as in rheumatoid arthritis. Function should be carefully assessed and monitored using validated outcome measures.	IIb	57 (42 to 73)
5	Patients with polyarticular HOA are at increased risk of knee OA, hip OA and OA at other common target sites (generalised OA) and should be assessed and examined accordingly.	IIa–IIb	77 (62 to 92)
6	Recognised subsets with different risk factors, associations and outcomes (requiring different assessment and management) include IPJ OA (with or without nodes), thumb base OA and erosive OA. Each may be symptomatic or asymptomatic.	IIa–IIb	68 (56 to 79)
7	Erosive hand OA targets IPJs and shows radiographic subchondral erosion, which may progress to marked bone and cartilage attrition, instability and bony ankylosis. Typically it has an abrupt onset, marked pain and functional impairment, inflammatory symptoms and signs (stiffness, soft tissue swelling, erythaema, paraesthesiae), mildly elevated CRP levels, and a worse outcome than non-erosive IPJ OA.	IIa–IIb	87 (81 to 93)
8	The differential diagnosis for HOA is wide. The commonest conditions to consider are psoriatic arthritis (which may target DIPJs or affect just one ray), rheumatoid arthritis (mainly targeting MCPJs, PIPJs, wrists), gout (which may superimpose on pre-existing HOA), and haemochromatosis (mainly targeting MCPJs, wrists).	Ib–IIb	81 (73 to 89)
9	Plain radiographs provide the gold standard for morphological assessment of HOA. A posteroanterior radiograph of both hands on a single film/field of view is adequate for diagnosis. Classical features are joint space narrowing, osteophyte, subchondral bone sclerosis and subchondral cyst, and subchondral erosion occurs in erosive hand OA. Further imaging modalities are seldom indicated for diagnosis.	Ib–IIb	87 (81 to 93)
10	Blood tests are not required for diagnosis of HOA but may be required to exclude coexistent disease. In a patient with HOA who has marked inflammatory symptoms and/or signs, especially involving atypical sites, blood tests should be undertaken to screen for additional inflammatory arthritides.	Ib–IIb	78 (63 to 92)

CRP, C-reactive protein; DIPJ, distal IPJ; IPJ, interphalangeal joint; HOA, hand osteoarthritis; LoE, level of evidence (see table 2 for further details), presented in range upon components assessed; MCPJ, metacarpophalangeal joints; PIPJ, proximal IPJ; SOR, strength of recommendation on visual analogue scale (0–100 mm, 0 = not recommended at all, 100 = fully recommended).

Ann Rheum Dis 2009;68:8–17. doi:10.1136/ard.2007.084772



Target sites of involvement with hand osteoarthritis (HOA),erosive OA, psoriatic arthritis, rheumatoid arthritis and haemochromatosis.



Ann Rheum Dis 2009;68:8–17. doi:10.1136/ard.2007.084772

EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis.

- **RESULTS:**
- Recommendations covered the definition of knee OA and its risk factors, subsets, typical symptoms and signs, the use of imaging and laboratory tests and differential diagnosis. Three symptoms (persistent knee pain, limited morning stiffness and reduced function) and three signs (crepitus, restricted movement and bony enlargement) appeared to be the most useful. Assuming a 12.5% background prevalence of knee OA in adults aged > or =45 years, the estimated probability of having radiographic knee OA increased with increasing number of positive features, to 99% when all six symptoms and signs were present. The performance of the recommendations in the study populations varied according to the definition of knee OA, background risk and number of tests applied.
- **CONCLUSION:**
- 10 key recommendations for diagnosis of knee OA were developed using both research evidence and expert consensus. Although there is no agreed reference standard, thorough clinical assessment alone can provide a confident rule-in diagnosis

Ann Rheum Dis 2010 Mar;69(3):483-9

. «Συγκριτική εφαρμογή των θεραπειών της οστεοαρθρίτιδας»

Συντηρητική θεραπεία:

πώς και γιατί;

1. ΧΕΡΙΑ

EXTENDED REPORT

EULAR evidence based recommendations for the management of hand osteoarthritis: Report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT)

W Zhang, M Doherty, B F Leeb, L Alekseeva, N K Arden, J W Bijlsma, F Dinçer, K Dziedzic, H J Häuselmann, G Herrero-Beaumont, P Kaklamanis, S Lohmander, E Maheu, E Martín-Mola, K Pavelka, L Punzi, S Reiter, J Sautner, J Smolen, G Verbruggen, I Zimmermann-Górska

Ann Rheum Dis 2007;66:377–388 doi:10.1136/ard.2006.062091

Experts' propositions developed through three Delphi rounds—order according to topic (general, non-pharmacological, pharmacological, invasive, and surgical)

No	Proposition	SOR (95% CI) VAS 100	A-B (%)
1	Optimal management of hand OA requires a combination of non-pharmacological and pharmacological treatment modalities individualised to the patient's requirements	95 (92 to 98)	100
2	Treatment of hand OA should be individualised according to localisation of OA; risk factors (age, sex, adverse mechanical factors); type of OA (nodal, erosive, traumatic); presence of inflammation; severity of structural change; level of pain, disability and restriction of quality of life; comorbidity and co-medication (including OA at other sites); and the wishes and expectations of the patient	84 (76 to 92)	92
3	Education concerning joint protection (how to avoid adverse mechanical factors) together with an exercise regimen (involving both range of motion and strengthening exercises) are recommended for all patients with hand OA	59 (45 to 74)	38
4	Local application of heat (for example, paraffin wax, hot pack), especially before exercise, and ultrasound are beneficial treatments		
	Overall	56 (40 to 71)	33
	Heat	77 (69 to 85)	77
	Ultrasound	25 (15 to 36)	0
5	Splints for thumb base OA and orthoses to prevent/correct lateral angulation and flexion deformity are recommended	67 (57 to 77)	69
6	Local treatments are preferred over systemic treatments, especially for mild to moderate pain and when only a few joints are affected. Topical NSAIDs and capsaicin are effective and safe treatments for hand OA	75 (68 to 83)	86
7	Because of its efficacy and safety paracetamol (up to 4 g/day) is the oral analgesic of first choice and, if successful, is the preferred long term oral analgesic	87 (78 to 96)	92
8	Oral NSAIDs should be used at the lowest effective dose and for the shortest duration in patients who respond inadequately to paracetamol. The patient's requirements and response to treatment should be re-evaluated periodically. In patients with increased gastrointestinal risk, non-selective NSAIDs plus a gastroprotective agent, or a selective COX-2 inhibitor (coxib) should be used. In patients with increased cardiovascular risk, coxibs are contraindicated and non-selective NSAIDs should be used with caution	81 (74 to 88)	100
9	SYSADOA (for example, glucosamine, chondroitin sulphate, avocado soybean unsaponifiables, diacerhein, intra-articular hyaluronan) may give symptomatic benefit with low toxicity, but effect sizes are small, suitable patients are not defined and clinically relevant structure modification, and pharmacoeconomic benefits have not been established	63 (48 to 76)	69
10	Intra-articular injection of long-acting corticosteroid is effective for painful flares of OA, especially trapeziometacarpal joint OA.	60 (47 to 74)	46
11	Surgery (for example, interposition arthroplasty, osteotomy or arthrodesis) is an effective treatment for severe thumb base OA and should be considered in patients with marked pain and/or disability when conservative treatments have failed	68 (56 to 79)	62

SOR, strength of recommendation; VAS, visual analogue scale; OA, osteoarthritis; NSAIDs, non-steroidal anti-inflammatory drugs; SYSADOAs, symptomatic slow acting drugs for osteoarthritis.

Ann Rheum Dis 2007;66:377–388 doi:10.1136/ard.2006.062091

Evidence of efficacy—pooled effect size (ES) and number needed to treat (NNT) for hand OA

Intervention*	Studies: Level*	No of studies (patients)	Duration	ES_{pain} (95% CI)	$ES_{function}$ (95% CI)	NNT (95% CI)	References
Education+exercise v OA information	Ib	1 (40)	3 months	–	–	2 (1 to 6)	19
Splint (full v half)	Ia	2 (47)	1 week	0.64 (0.02 to 1.26)	–	4 (2 to 13)	21, 22
NSAIDs	Ia	2 (654)	2–4 weeks	0.40 (0.20 to 0.60)	0.17 (−0.03 to 0.36)	3 (2 to 6)	23, 24
Topical NSAIDs	Ia	2 (131)	2–3 hours	0.77 (0.32 to 1.22)	–	NS	25
Topical capsaicin	Ia	2 (318)	4 weeks	–	–	3 (2 to 5)	26
Chondroitin sulphate	Ib	1 (92)	3 years	–	–	NS	27
Chondroitin polysulphate	Ib	1 (130)	3 years	–	–	8 (4 to 166)	27
IA corticosteroid	Ib	1 (40)	24 weeks	NS	NS	NS	28
Surgery	Ia	7 (384)	3–66 months				
T+LRTI/IA v T				−0.17 (−0.57 to 0.24)	0.03 (−0.37 to 0.44)	NS	29
TJR v T+IA				−0.3 (−1.07 to 0.47)	–	–	29

*Compared with placebo, unless otherwise stated; †see table 1 for definitions

No, number of studies; ES, effect size of treatment compared with placebo unless otherwise stated; NNT, number needed to treat to obtain moderate to excellent (more than 50%) pain relief or symptomatic improvement; –, not available; NS, not significant; T, trapeziectomy; LRTI, ligament reconstruction and tendon interposition; IA, interposition arthroplasty; TJR, total joint replacement.

Ann Rheum Dis 2007;66:377–388 doi:10.1136/ard.2006.062091

Evidence of safety—pooled relative risk (RR) or odds ratio (OR)* and 95% confidence interval (CI)

Intervention†	Adverse events	RR/OR (95% CI)	Evidence	References
Paracetamol	GI discomfort	0.80 (0.27 to 2.37)	RCTs	48
	GI perforation/bleed	3.60 (2.60 to 5.10)	Case-control study	49
	GI bleeding	1.2 (0.8 to 1.7)	Case-control studies	50
	Renal failure	2.5 (1.7 to 3.6)	Case-control study	51
	Renal failure	0.83 (0.50 to 1.39)	Cohort study	52
Topical NSAIDs	GI events	0.81 (0.43 to 1.56)	RCTs	25
	GI bleed/perforation	1.45 (0.84 to 2.50)	Case-control	42
Glucosamine sulphate preparations	Any	0.97 (0.88 to 1.08)	RCTs	53
Diacerhein	Diarrhoea	3.98 (2.90 to 5.47)	RCTs	54, 55
NSAIDs	GI perforation/ulcer/bleed	5.36 (1.79 to 16.10)	RCTs	56
	GI perforation/ulcer/bleed	2.70 (2.10 to 3.50)	Cohort studies	56
	GI perforation/ulcer/bleed	3.00 (2.70 to 3.70)	Case-control studies	56
GI protective strategies versus NSAID alone				
H2 blocker+NSAID	Serious GI complications	0.33 (0.01 to 8.14)	RCTs	57
	Symptomatic ulcers	1.46 (0.06 to 35.53)	RCTs	57
	Serious CV or renal events	0.53 (0.08 to 3.46)	RCTs	57
PPI+NSAID	Serious GI complications	0.46 (0.07 to 2.92)	RCTs	57
	Symptomatic ulcers	0.09 (0.02 to 0.47)	RCTs	57
	Serious CV or renal events	0.78 (0.10 to 6.26)	RCTs	57
Misoprostol+NSAID	Serious GI complications	0.57 (0.36 to 0.91)	RCTs	57
	Symptomatic ulcers	0.36 (0.20 to 0.67)	RCTs	57
	Serious CV or renal events	1.78 (0.26 to 12.07)	RCTs	57
	Diarrhoea	1.81 (1.52 to 2.61)	RCTs	58
COX-2 selective	Serious GI complications	0.61 (0.34 to 1.10)	RCTs	57
	Symptomatic ulcers	0.41 (0.26 to 0.65)	RCTs	57
	Serious CV or renal events	0.95 (0.55 to 1.66)	RCTs	57
COX-2 specific (coxibs)	Serious GI complications	0.55 (0.38 to 0.80	RCTs	57
	Symptomatic ulcers	0.49 (0.38 to 0.62)	RCTs	57
	Serious CV or renal events	1.19 (0.80 to 1.75)	RCTs	57
Surgery				
T+LRTI/IA *v* T	Any	2.12 (1.24 to 3.60)	RCTs	29
TJR *v* T+IA	Any	5.00 (0.26 to 95.02)	RCTs	29

Ann Rheum Dis 2007;66:377–388 doi:10.1136/ard.2006.062091

*RR was calculated for an RCT or cohort study and OR was for a case-control study. RR (or OR) = 1: no difference between treatment and control; RR (or OR)>1: more risky with treatment; RR <1: less risky with treatment. The results were pooled if more than one study was involved; †compared with placebo/non-exposure unless otherwise stated.

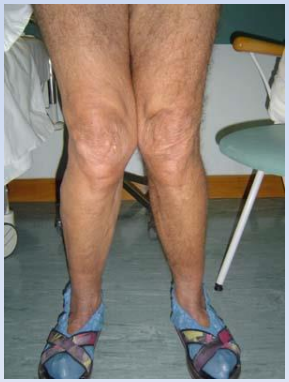
H_2-blockers, histamine type 2 receptor antagonists; PPIs, proton pump inhibitors; GI, gastrointestinal; CV, cardiovascular; CNS, central nervous system; T, trapeziectomy; LRTI, ligament reconstruction and tendon interposition; IA, interposition arthroplasty; TJR, total joint replacement.

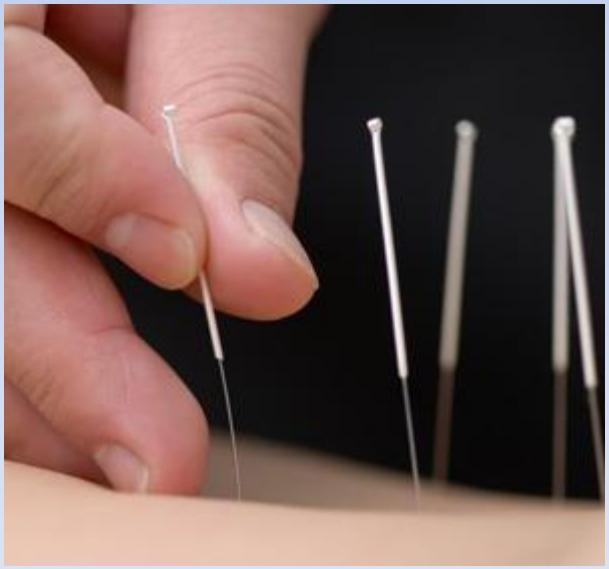
. «Συγκριτική εφαρμογή των θεραπειών της οστεοαρθρίτιδας»

Συντηρητική θεραπεία:

πώς και γιατί;

1. ΙΣΧΙΟ-ΓΟΝΑΤΟ





Osteoarthritis and Cartilage (2008) **16**, 137–162

doi:10.1016/j.joca.2007.12.013

Osteoarthritis and Cartilage

ICRS International Cartilage Repair Society

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines

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Συστάσεις μη φαρμακευτικής αντιμετώπισης (1-2)

1. Η θεραπεία της οστεορθρίτιδας συμπεριλαμβάνει μη φαρμακευτική και φαρμακευτική αντιμετώπιση
2.

- Οι ασθενείς με ΟΑ ισχίου ή γόνατος πρέπει να έχουν πρόσβαση στην ενημέρωση και εκπαίδευση για τους θεραπευτικούς στόχους και την σημασία της αλλαγής τρόπου ζωής και δραστηριοτήτων, άσκησης, απώλειας βάρους και άλλων μέτρων που είναι αναγκαία για την αποφόρτιση της πάσχουσας άρθρωσης.
- Επικέντρωση στην σημασία του ενεργού ρόλου του ασθενούς στην θεραπευτική παρέμβαση και όχι στην παθητική συμμετοχή
- Έμφαση στην συμμόρφωση στις μη φαρμακευτικές παρεμβάσεις

Osteoarthritis and Cartilage (2008) 16, 137e162

Συστάσεις μη φαρμακευτικής αντιμετώπισης (3-6)

- 3. The clinical status of patients with hip or knee OA can be improved if patients are contacted regularly by phone.
- 4. Patients with symptomatic hip and knee OA may benefit from referral to a physical therapist for evaluation and instruction in appropriate exercises to reduce pain and improve functional capacity. This evaluation may result in provision of assistive devices such as canes and walkers, as appropriate.
- 5. Patients with hip and knee OA should be encouraged to undertake, and continue to undertake, regular aerobic, muscle strengthening and range of motion exercises. For patients with symptomatic hip OA, exercises in water can be effective.
- 6. Patients with hip and knee OA, who are overweight, should be encouraged to lose weight and maintain their weight at a lower level

Osteoarthritis and Cartilage (2008) 16, 137e162

Συστάσεις μη φαρμακευτικής αντιμετώπισης (7-12)

- 7. Walking aids can reduce pain in patients with hip and knee OA. Patients should be given instruction in the optimal use of a cane or crutch in the contralateral hand. Frames or wheeled walkers are often preferable for those with bilateral disease.
- 8. In patients with knee OA and mild/moderate varus or valgus instability, a knee brace can reduce pain, improve stability and diminish the risk of falling.
- 9. Every patient with hip or knee OA should receive advice concerning appropriate footwear. In patients with knee OA insoles can reduce pain and improve ambulation. Lateral wedged insoles can be of symptomatic benefit for some patients with medial tibio-femoral compartment OA.
- 10. Some thermal modalities may be effective for relieving symptoms in hip and knee OA.
- 11. TENS can help with short-term pain control in some patients with hip or knee OA.
- 12. Acupuncture may be of symptomatic benefit in patients with kneeOA.

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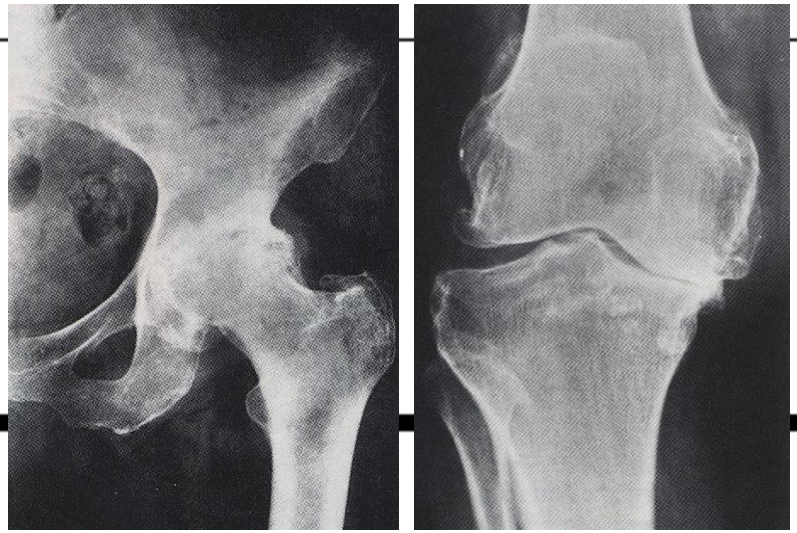
Osteoarthritis and Cartilage 18 (2010) 476–499

Osteoarthritis and Cartilage



OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

OARSI recommendations for the management of hip and knee osteoarthritis Part III: changes in evidence following systematic cumulative update of research published through January 2009

W. Zhang*, G. Nuki, R.W. Moskowitz, S. Abramson, R.D. Altman, N.K. Arden, S. Bierma-Zeinstra, K.D. Brandt, P. Croft, M. Doherty, M. Dougados, M. Hochberg, D.J. Hunter, K. Kwoh, L.S. Lohmander, P. Tugwell

Affiliations for Committee members' can be found in the following section: Members of the OARSI Treatment Guidelines Committee

Table I

Best evidence for efficacy for various modalities of therapy for hip and knee OA available 31 January 2009

Modality	Joint	QoS (%)	LoE	Best evidence until 31 January 2009			
				ES_{pain} (95% CI)	$ES_{function}$ (95% CI)	$ES_{stiffness}$ (95% CI)	NNT (95% CI)
Non-pharmacological							
Self-management	Both	100	Ia	0.06 (0.02, 0.10)[10,11,*]	0.06 (0.02, 0.10)[10,11,*]	0.01 (−0.12, 0.15)[10,*]	
Telephone	Both	100	Ia	0.12 (0.00, 0.24)[154]	0.07 (0.00, 0.15)[154]		
Education	Both	100	Ia	0.06 (0.03, 0.10)[11,12,*]	0.06 (0.02, 0.10)[11]		
Strengthening	Knee	100	Ia	0.32 (0.23, 0.42)[20]	0.32 (0.23, 0.41)[20]		
	Hip*	100*	Ia*	0.38 (0.08, 0.68)[15,*]			
Aerobic	Knee	100	Ia	0.52 (0.34, 0.70)[20]	0.46 (0.25, 0.67)[20]		
Water-based exercise	Both	100*	Ia*	0.19 (0.04, 0.35)[13,*]	0.26 (0.11, 0.42)[13,*]	0.17 (−0.05, 0.39)[155]	
Balneotherapy	Knee	75	Ia				NS[156]
Spa/sauna	Both	75	Ib	0.46 (0.17, 0.75)[157]			NS
Weight reduction	Knee	100*	Ia*	0.20 (0.00, 0.39)[21,*]	0.23 (0.04, 0.42)[21,*]	0.36 (−0.08, 0.80)[158]	3 (2, 9)[158]
TENS	Both	75	Ia				2 (1, 5)[159]
Laser	Both	100	Ia				4 (2,17)[160]
Ultrasound	Both	50	Ia	0.06 (−0.39, 0.52)[161]			
Radiotherapy	Both	50	IIb	Similar effects between OA and RA from an MA of uncontrolled trial[162]			
Heat/ice	Knee	75	Ia	0.69 (−0.07, 1.45)[163]	1.03 (0.44, 1.62)[163] for quads strength; 1.13 (0.54, 1.73)[163] for flexion	0.83(−0.03, 1.69)[163] for swelling	
Massage	Knee	40	Ib	0.10 (−0.23, 0.43)[164]			
Acupuncture	Knee	100*	Ia*	0.35 (0.15, 0.55)[23,*]	0.35 (0.14, 0.56)[23,*]	0.41 (0.13, 0.69)[30]	4 (3, 9)[30]
Insoles	Knee	100	Ia	No different between type of insoles, no placebo/usual care comparisons[165]			
Joint protection (braces)	Knee	100	Ia	More benefits with a knee brace than a neoprene sleeve[165]			
Electrotherapy/EMG	Knee	100*	Ia*	0.16 (−0.08, 0.39)[31,*]	0.33 (0.07, 0.59)[31,*]		

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Non-pharmacological therapies, ES for pain relief

Table II
Comparison of ESs and LoE for pain relief with different modalities of therapy in 2006 and 2009

	31 January 2006 ES (95% CI), LoE	31 January 2009 ES (95% CI), LoE
Self-management	0.06 (0.02, 0.10), Ia	0.06 (0.02, 0.10), Ia
Education/information	0.06 (0.02, 0.10), Ia	0.06 (0.03, 0.10), Ia
Exercise for knee OA		
Strengthening	0.32 (0.23, 0.42), Ia	0.32 (0.23, 0.42), Ia
Aerobic	0.52 (0.34, 0.70), Ia	0.52 (0.34, 0.70), Ia
Exercise for hip OA	NA	0.38 (0.08, 0.68), Ia
Exercise in water for knee & hip OA	0.25 (0.02, 0.47), Ib	0.19 (0.04, 0.35), Ia
Weight reduction	0.13 (−0.12, 0.36), Ib	0.20 (0.00, 0.39), Ia
Acupuncture	0.51 (0.23, 0.79), Ib	0.35 (0.15, 0.55), Ia
Electromagnetic therapy	0.77 (0.36, 1.17), Ia	0.16 (−0.08, 0.39), Ia
Acetaminophen	0.21 (0.02, 0.41), Ia	0.14 (0.05, 0.22), Ia
NSAIDs	0.32 (0.24, 0.39), Ia	0.29 (0.22, 0.35), Ia
Topical NSAIDs	0.41 (0.22, 0.59), Ia	0.44 (0.27, 0.62), Ia
Opioids	NA	0.78 (0.59, 0.98), Ia
IA corticosteroid	0.72 (0.42, 1.02), Ia	0.58 (0.34, 0.75), Ia
IAHA	0.32 (0.17, 0.47), Ia	0.60 (0.37, 0.83), Ia
GS	0.61 (0.28, 0.95), Ia	0.58 (0.30, 0.87), Ia
GH	NA	−0.02 (−0.15, 0.11), Ib
CS	0.52 (0.37, 0.67), Ia	0.75 (0.50, 1.01), Ia
Diacerein	0.22 (0.01, 0.42), Ib	0.24 (0.08, 0.39), Ib
ASU	NA	0.38 (0.01, 0.76), Ia
Rosehip	NA	0.37 (0.13, 0.60), Ia
Lavage/debridement	0.09 (−0.27, 0.44), Ib	0.21 (−0.12, 0.54), Ib

NA: not available.

- Unchanged for self management, education, exercise and acupuncture.
- Statistical significance increasing , or weight reduction from 0.13 [in 2006 to 0.20 in 2009.
- By contrast, the ES for electromagnetic therapy which was large in 2006 (ES Ó 0.77, was no longer significant (ES Ó 0.16)

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Table I

Best evidence for efficacy for various modalities of therapy for hip and knee OA available 31 January 2009

Modality	Joint	QoS (%)	LoE	Best evidence until 31 January 2009			
				ES_{pain} (95% CI)	$ES_{function}$ (95% CI)	$ES_{stiffness}$ (95% CI)	NNT (95% CI)
Pharmacological							
Acetaminophen	Both	100	Ia	0.14 (0.05, 0.23)[32,34,*]	0.09 (−0.03, 0.22)[34,166,167,*]	0.16 (−0.05, 0.37)[166,168,*]	3 (2, 52)[34–36,*]
NSAIDs	Both	100	Ia	0.29 (0.22, 0.35)[44,*]			
NSAIDs + PPIs	OA/RA	100	Ia				
NSAIDs + H2-blockers	OA/RA	100	Ia				
NSAIDs + misoprostol	OA/RA	100	Ia				
Cox-2 inhibitors	Both	100	Ia	0.44 (0.33, 0.55)[169] (exc Deek's for OA/RA)			
Topical NSAIDs	Knee	100	Ia	0.44 (0.27, 0.62)[48–51,*]	0.36 (0.24, 0.48)[48]	0.49 (0.17, 0.80)[48]	3 (2, 4)[48]
Topical capsaicin	Knee	75	Ia				4 (3, 5)[170]
Opioids	Any*	100*	Ia*	0.78 (0.59, 0.98)[58,*]	0.31 (0.24, 0.39)[58,*]		
IA corticosteroid	Knee	100	Ia	0.58 (0.34, 0.75)[44,*]	0.20 (−0.14, 0.53)[61,*]	0.25 (−0.23, 0.74)[61,*]	5 (3, 38)[61,*]
IAHA	Knee	100	Ia	0.60 (0.37, 0.83)[65,*]	0.61 (0.35, 0.87)[65,*]	0.54 (−0.17, 1.26)[65,*]	7 (3, 119)[65,*]
GS	Both	100	Ia	0.58 (0.30, 0.87)[34,80,82,*]	0.07 (−0.08, 0.21)[84]	0.06 (−0.11, 0.23)[84]	5 (4, 7)[96]
GH*	Knee*	–	Ib*	−0.02 (−0.15, 0.11)[81,171,172,*]			
CS	Knee	100	Ia	0.75 (0.50, 1.01)[95,*]			5 (4, 7)[96]
Diacerhein	Both	–	Ib	0.24 (0.08, 0.39)[112–115,119,120,*]	0.14 (0.03, 0.25)[112–115,119,120,*]		
ASU	Both*	100*	Ia*	0.38 (0.01, 0.76)[99,*]	0.45 (0.21, 0.70)[99,*]		6 (4, 21)[99,*]
Rosehip*	Both*	100*	Ia*	0.37 (0.13, 0.60)[108,*]			6 (4, 13)[108,*]
SAM-e	Knee	100	Ia	0.22 (−0.25, 0.69)[106]	0.31 (0.10, 0.52)[106]		

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Ακεταμινοφαίνη

OARSI recommendations for the management of hip and knee osteoarthritis, Part II, 2008

- **13.** Η ακεταμινοφαίνη (paracetamol) (up to 4 g/day) μπορεί να χρησιμοποιηθεί με αποτελεσματικότητα για την αντιμετώπιση ελαφρού έως μέτριου πόνου σε ασθενείς με ΟΑ ισχίου ή γόνατος
- Σε περίπτωση μη αποτελεσματικότητας ή σε περίπτωση έντονου πόνου ή φλεγμονής πρέπει να σκεφτούμε εναλλακτικές αγωγές συνυπολογίζοντας την αποτελεσματικότητα, ασφάλεια, άλλα φάρμακα που λαμβάνει ο ασθενείς και συννοσηρότητα
- SOR: 92% (95% CI 88e99)

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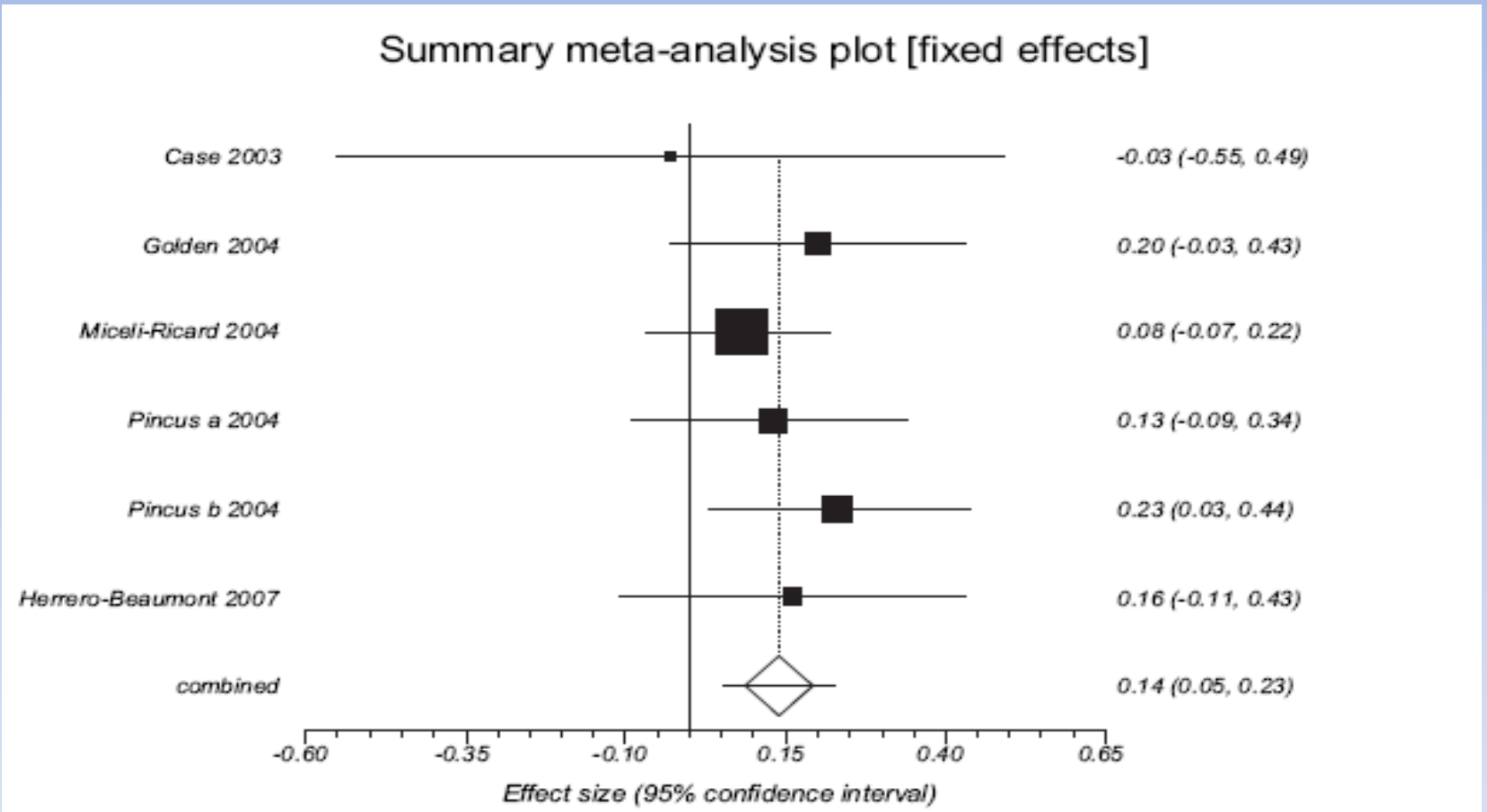
Ακεταμινοφαίνη

Ομοιγένεια μελετών με μέγεθος επίδρασης μείωση μη στατιστικά σημαντική στον πόνο (ES) 0.14 (0.05, 0.23)



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Test for heterogeneity:
Cochran Q = 2.10 (df = 5) P = 0.8353
I^2 (inconsistency) = 0% (95% CI = 0% to 61%)

Ακεταμινοφαίνη
Ανεπιθύμητες ενέργειες

- Επιδημιολογική μελέτη (cohort study n 644,183) έδειξε ότι αγωγή με υψηλές δόσεις (>3 g/day) acetaminophen σχετίστηκε με αυξημένο κίνδυνο νοσηλείας λόγω διάτρησης στομάχου, έλκους και γαστορραγίας από ότι η αγωγή με χαμηλές δόσεις (3 g/day) με HR of 1.20 (1.03, 1.40)
- Στοιχεία για ήπια έκπτωση νεφρικής λειτουργίας σε ασθενείς με μακροχρόνια χορήγηση υψηλών δόσεων (OR= 2.04, 95% CI 1.28, 3.24) για μείωση της GFR)> 30 ml/min
- Στοιχεία από προοπτική μελέτη για αύξηση της συχνότητας υπερτασης σε γυναίκες που ελάμβαναν > 500 mg acetaminophen ημερησίως και άνδρες που ελάμβαναν καθημερινά acetaminophen σε σχέση με μη χρήστες (RR =1.34, 95% CI 1.00, 1.79)

1)Am J Gastroenterol 2008;103:872–82. 2)Arch Intern Med 2004;164:1519–24. 3)Arch Intern Med 2002;162:2204–8. 4)Arch Intern Med 2007;167:394–9.

Ακεταμινοφαίνη Ανεπιθύμητες ενέργειες– Νέες Συστάσεις

- Λόγω αυξανόμενων αμφιβολιών για το στενό παράθυρο της ακεταμινοφαίνης για ηπατοτοξικότητα, συμβουλευτική επιτροπή του FDA πρόσφατα συστήνει η μέγιστη ημερήσια δόση να είναι χαμηλότερη από 4g και η περιεκτικότητα ανά δόση των OTC να μην υπερβαίνει τα 650 mg

FDA. Drug Safety Information, http://www.fda.gov/Drugs/DrugSafety/informationbydrugclass/ucm165107.htm; 2009.

Μη στεροειδή αντιφλεγμονώδη (NSAIDs)

OARSI recommendations for the management of hip and knee osteoarthritis, Part II, 2008

- **14.** Σε ασθενείς με συμπτωματική ΟΑ ισχίου, γόνατος NSAIDs μπορεί να χορηγηθούν στην χαμηλότερη δραστική δόση, αλλά η μακροχρόνια χορήγηση πρέπει να αποφεύγεται
- Σε ασθενείς με αυξημένο κίνδυνο από το γαστρεντερικό μπορεί να χορηγηθούν εκλεκτικοί COX-2 αναστολείς ή μη εκλεκτικοί COX-2 αναστολείς με συνχορήγηση αναστολέα της αντλίας πρωτονίων (PPI) ή μικροπροστόλης
- Τα NSAIDs, συμπεριλαμβανομένων εκλεκτικών ή μη εκλεκτικών COX-2 αναστολείς πρέπει να χορηγούνται με προσοχή σε ασθενείς με αυξημένο καρδιαγγειακό (CV) κίνδυνο
- SOR: 93% (95% CI 88e99)

Osteoarthritis and Cartilage (2008) 16, 137e162

Μη στεροειδή αντιφλεγμονώδη (NSAIDs)-Επίδραση στον πόνο

OARSI recommendations for the management of hip and knee osteoarthritis, Part III, 2010

Comparison of ESs and LoE for pain relief with different modalities of therapy in 2006 and 2009

	31 January 2006 ES (95% CI), LoE	31 January 2009 ES (95% CI), LoE
NSAIDs	0.32 (0.24, 0.39), Ia	0.29 (0.22, 0.35), Ia

- Αν και η επίδραση στον πόνο είναι μικρή ή μέτρια είναι διπλάσια από αυτήν της acetaminophen (ES=0.14, 95% CI 0.05, 0.23)
- Υπεροχή των NSAIDs σε σχέση με την acetaminophen από Head to head συγκρίσεις (ES =0.20, 95% CI 0.10, 0.30)
- Αυξημένη κλινική ανταπόκριση (RR=1.24, 95% CI 0.10, 1.41) και αριθμός ασθενών που προτιμούν NSAIDs από acetaminophen (RR = 2.46, 95% CI 1.50, 4.12)33.

•Osteoarthritis and Cartilage 18 (2010) 476–499
•Ann Rheum Dis 2004;63:901–7.

Μη στεροειδή αντιφλεγμονώδη (NSAIDs)- Ανεπιθύμητες ενέργειες

Table IV
Side effects associated with pharmacological therapies

Intervention*	Adverse events	RR/OR (95% CI)	Evidence (references)
NSAIDs	GI perforation/ulcer/bleed	5.36 (1.79, 16.10)	Meta-RCTs[180]
	GI perforation/ulcer/bleed	2.70 (2.10, 3.50)	Meta-CSs[180]
	GI perforation/ulcer/bleed	3.00 (2.50, 3.70)	Meta-CCs[180]
	GI hospitalisation†	1.63 (1.44, 1.85)†	CS[37],†
	Myocardial infarction	1.09 (1.02, 1.15)	Meta-CSs[181]
Topical NSAIDs	GI events	0.81 (0.43, 1.56)	Meta-RCTs[48]
	GI bleed/perforation	1.45 (0.84, 2.50)	Case–control[53]
NSAID + H2-blocker vs NSAID	Serious GI complications	0.33 (0.01, 8.14)	Meta-RCTs[182]
	Symptomatic ulcers	1.46 (0.06, 35.53)	Meta-RCTs[182]
	Serious CV or renal events	0.53 (0.08, 3.46)	Meta-RCTs[182]
NSAID + PPI vs NSAID	Serious GI complications	0.46 (0.07, 2.92)	Meta-RCTs[182]
	Symptomatic ulcers	0.09 (0.02, 0.47)	Meta-RCTs[182]
	Serious CV or renal events	0.78 (0.10, 6.26)	Meta-RCTs[182]
Cox-2 inhibitors + PPI vs Cox-2 inhibitors†	Recurrent ulcer bleeding†	8.9% vs 0%†	RCT[45],†
	GI hospitalisation†	0.69 (0.52, 0.93)†	CS[46],†
NSAID + misoprostol vs NSAID	Serous GI complications	0.57 (0.36, 0.91)	Meta-RCTs[182]
	Symptomatic ulcers	0.36 (0.20, 0.67)	Meta-RCTs[182]
	Serious CV or renal events	1.78 (0.26, 12.07)	Meta-RCTs[182]
	Diarrhea	1.81 (1.52, 2.61)	Meta-RCTs[183]
Cox-2 inhibitors			
Coxibs vs NSAID	Serious GI complications	0.55 (0.38, 0.80)	Meta-RCTs[182]
	Symptomatic ulcers	0.49 (0.38, 0.62)	Meta-RCTs[182]
	Serious CV or renal events	1.19 (0.80, 1.75)	Meta-RCTs[182]
Celecoxib	Myocardial infarction	2.26 (1.00, 5.10)	Meta-RCTs[184]
	Myocardial infarction	0.97 (0.86, 1.08)	Meta-CSs/CCs[181]
Rofecoxib	Myocardial infarction	2.24 (1.24, 4.02)	Meta-RCTs[149]
	Myocardial infarction	1.27 (1.12, 1.44)	Meta-CSs/CCs[181]
Valdecoxib	CV events	2.30 (1.10, 4.70)	Meta-RCTs[185]

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Σύσταση 15. Τοπική χρήση NSAIDs

Table I
Best evidence for efficacy for various modalities of therapy for hip and knee OA available 31 January 2009

Modality	Joint	QoS (%)	LoE	Best evidence until 31 January 2009			
				ES_{pain} (95% CI)	$ES_{function}$ (95% CI)	$ES_{stiffness}$ (95% CI)	NNT (95% CI)
Topical NSAIDs	Knee	100	Ia	0.44 (0.27, 0.62)	0.36 (0.24, 0.48)	0.49 (0.17, 0.80)	3 (2, 4)

- Η τοπική χρήση NSAIDs συνιστάται σαν εναλλακτική αγωγή της συμπτωματικής ΟΑ γόνατος σε 7/9 guidelines έως το 2006 και πιο πρόσφατα (NICE και OARSI)
- Στις παλαιότερες μελέτες ετερογένεια αποτελεσματικότητας μεταξύ διαφόρων προιόντων (I=69%) →Publication bias με υποεκτίμηση των μελετών με μη ευνοικά αποτελέσματα
- Στις νεώτερες μελέτες αποτελεσματικότητα παρόμοια και ασφάλεια μεγαλύτερη από την συστηματική χορήγηση αν και πρόσφατη cost-utility μελέτη έδειξε ότι στον δεύτερο χρόνο χορήγησης ibuprofen από το στόμα ήταν αποτελεσματικότερη από τα την τοπική εφαρμογή (cost per QALY oral ibuprofen/topical ibuprofen: £27,130 το 2009)

Evans JM, MacDonald TM. Tolerability of topical NSAIDs in the elderly: do they really convey a safety advantage? Drugs Aging 1996;9:101–8.
Evans JMM, McMahon AD, McGilchrist MM, White G, Murray FE, McDevitt DG, *et al*. Topical non-steroidal anti-inflammatory drugs and admission to hospital for upper gastrointestinal bleeding and perforation: a record linkage case–control study. BMJ 1995;311:22–6.
Tugwell PS, Wells GA, Shainhouse JZ. Equivalence study of a topical diclofenac solution (Pennsaid) compared with oral diclofenac in symptomatic treatment of osteoarthritis of the knee: a randomized controlled trial. J Rheumatol 2004;10:2002–12.
Underwood M, Ashby D, Cross P, Hennessy E, Letley L, Martin J, *et al*. Advice to use topical or oral ibuprofen for chronic knee pain in older people: randomised controlled trial and patient preference study. BMJ 2008;336:138–42.

Σύσταση 15. Τοπική χρήση Καπσαικίνης

- Lipophilic alkaloid extracted from chilli peppers
- Burning pain at the site of application, it can also be an effective topical analgesic which is recommended as an alternative or adjunctive treatment for knee OA in 8/9 existing treatment guidelines
- Evidence for the efficacy of topical capsaicin (0.025% cream 4 daily) in patients with knee OAis supported by an MA of RCTs of topical capsaicin in the treatment of chronic painful conditions
- The mean reduction in pain was 33% with an NNT of 4 (95% CI 3, 5) after 4 weeks of therapy but adequate blinding is not possible in trials with this agent
- Treatment with topical capsaicin is safe but 40% of patients are troubled by local burning, stinging or erythema

Baron R. Capsaicin and nociception: from basic mechanisms to now drugs. Lancet 2000;356:785–7.
Zhang WY, Li Wan Po A. The effectiveness of topically applied capsa icin. A meta-analysis. Eur J Clin Pharmacol 1994;46:517–22.
Deal CL, Schnitzer TJ, Lipstein E, Seibold JR, Stevens RM, Levy MD *et al*. Treatment of arthritis with topical capsaicin: a double-blind tria Clin Ther 1991;13:383–95.

Ενδαρθρική έγχυση κορτικοστεροειδών

OARSI recommendations for the management of hip and knee osteoarthritis, Part II, 2008

- **16.**Ενδαρθρικές εγχύσεις κορτικοστεροειδών μπορεί να χρησιμοποιηθούν στην θεραπεία ΟΑ ισχίου και γόνατος ειδικά σε ασθενείς με μέτριο έως σοβαρό πόνο που δεν απαντά στα αναλγητικά/αντιφλεγμονώδη και σε ασθενείς με συμπτωματική ΟΑ γόνατος με ύδραρθρο και άλλα σημεία τοπικής φλεγμονής
- SOR: 78% (95% CI 61e95)

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Ενδαρθρική έγχυση κορτικοστεροιδών

OARSI recommendations for the management of hip and knee osteoarthritis, Part III, 2010

Table I
Best evidence for efficacy for various modalities of therapy for hip and knee OA available 31 January 2009

Modality	Joint	QoS (%)	LoE	Best evidence until 31 January 2009			
				ES_{pain} (95% CI)	$ES_{function}$ (95% CI)	$ES_{stiffness}$ (95% CI)	NNT (95% CI)
IA corticosteroid	Knee	100	Ia	0.58 (0.34, 0.75)[44,*]	0.20 (−0.14, 0.53)[61,*]	0.25 (−0.23, 0.74)[61,*]	5 (3, 38)[61,*]

- The ES for relief of pain following single injections of IA corticosteroid was relatively large; 0.72, 1 week following injection. However, this fell to 0.28 (0.17, 0.73) after 4 weeks and 0.21
- Treatment may need to be repeated at frequent intervals to maintain efficacy
- A long-term trial of IA corticosteroid injections every 3 months for 2 years showed that while there was efficacy for relief of pain after 1 year (ES =0.67) this was not demonstrable after 2 years (ES =0.25)

- Osteoarthritis and Cartilage 18 (2010) 476–499
- Eur J Pain 2007;11:125–38.
- Cochrane Database Syst Rev 2006. CD005328.

Υαλουρονικό οξύ ή υαλουρονάνη

OARSI recommendations for the management of hip and knee osteoarthritis, Part II, 2008

- **17.** Εγχύσεις υαλουρονικού οξέως μπορεί να βοηθήσουν ασθενείς με ΟΑ γόνατος ή ισχίου
- Δεν έχουν άμεσο αποτέλεσμα αλλά έχουν παρατεταμένη δράση στα συμπτώματα σε σχέση με τις ενδαρθρικές εγχύσεις κορτικοστεροειδών
- SOR: 64% (95% CI 43e85)

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Γλυκοζαμίνη

OARSI recommendations for the management of hip and knee osteoarthritis, Part II, 2008

- **18.** Θεραπεία με γλυκοζαμίνη και/ή θεική χονδροιτίνη μπορεί να έχει ευνοικά αποτελέσματα στα συμπτώματα ασθενών με ΟΑ γόνατος
- Εάν δεν απαντήσουν σε 6 μήνες η θεραπεία πρέπει να διακόπτεται
- SOR: 63% (95% CI 44-82)
  - ES_{pain} = 0.61 (95% CI: 0.28-0.95)
    $ES_{function}$ = 0.51 (95% CI: 0.05-0.96)
  - Μεγάλη ετερογένεια αποτελεσμάτων στις διάφορες μελέτες
  - Η μεγαλύτερη διαφορά ανάμεσα σε διαφορετικά σκευάσματα GS και μεταξύ GS και GH

Osteoarthritis and Cartilage (2008) 16, 137e162

Γλυκοζαμίνη

OARSI recommendations for the management of hip and knee osteoarthritis, Part III, 2010

Modality	Joint	Best evidence until 31 January 2009		
		ES pain (95% CI)	ES function (95% CI)	ES stiffness (95%CI)
GS	Both	0.58 (0.30, 0.87)	0.07 (0.08, 0.21)	0.06 (0.11, 0.23)
GH*	Knee	0.02 (0.15, 0.11)		

- Σημαντική ετερογένεια ευρημάτων (I2=87%, P <0.0001)
- Σημαντικά στοιχεία publication bias (P =0.002 using the Egger test)

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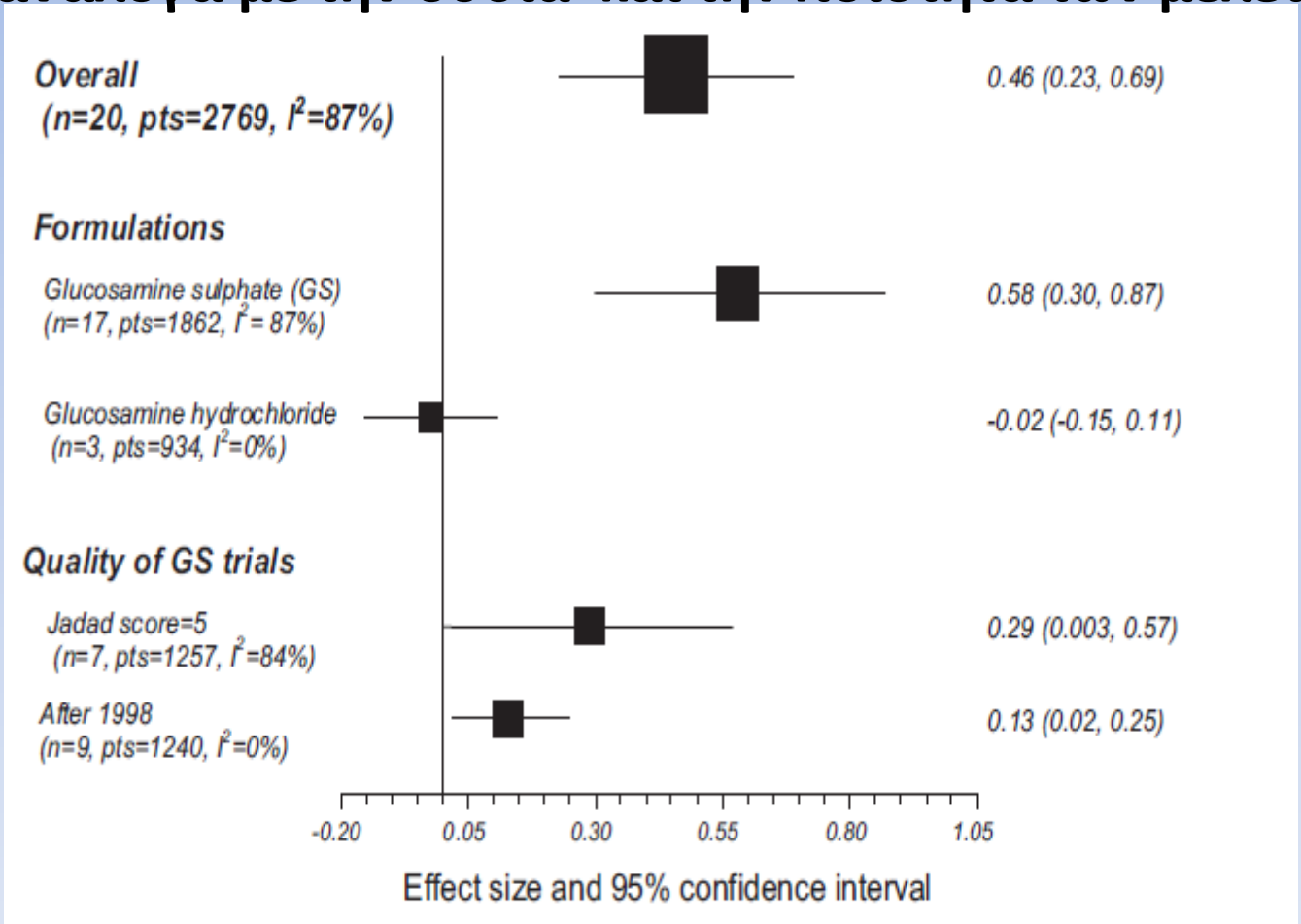
Γλυκοζαμίνη

OARSI recommendations for the management of hip and knee osteoarthritis, Part III, 2010

Αναλγητική επίδραση της glucosamine στην OA: ανάλυση RCTsανάλογα με την ουσία και την ποιότητα των μελετών



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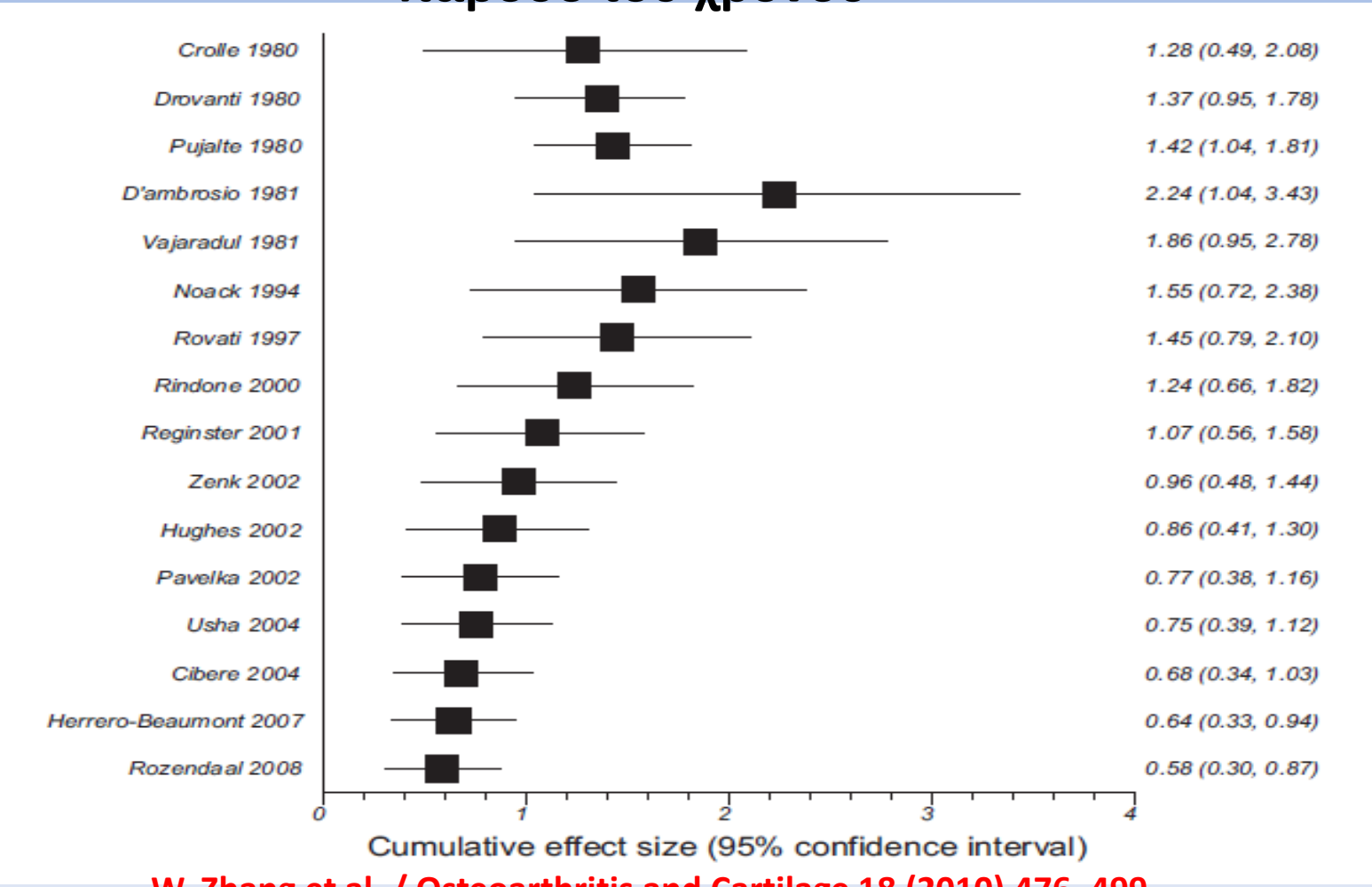
Γλυκοζαμίνη

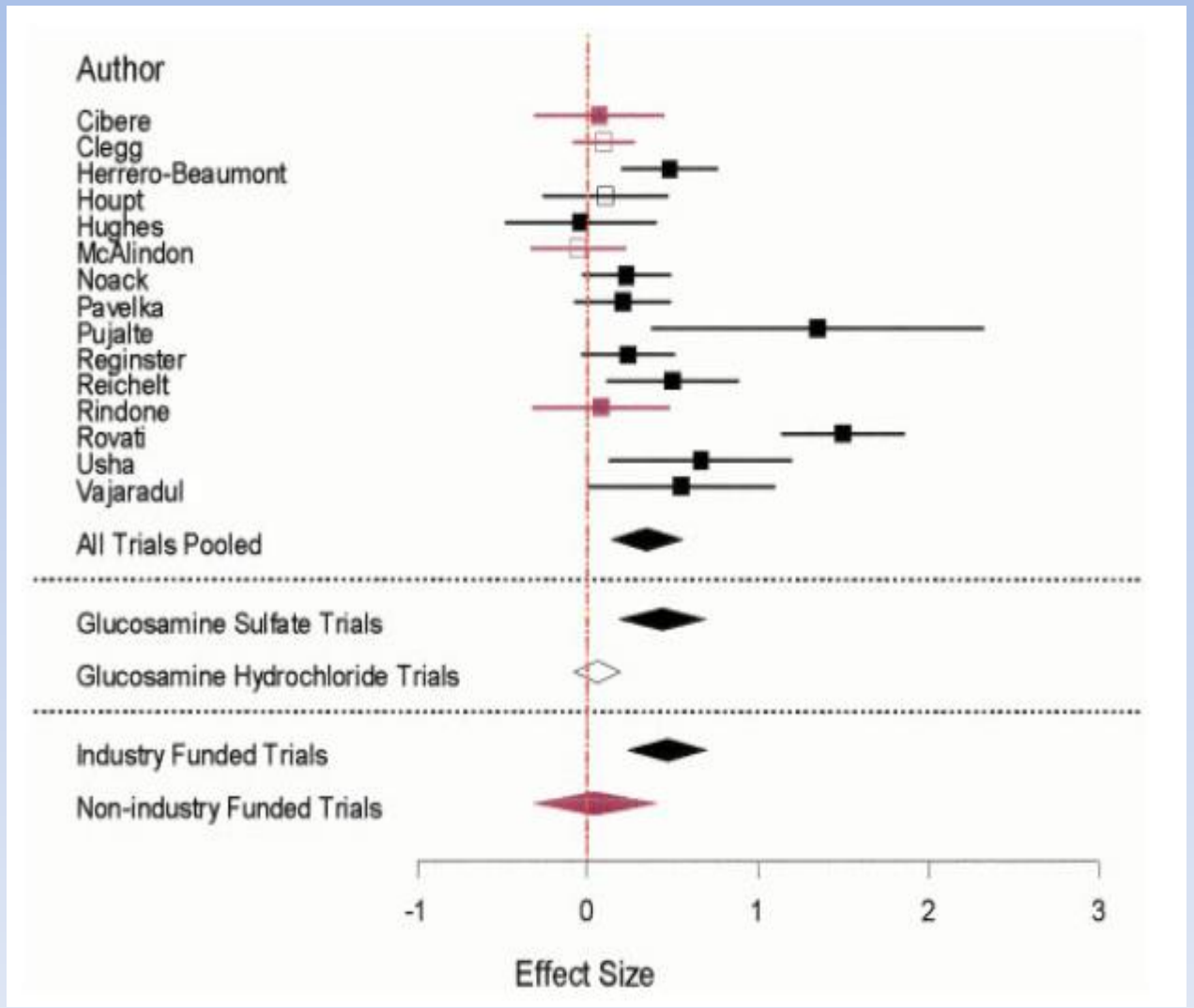
OARSI recommendations for the management of hip and knee osteoarthritis, Part III, 2010

Αναλγητική επίδραση της GS στην OA: ανάλυση των RCTs στην πάροδο του χρόνου



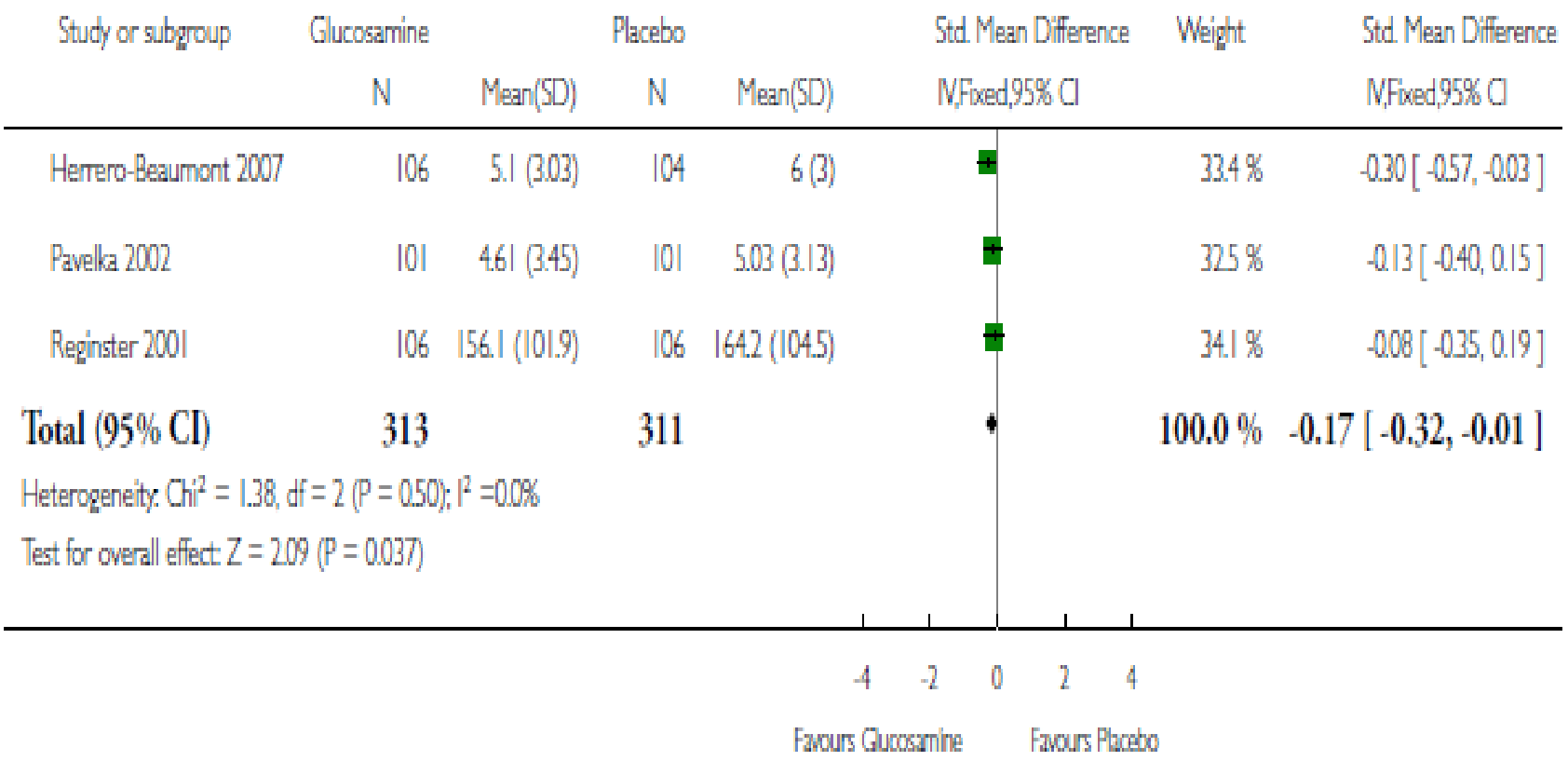
W. Zhang et al. / Osteoarthritis and Cartilage 18 (2010) 476–499

Glucosamine for pain in osteoarthritis: why do trial results differ?



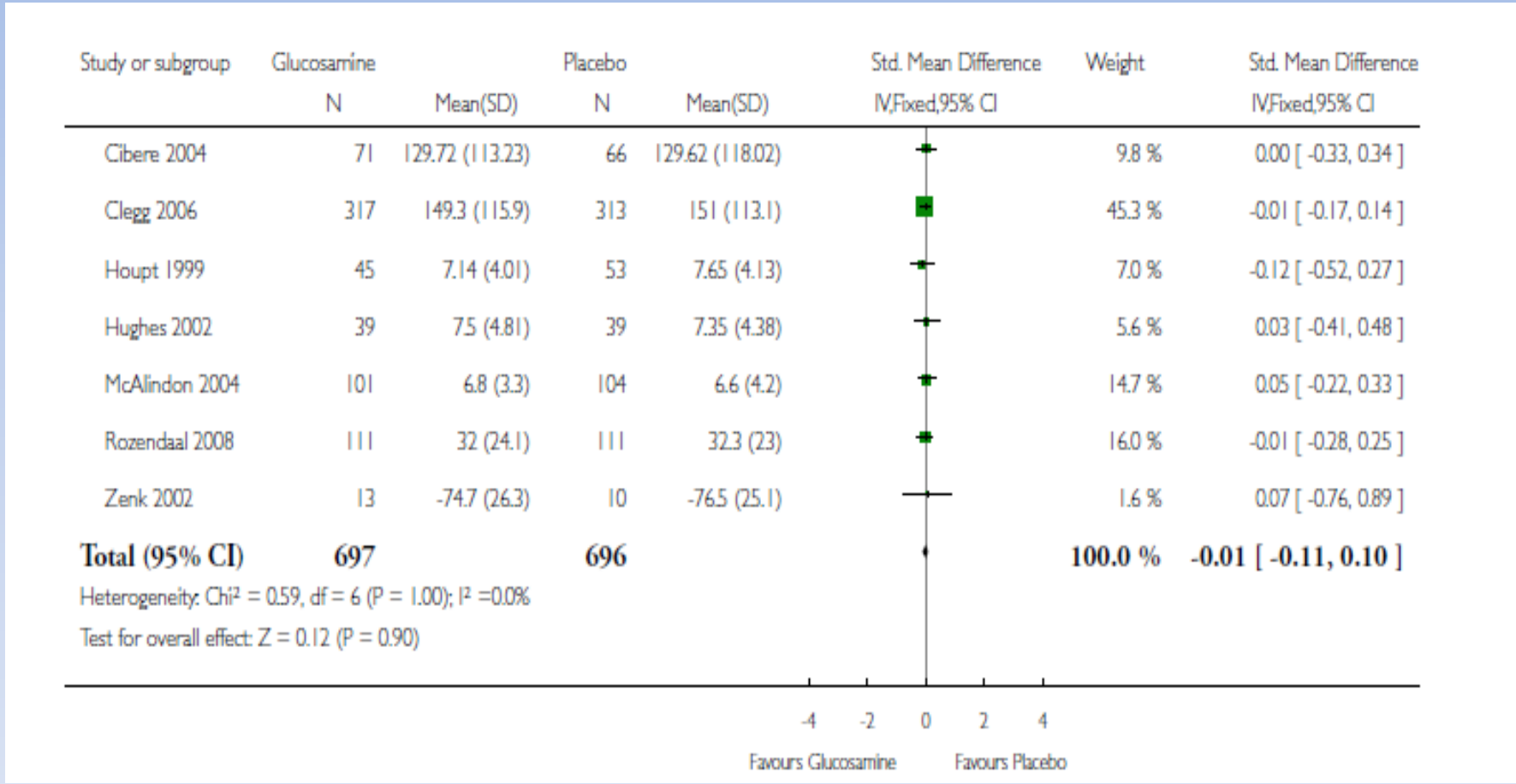
- Trials represented in red are non–industry funded
- Solid squares represent trials
- of glucosamine sulfate
- Open squares represent trials of glucosamine hydrochloride.

The Cochrane Review of glucosamine in OA: Crystalline glucosamine sulfate (Rottapharm) vs placebo
- WOMAC Pain -



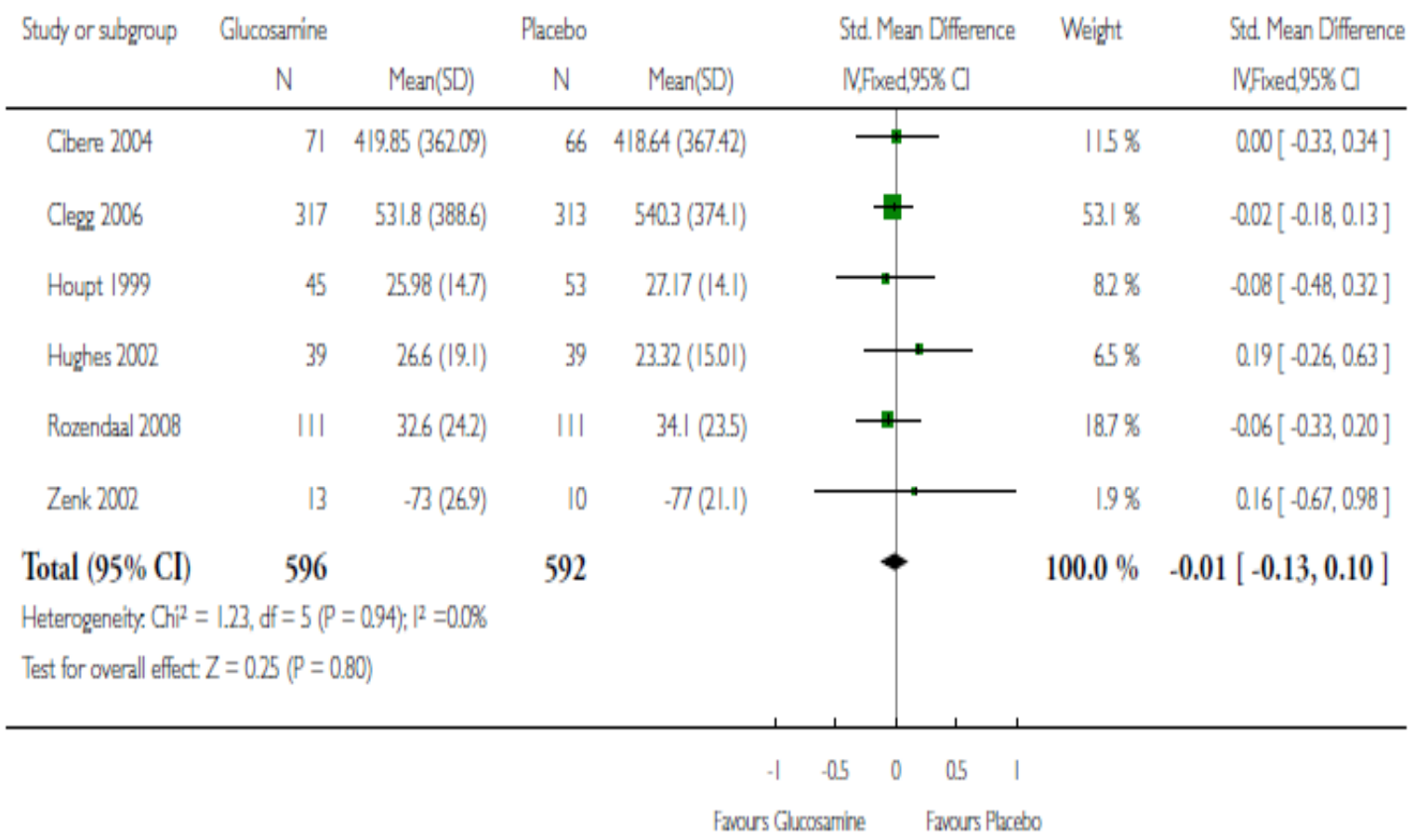
Towheed et al, Cochrane Database 2009; issue 2

The Cochrane Review of glucosamine in OA: Other glucosamines vs placebo - WOMAC Pain -



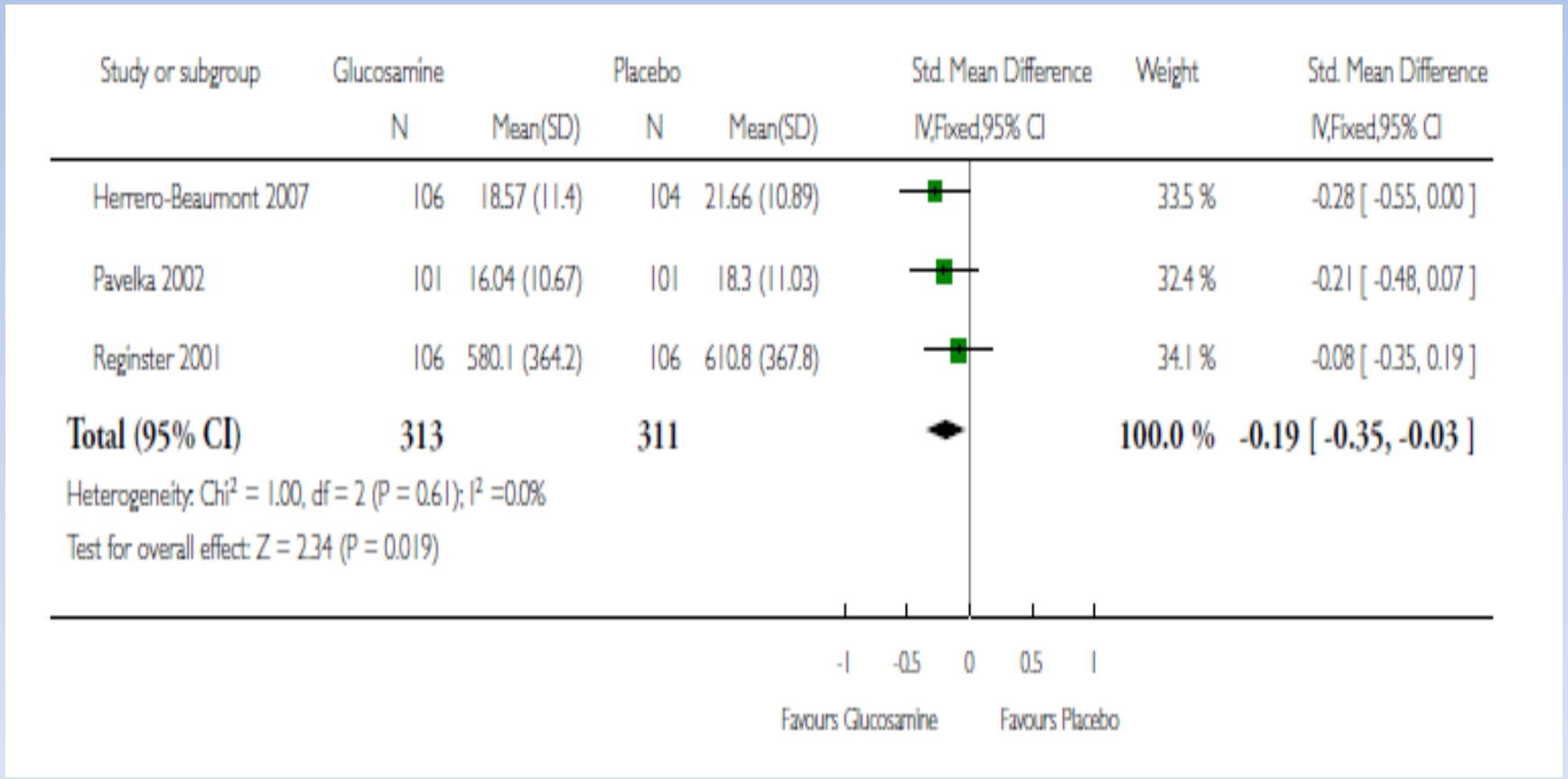
Towheed et al, Cochrane Database 2009; issue 2

The Cochrane Review of glucosamine in OA: Other glucosamines vs placebo - WOMAC Function -



Towheed et al, Cochrane Database 2009; issue 2

The Cochrane Review of glucosamine in OA: Crystalline glucosamine sulfate (Rottapharm) vs placebo
- WOMAC Function -



Towheed et al, Cochrane Database 2009; issue 2

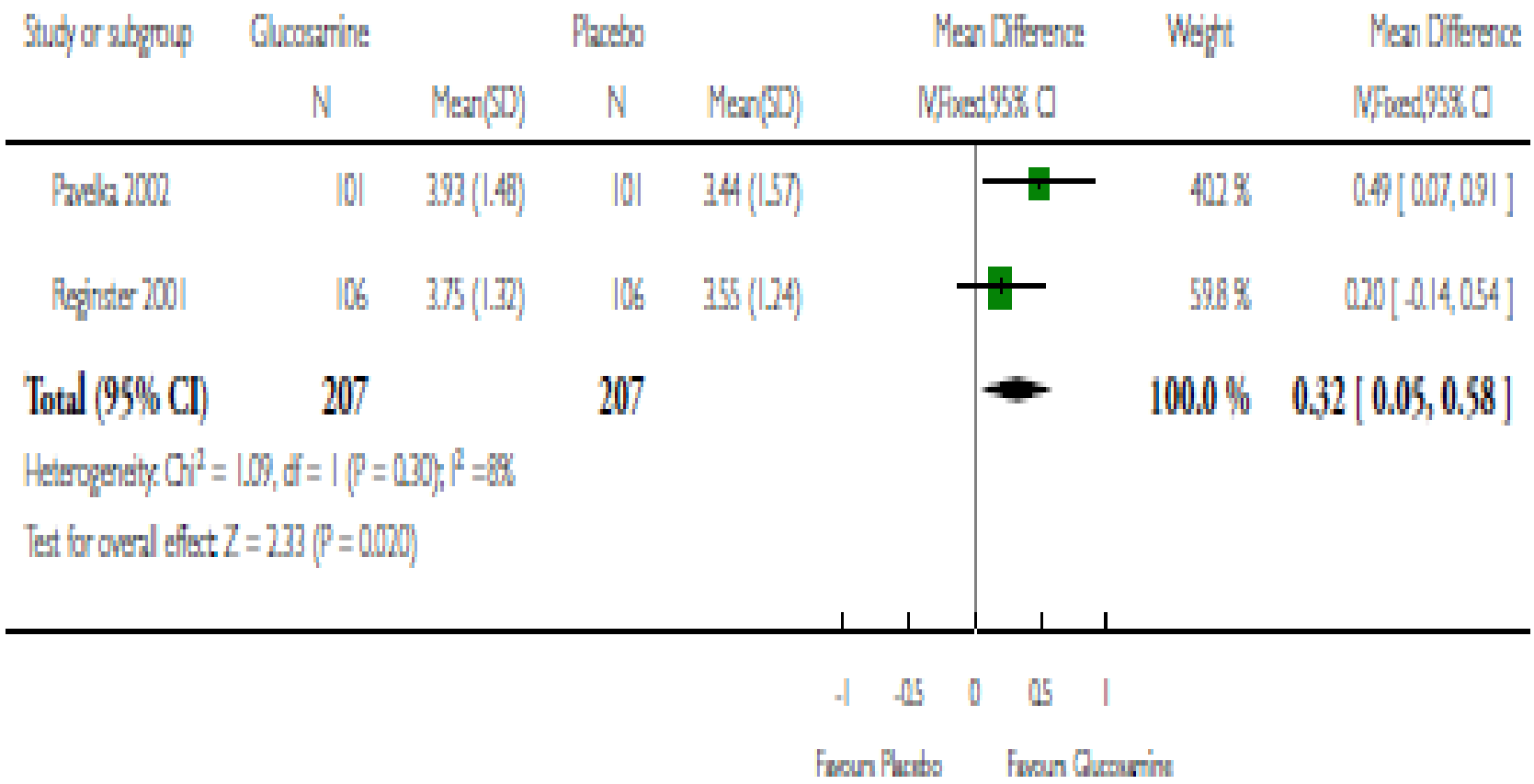
Characteristics and quality of placebo- controlled, high-quality, pivotal trials of prescription glucosamine sulfate 1500 mg once-a-day in knee OA

Study	Duration, Months	Size, N	Jadad Quality Score	Allocation Concealment	ITT Analysis
Reginster 2001 (Lancet; 357:251-6)	36	212	4/5	Adequate	Yes
Pavelka 2002 (Arch Intern Med;1162: 2113-23)	36	202	5/5	Adequate	Yes
Herrero-Beaumont (GUIDE) 2007 (A&R; 56:555-67)	6	214	5/5	Adequate	Yes

All trials used the WOMAC and/or the Lequesne index as primary/secondary outcomes

Reginster JY, Arthritis Rheum 2007;2105-10

The Cochrane Review of glucosamine in OA: Glucosamine sulfate vs placebo - Minimum Joint Space Width -



Towheed et al, Cochrane Database 2009; issue 2

Total joint replacement after glucosamine sulphate treatment in knee osteoarthritis: results of a mean 8-year observation of patients from two previous 3-year, randomised, placebo-controlled trials.

Bruyere O, Pavelka K, Rovati LC, Gatterova J, Giacovelli G,Olejarova M, et al

- The 5-year incidence of total knee replacement (TKR) in patients who had taken GS 1500 mg/day for at least 12 months was less than half of that in those who had taken placebo (6.3 vs 14.5%) (P =0.0024)

Osteoarthritis Cartilage 2008;16:254–60.

Θεική χονδριτίνη (CS)

OARSI recommendations for the management of hip and knee osteoarthritis, Part III, 2010

Modality	Joint	Best evidence until 31 January 2009		
		ES pain (95% CI)	ES function (95% CI)	ES stiffness (95%CI)
CS	Knee	0.75 (0.50, 1.01)		

- Σημαντική ετερογένεια ευρημάτων(I2= 92%).
- Σημαντικά στοιχεία publication bias
- Μείωση της αποτελεσματικότητας στις νεώτερες μελέτες
- Στις υψηλής αξιολόγησης μελέτες (Jadad score 5) δεν υπήρχε σημαντική μείωση στον πόνο, (ES=0.005, 95% CI 0.11, 0.12)

W. Zhang et al. / Osteoarthritis and Cartilage 18 (2010) 476–499

Θεική χονδριτίνη (CS)
Επίδραση στον χόνδρο

- Από μετανάλυση μικρή αλλά σημαντική σε σχέση με το placebo επίδραση στην στένωση του μεσαρθρίου διαστήματος (ES=0.26, 95% CI 0.16, 0.36)

Hochberg MC, Zhan M, Langenberg P. The rate of decline of joint space width in patients with osteoarthritis of the knee: a systematic review and meta-analysis of randomized placebo-controlled trials of chondroitin sulfate. Curr Med Res Opin 2008;Sept 29 (Epub ahead of print).

- Η μείωση του πάχους του αρθρικού χόνδρου στα 2 έτη ήταν μικρότερη στην ομάδα των ασθενών με CS (0.07, S.E.M. 0.03) σε σχέση με το placebo (0.031, S.E.M. 0.04) (P< 0.0001)

Kahan A, Uebelhart D, De Vathaire F, Delmas PD, Reginster JY. Long-term effects of chondroitins 4 and 6 sulfate on knee osteoarthritis: the study on osteoarthritis progression prevention, a two-year, randomized, double-blind, placebo-controlled trial. Arthritis Rheum 2009;60:524–33.

Διασερείνη (Diacerhein)

OARSI recommendations for the management of hip and knee osteoarthritis, Part III, 2010

Modality	Joint	Best evidence until 31 January 2009		
		ES pain (95% CI)	ES function (95% CI)	ES stiffness (95%CI)
Diacerhein	Both	0.24 (0.08, 0.39)	* 0.14 (0.03, 0.25)	

Σημαντικό πρόβλημα η διάρροια (RR compared to placebo is 3.51 (2.55, 4.83)]

W. Zhang et al. / Osteoarthritis and Cartilage 18 (2010) 476–499

Οπιοειδή

Avouac J, Gossec L, Dougados M. Efficacy and safety of opioids for osteoarthritis: a meta-analysis of randomized controlled trials. Osteoarthritis Cartilage 2007;15:957–65.
Ehrich EW, Davies GM, Watson DJ, Bolognese JA, Seidenberg BC, Bellamy N. Minimal perceptible clinical improvement with the Western Ontario and McMaster Universities Osteoarthritis Index questionnaire and global assessments in patients with osteoarthritis. J Rheumatol 2000;27:2635–41.
Furlan AD, Sandoval JA, Mailis-Gagnon A, Tunks E. Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects. CMAJ 2006;174:1589–94.

Table I
Best evidence for efficacy for various modalities of therapy for hip and knee OA available 31 January 2009

Modality	Joint	QoS (%)	LoE	Best evidence until 31 January 2009			
				ES_{pain} (95% CI)	$ES_{function}$ (95% CI)	$ES_{stiffness}$ (95% CI)	NNT (95% CI)
Opioids	Any*	100*	Ia*	0.78 (0.59, 0.98)[58,*]	0.31 (0.24, 0.39)[58,*]		

Table IV
Side effects associated with pharmacological therapies

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Intervention*	Adverse events	RR/OR (95% CI)	Evidence (references)
Opioids	Any	1.40 (1.30, 1.60)	Meta-RCTs[186]
	Constipation†	4.08 (3.30, 5.05)†	Meta-RCTs[58,†]
	Nausea†	3.15 (2.68, 3.72)†	Meta-RCTs[58,†]
	Vomiting†	5.99 (4.20, 8.54)†	Meta-RCTs[58,†]
	Dizziness†	3.74 (3.00, 4.66)†	Meta-RCTs[58,†]
	Somnolence†	4.78 (3.65, 6.26)	Meta-RCTs[58,†]

- 25% of patients treated with opioids withdrew from studies compared with 7% of placebo-treated patients
- The withdrawal rate was higher (31%) for strong opioids (oxymorphone, oxycodone, oxytrex, fentanyl, morphine sulphate) than for the weaker opioids (tramadol, tramadol/paracetamol, codeine and propoxyphene)(19%)
- MA of 41 RCTs for chronic non-cancer pain involving 6019 patients, only strong opioids were significantly more effective than acetaminophen or NSAIDs (ES=0.34)