

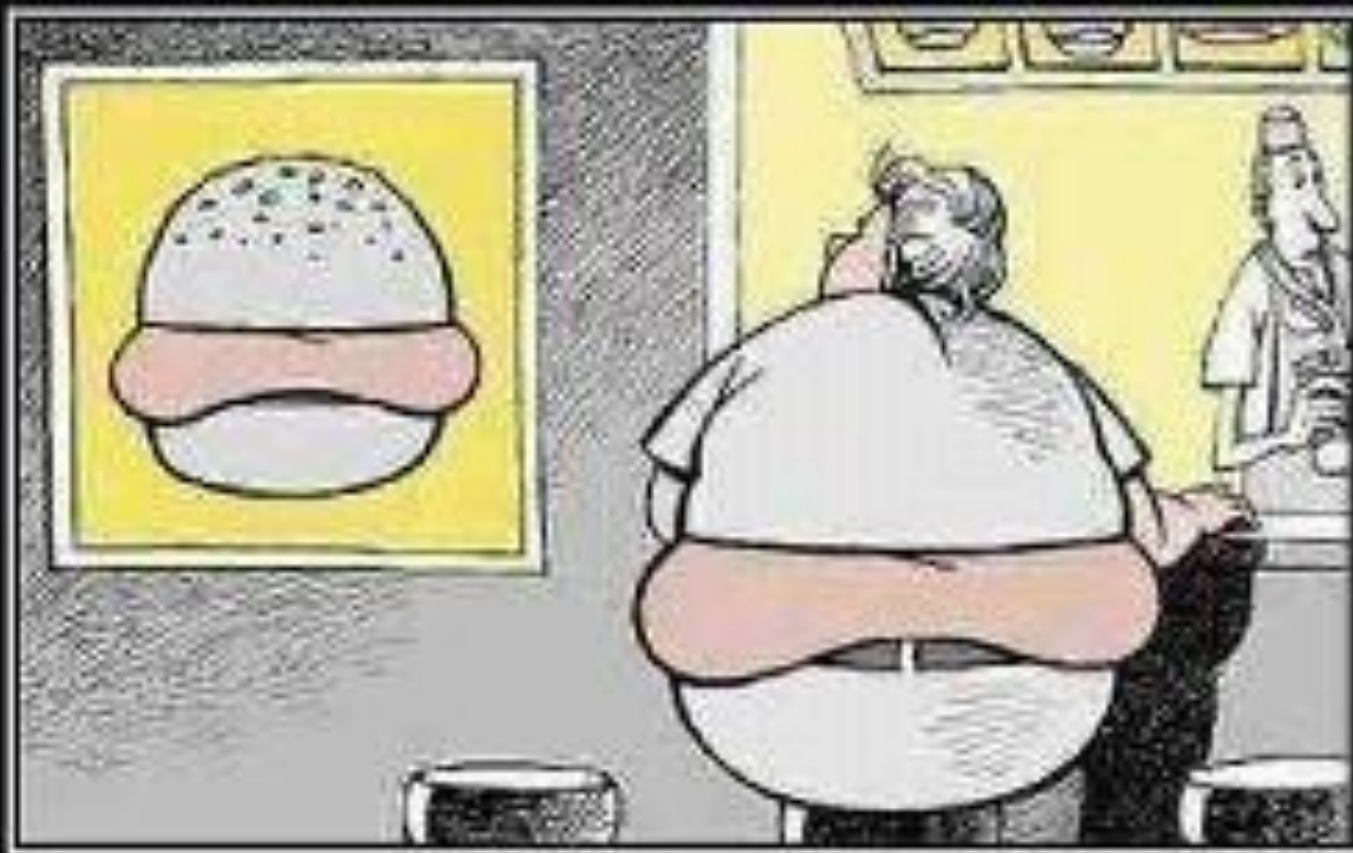
Nutraceutica clinica, infiammazione e rischi correlati: tra dieta e farmaco

Arrigo F.G. Cicero

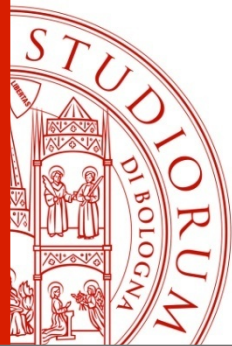
Presidente SINut

Dip. di Scienze Mediche e Chirurgiche

Alma Mater Studiorum Università di Bologna

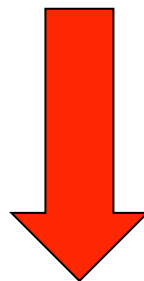


TU SEI COSA MANGI !!!



Bersagli dell'inflammazione

Tutti gli organi ed apparati



Invecchiamento

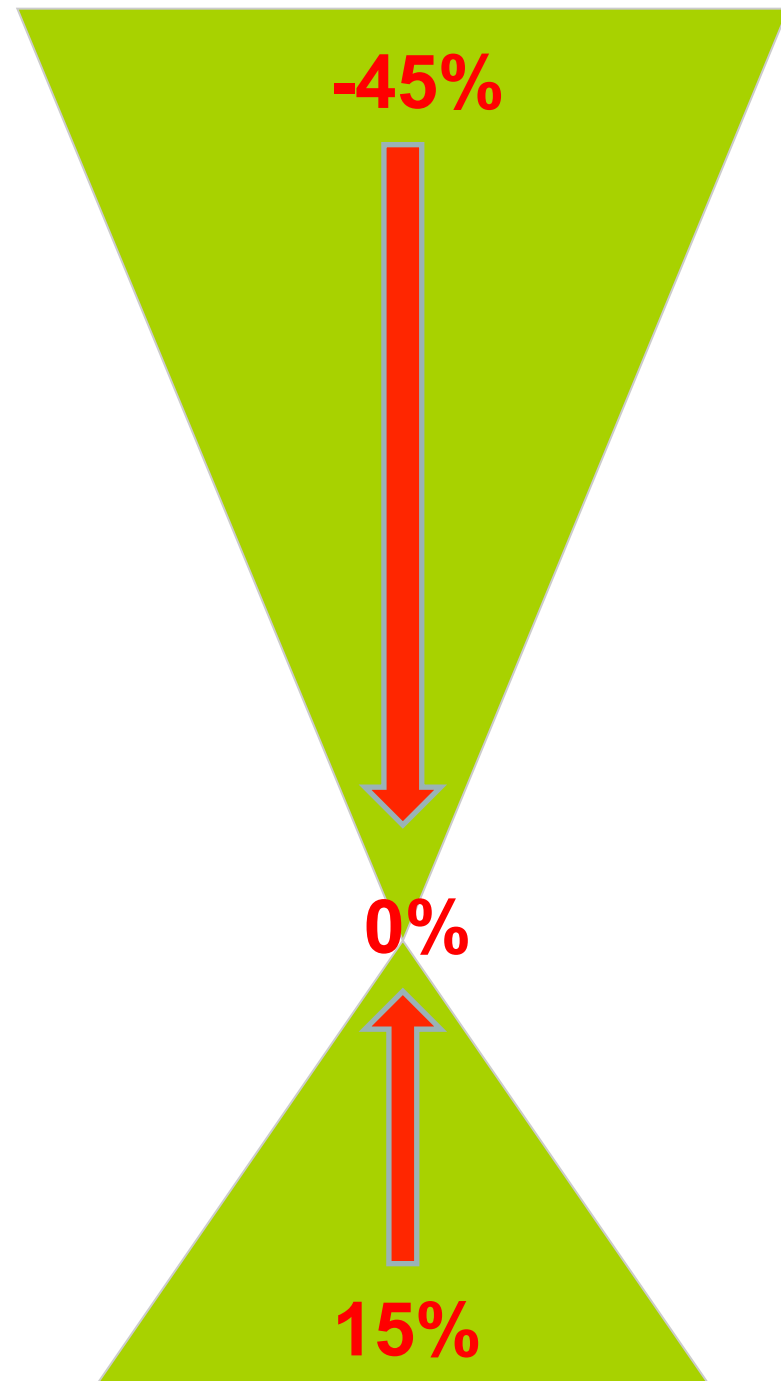


La dieta «antinfiammatoria»

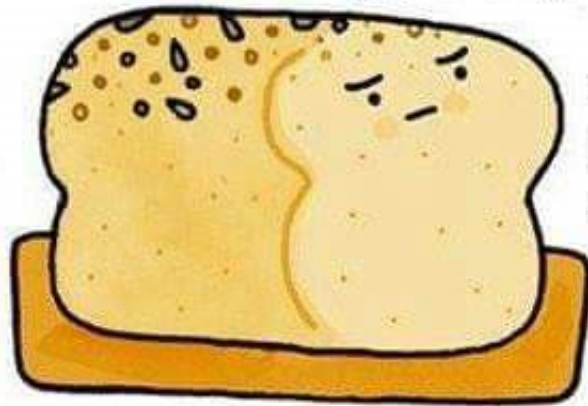
- **Dieta «ipocalorica» associata ad attività fisica moderata**
- **Importante idratazione**
- **Basso contenuto di sodio**
- **Ricca in carboidrati complessi e povera in zuccheri semplici**
- **Ricca in vegetali (ogni tipo, comprese spezie e bacche)**
- **Ricca in pesce, specie se azzurro e cotto a basse temperature**
- **Piccole quantità di cioccolato extra-fondente di alta qualità (senza zucchero) e modiche quantità di alcool**

Cicero AFG, Stallone T. In: Encyclopedia of Food and Health. 2015

- **Trigliceridi**
- **Glicemia/IR**
- **Microinfiammazione**
- **Pressione arteriosa**
- **Colesterolo LDL**
- **Lipoproteina (a)**
- **Colesterolo HDL**

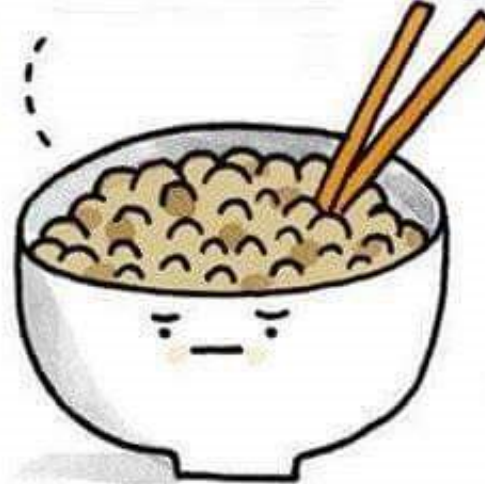
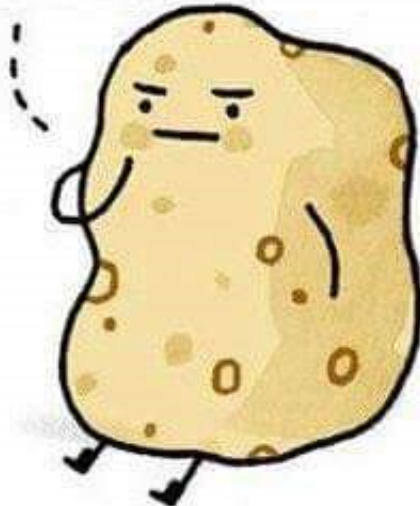


Se esistono infiniti universi paralleli,
può esistere un universo parallelo il cui
non esistono universi paralleli?

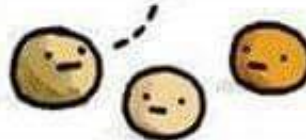


La vita è un pendolo che
oscilla tra dolore e noia

Io dubito.
Dunque sono!

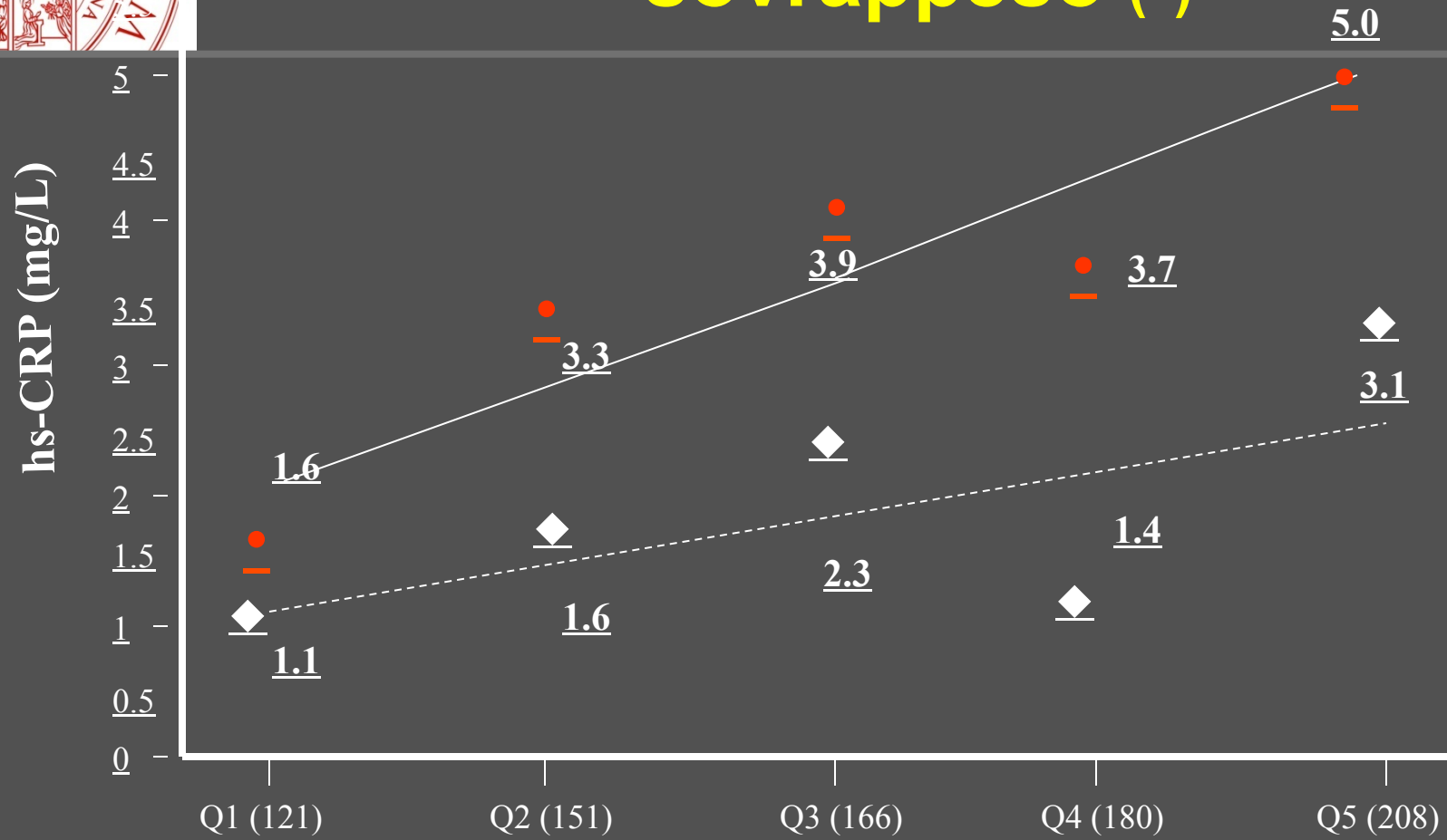


Qual è il significato
dell'esistenza?



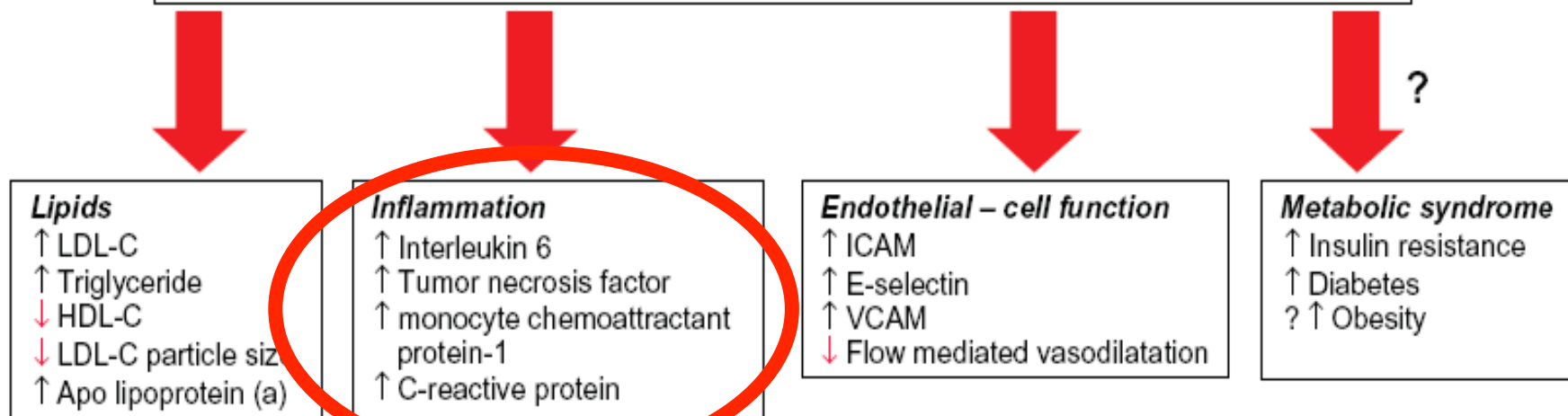
I carboidrati complessi

hsCRP per Quintili di Carico glicemico in donne normopeso (◆) e sovrappeso (•)



Quintili di carico glicemico aggiustati per l'introito calorico totale

Trans fatty acids

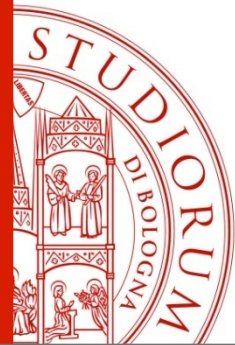


**ATHEROSCLEROSIS VULNERABLE
PLAQUE SUDDEN DEATH**

E COMUNQUE I BAMBINI



**NON CONTENGONO
OLIO DI PALMA**



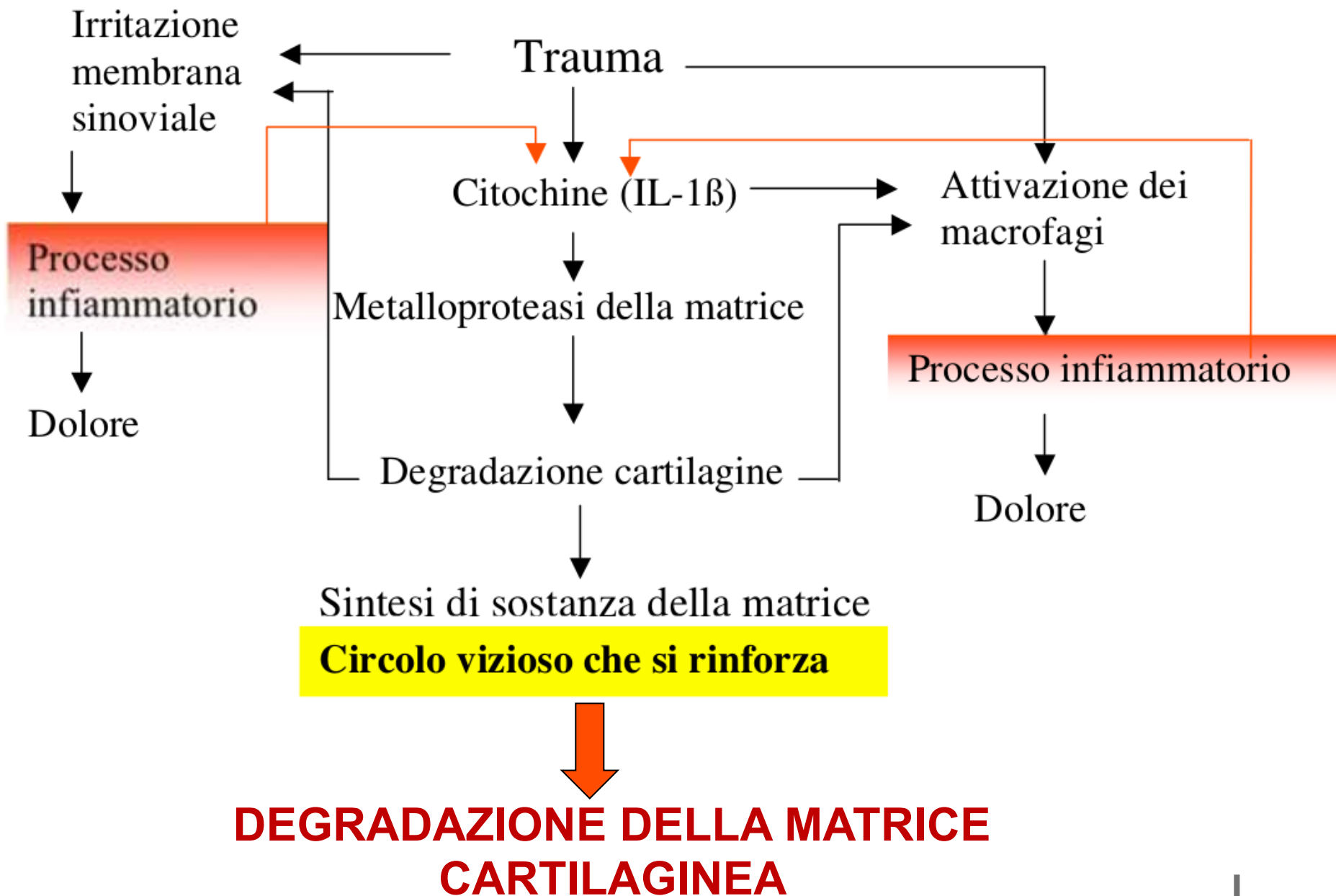
Ma è vero che il cacao fa bene?



- «Ni»
- Il cacao di alta qualità con molti antiossidanti sì!
- Effetti: riduzione della pressione arteriosa, miglioramento della funzione dei vasi, aumento del colesterolo «buono», miglioramento del metabolismo degli zuccheri, ...
- Gli antiossidanti si perdono col calore
- I prodotti commerciali usualmente sono molto calorici e poveri di antiossidanti
- Gli antiossidanti del cacao sono amaro-acidi

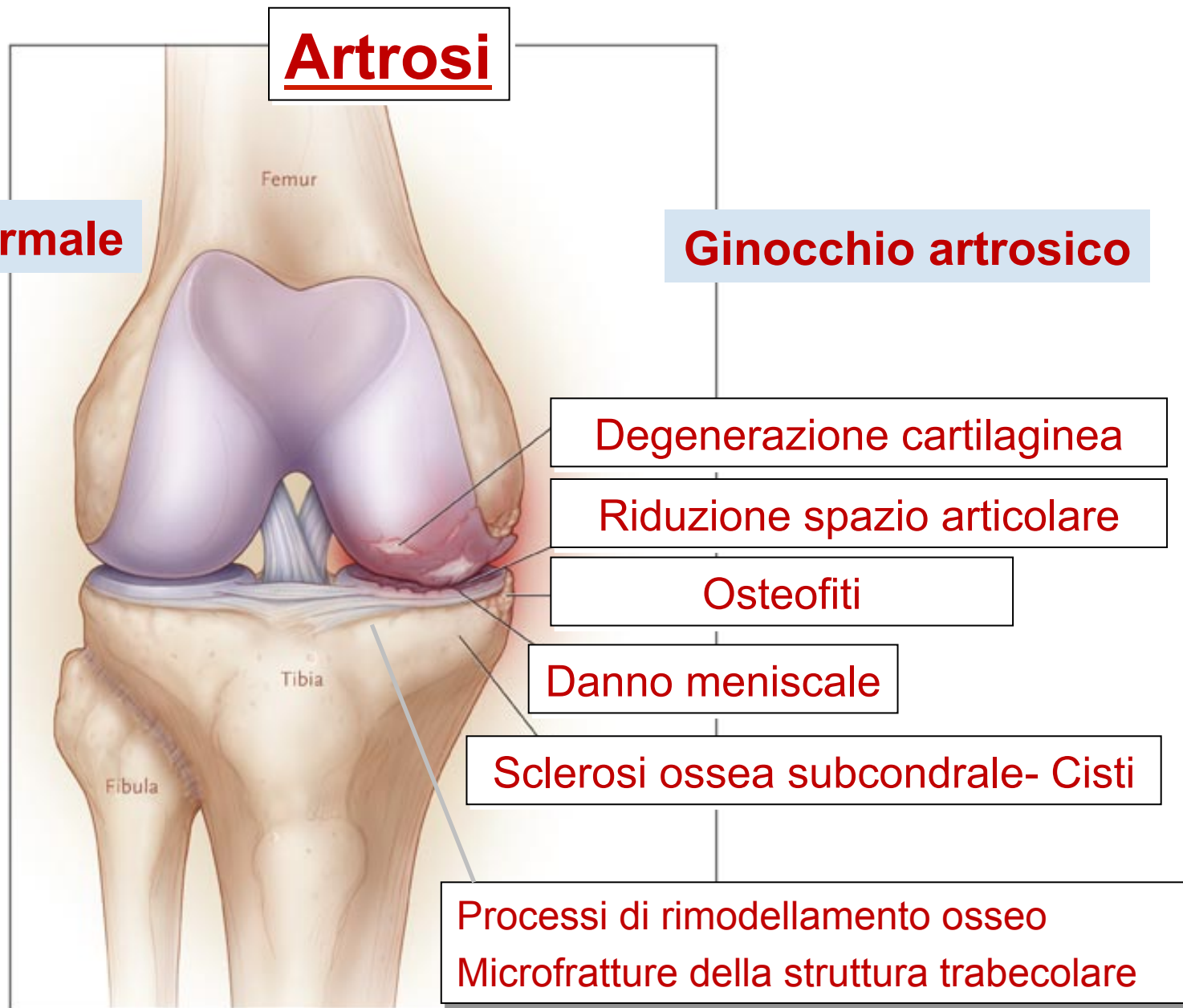
Ried K et al. *BMC Medicine* 2010, 8:39







Ginocchio normale



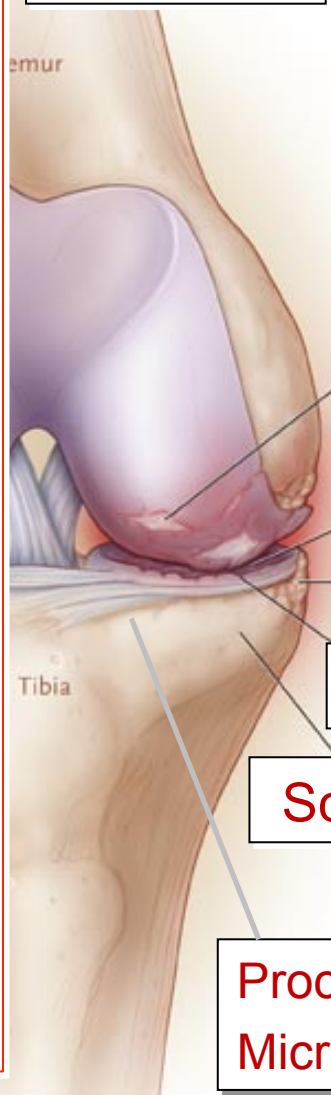
Artrosi

➤ SINTOMI

- Dolore articolare (↑ con l'attività, ↓ con il riposo)
- Rigidità mattutina (usualmente < 30')
- Instabilità articolare
- Impotenza funzionale
- Dolorabilità alla palpazione
- Dolore alla mobilizzazione

➤ SEGNI

- Limitazione alla mobilizzazione
- Rumore di scroscio (crepitio) al movimento
- Versamento endo-articolare
- Disallineamento e/o deformità articolare
- Deformità dei capi articolari



Ginocchio artrosico

Degenerazione cartilaginea

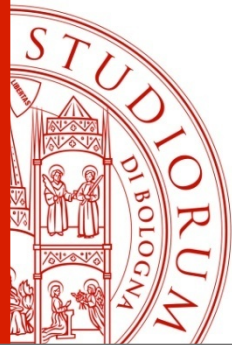
Riduzione spazio articolare

Osteofiti

Danno meniscale

Sclerosi ossea subcondrale- Cisti

Processi di rimodellamento osseo
Microfratture della struttura trabecolare

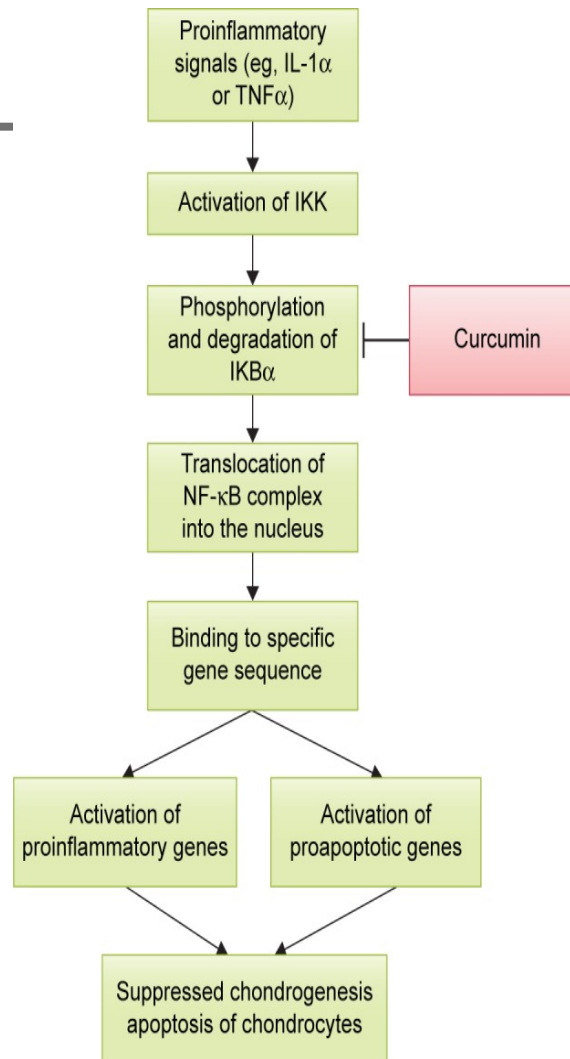
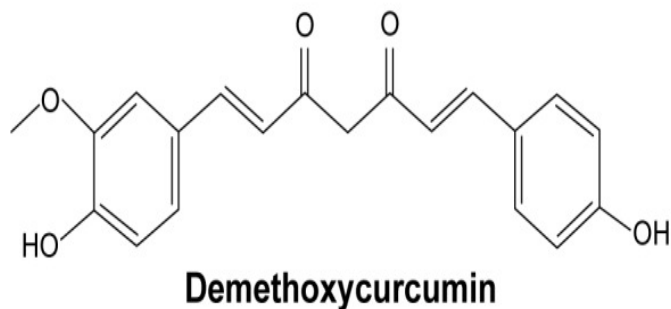
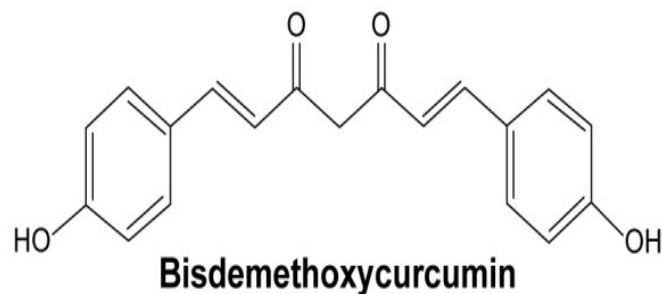
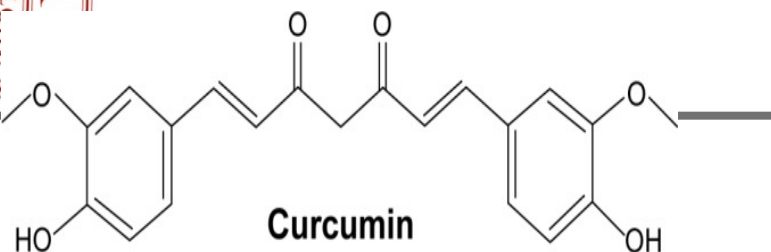


Indicazioni dei condroprotettori

- Condroprotezione (!)
- Miglioramento di performance e QoL
- Riduzione assunzione di FANS/
Corticosteroidi
- Ritardo trattamento invasivo
- Allungamento tempo intercorso senza dolore fra interventi invasivi

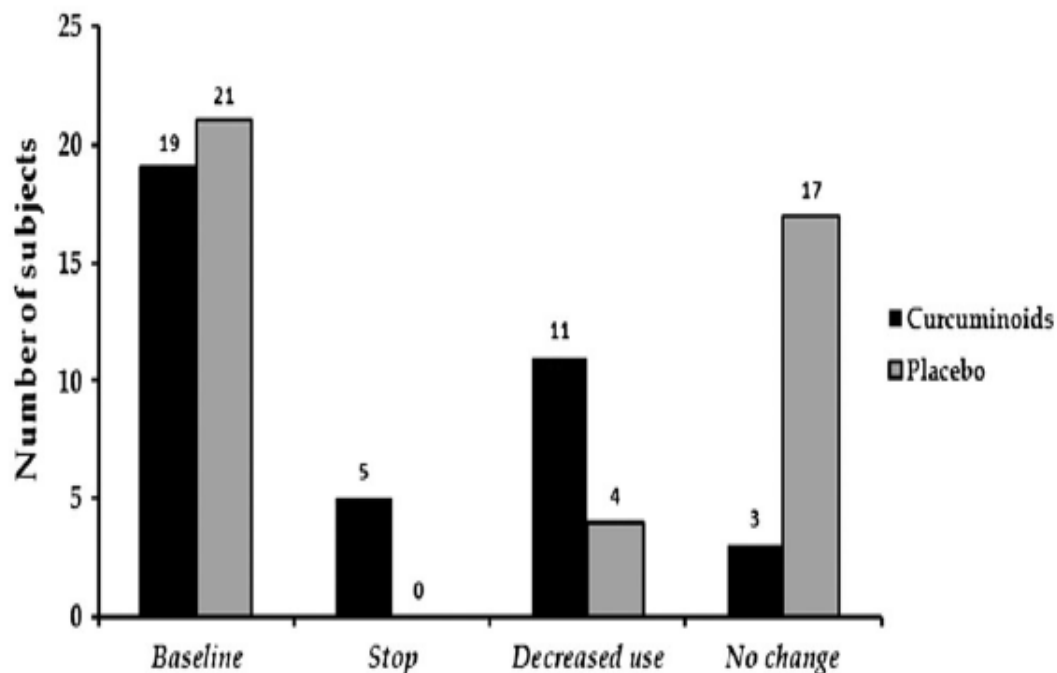


Curcuminoids and OA

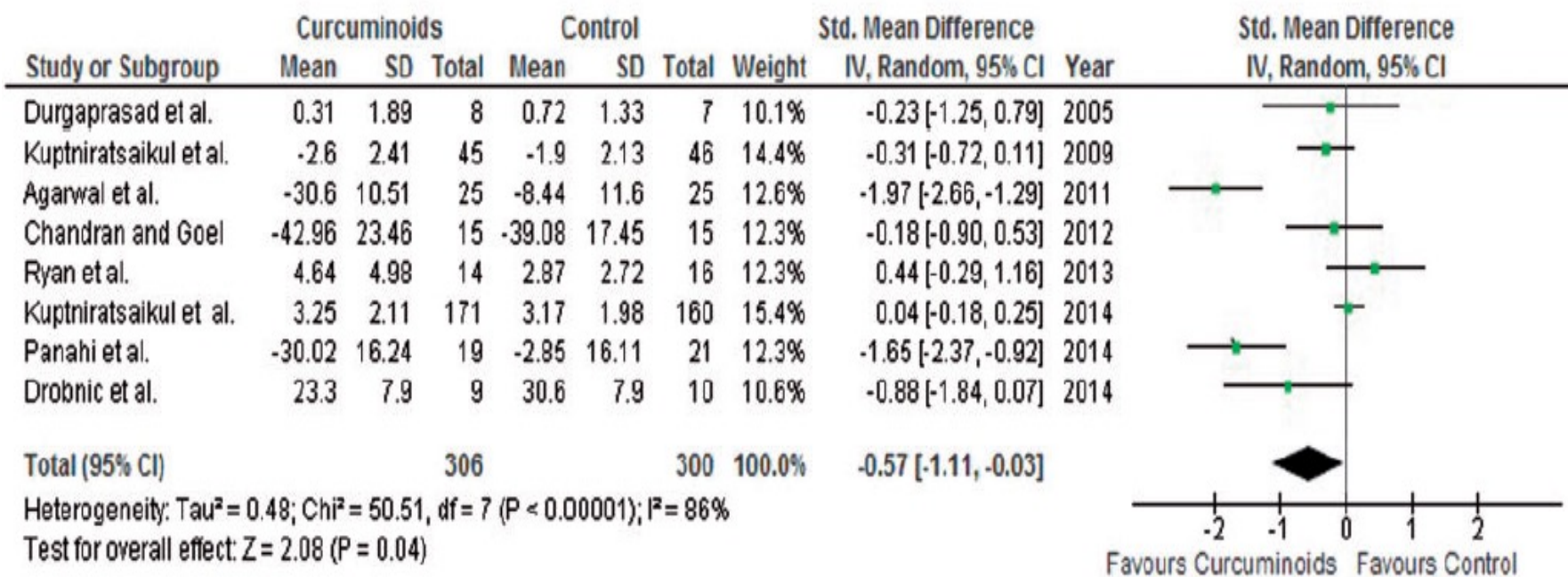
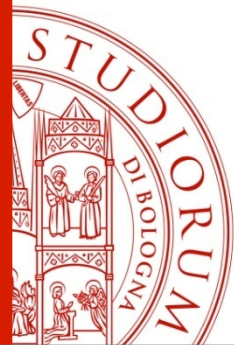


Curcuminoid Treatment for Knee Osteoarthritis: A Randomized Double-Blind Placebo-Controlled Trial

**Frequenza di
impiego di
antinfiammatori
pre e post
trattamento**

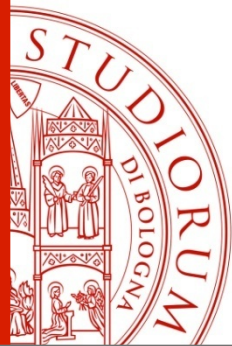


Effetto analgesico dei curcuminoidi

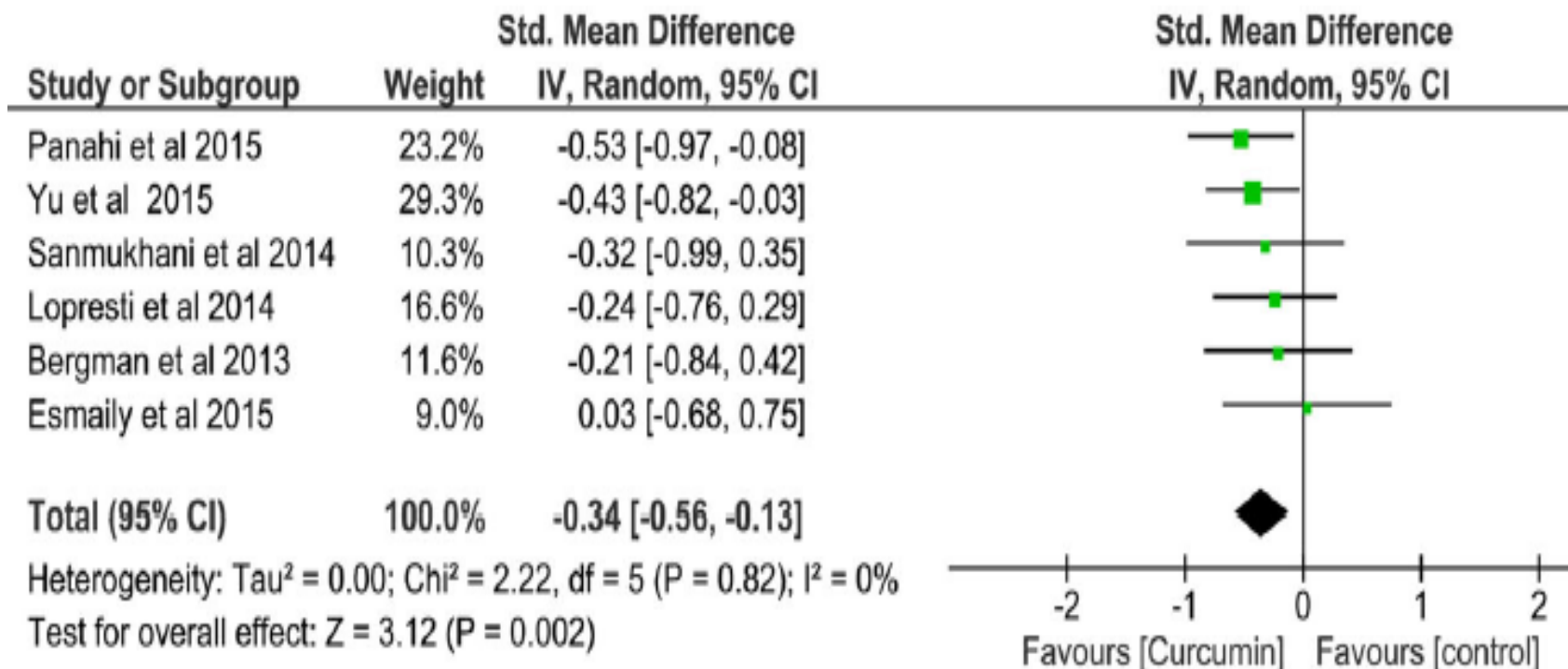


Forest plot detailing standardized mean difference and 95%CI for the impact of curcuminoid supplementation on the severity of pain.

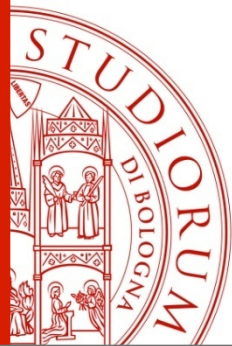
Pain Medicine 2015



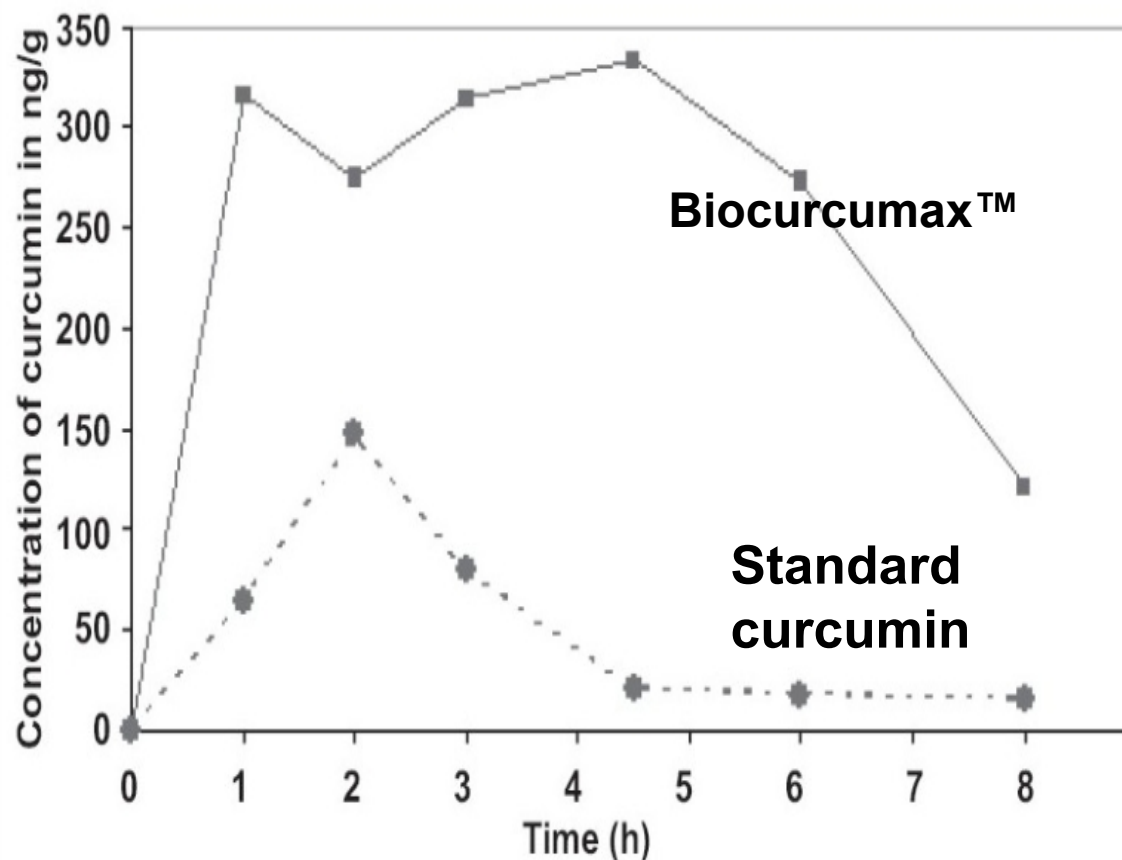
Effetto antidepressivo della curcumina



Phytother. Res. 30: 175–183 (2016)

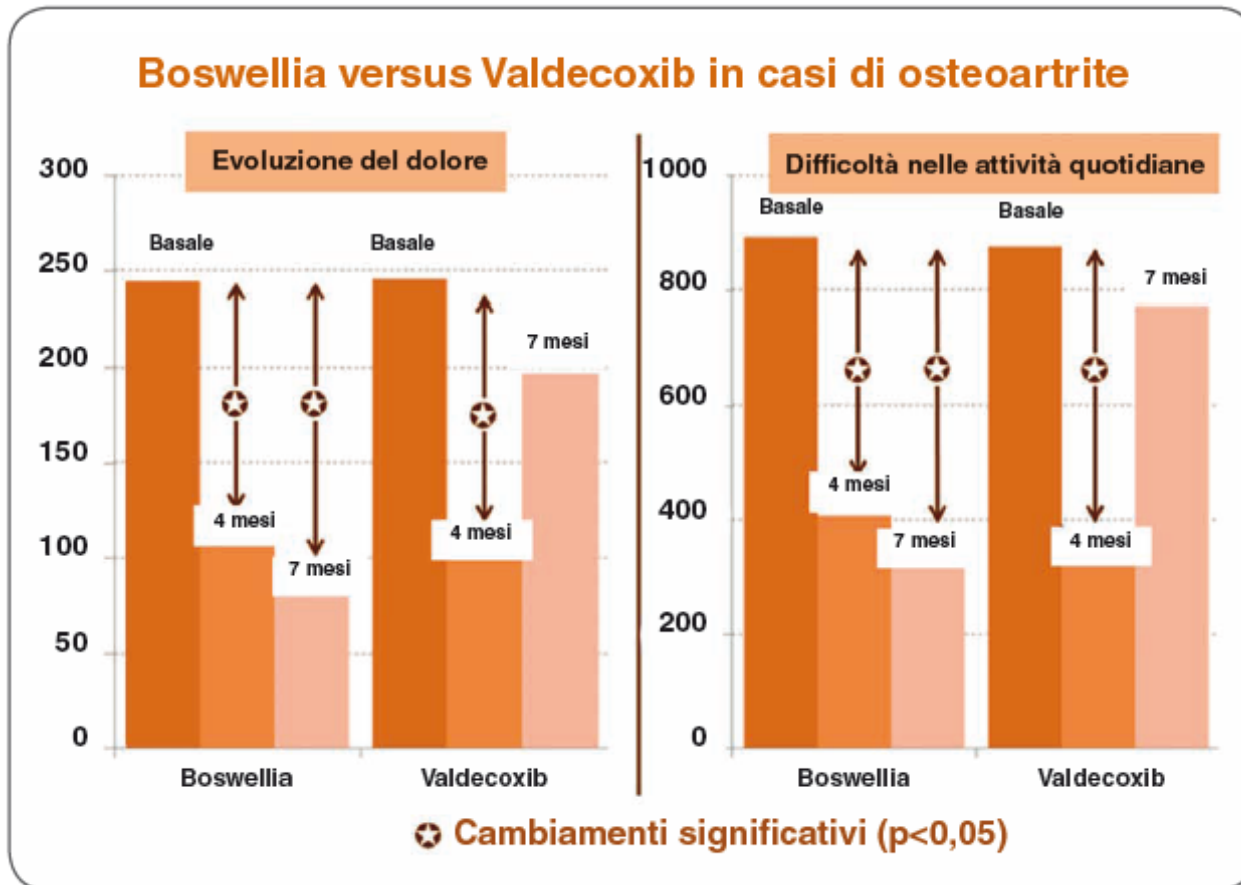


Non tutte le «curcumine» commerciali vengono assorbite allo stesso modo

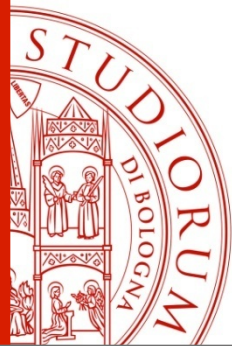


*Indian J
Pharm Sci.
2008;70(4):
445–449.*

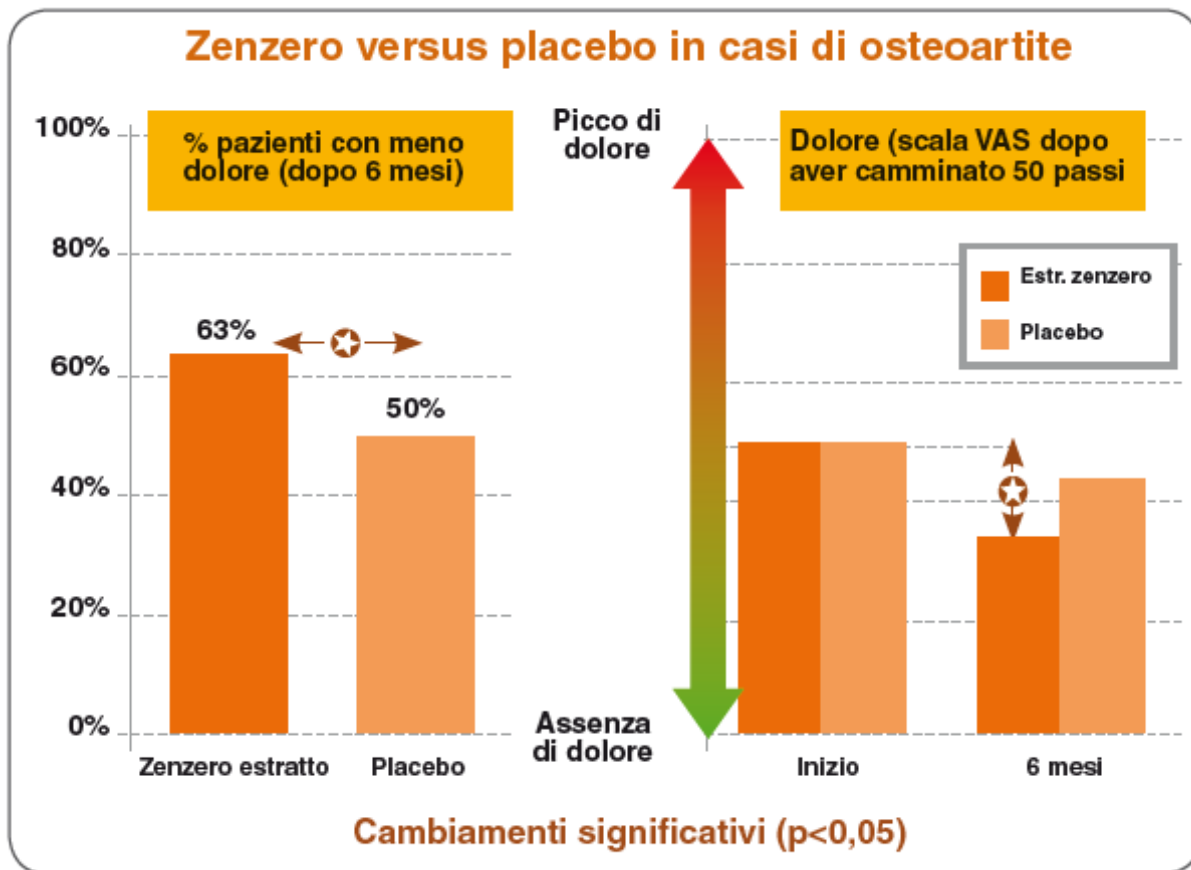
Boswellia serrata (40% in acidi boswellici)



Indian J
Pharmacol
2007;39(1):
27-29.



Zingiber officinalis: un Cox-2/Lox5 inibitore

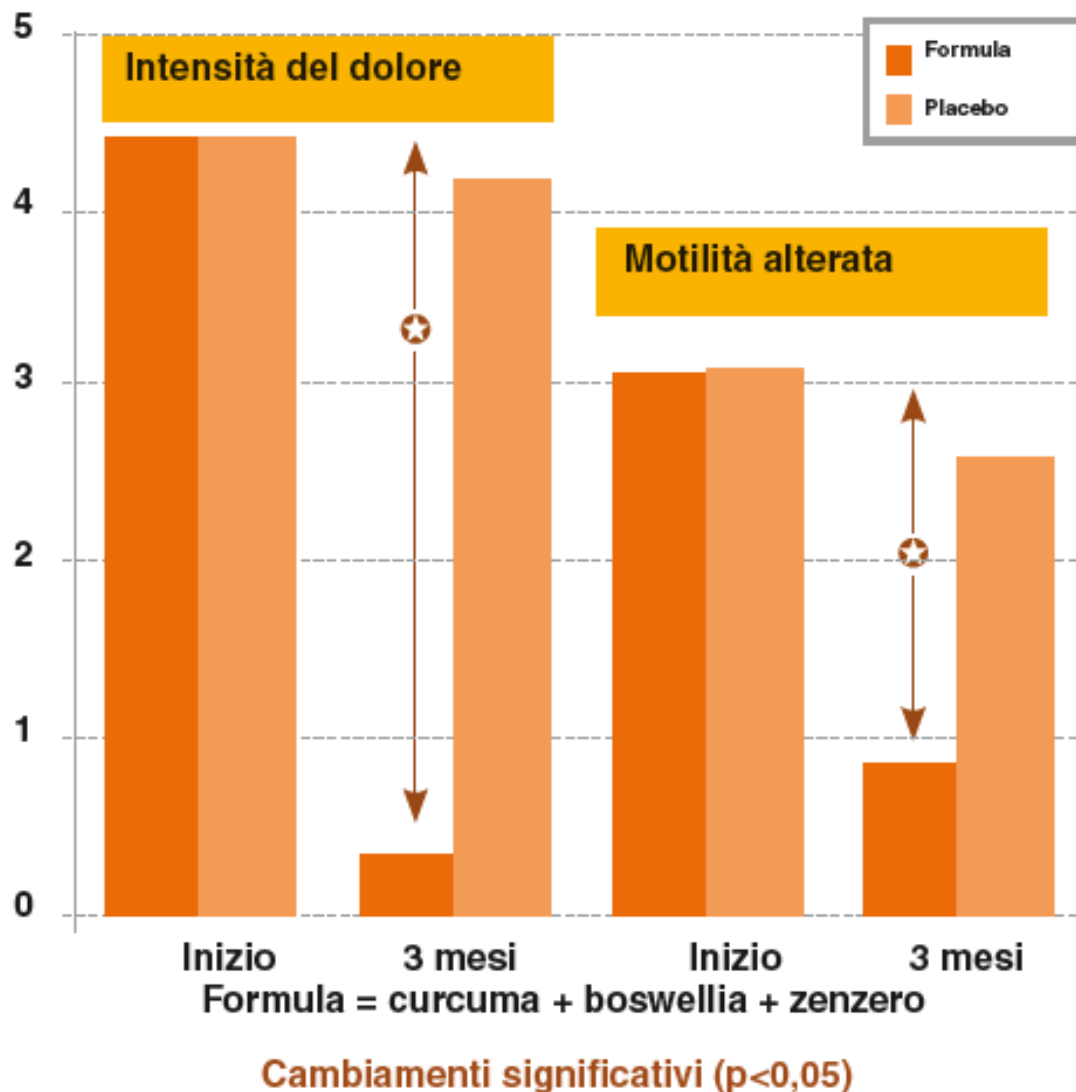


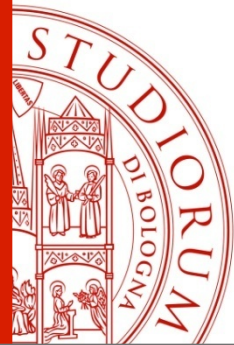
**Arthritis
Rheum.
2001;44(11):
2531-2538.**



Gli effetti di una triplice associazione

Curcuma, boswellia e zenzero versus placebo in casi di osteoartrite



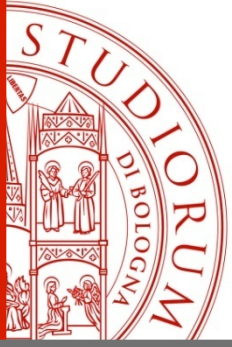


Glucosamine sulphate and OA: the results of a meta-analysis of 31 RCTs

Compared to placebo, glucosamine showed a significant improvement with unstandardized mean differences (UMD) in:

- **Total WOMAC: -2.49 (95%CI -4.14, -0.83)**
- **Pain WOMAC: -0.75 (95% CI: -1.18, -0.32)**
- **Function WOMAC: -4.78 (95% CI: -5.96, -3.59)**
- **Lequesne score: -1.03 (95% CI: -1.34, -0.72)**

Eur J Med Res. 2015;20:24.

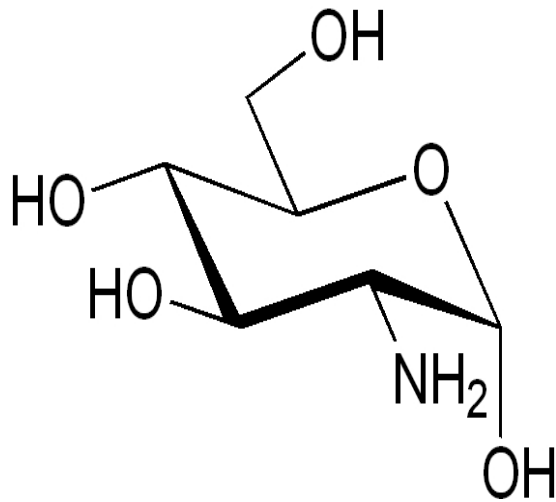


Chondroitin sulphate and OA: the results of a meta-analysis of 43 RCTs

- Participants treated with chondroitin achieved statistically significantly and clinically meaningful better pain scores (0–100) in studies less than 6 months than those given placebo with an absolute risk difference of 10% lower (95%CI 15% to 6%); NNT = 5 (95% CI, 3 to 8)
- In studies >6 months, the absolute risk difference for pain was 9% lower (95% CI 18 to 0)
- For the WOMAC MCII Pain subscale outcome, a reduction in knee pain by 20% was achieved by 53/100 in the chondroitin group versus 47/100 in the placebo group, an absolute risk difference of 6% (95% CI 1 to 11), (RR 1.12, 95% CI 1.01 to 1.24).
- Differences in Lequesne's index (composite of pain, function and disability) statistically significantly favoured chondroitin as compared with placebo in studies <6 months, with an absolute risk difference of 8% lower (95% CI 12 to 5)
- Loss of minimum joint space width in the chondroitin group was statistically significantly less than in the placebo group, with a relative risk difference of 4.7% less (95%CI 1.6 to 7.8).
- Chondroitin did not result in statistically significant numbers of adverse events or withdrawals due to adverse events compared with placebo or another drug.

[Cochrane Database Syst Rev. 2015 Jan 28;1:CD005614.](#)

Glucosamine sulphate and OA: level of evidence



B: Knee osteoarthritis

Evidence supports the use of glucosamine sulfate taken by mouth to treat knee osteoarthritis.

B: Osteoarthritis (general)

Several studies have found that glucosamine may benefit osteoarthritis in other body parts, aside from the knee. However, there is less evidence to support this compared to knee osteoarthritis. Knee osteoarthritis appears to respond better than other joints to any treatment.

B= Good scientific evidence for this use

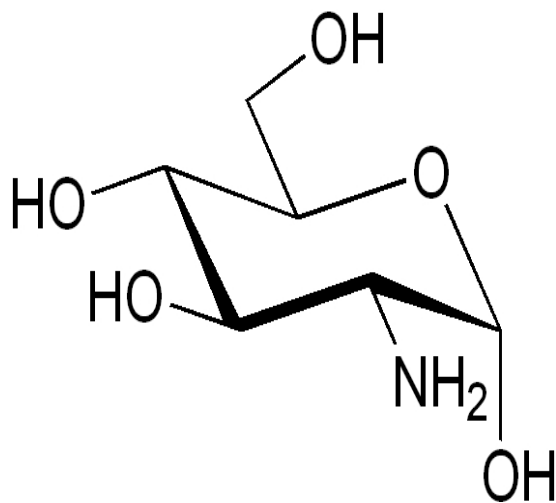
Chondroitin sulphate and OA: level of evidence

A: Osteoarthritis (general)

Chondroitin sulfate is considered a promising treatment for osteoarthritis. It is most often used to treat osteoarthritis of the finger, knee, hip joints, low back, and facial joints. Research has mostly focused on knee osteoarthritis, with fewer studies conducted on other joints. Clinical trials suggest that chondroitin may have significant effects when compared to placebo.

A: Osteoarthritis (knee)

Chondroitin sulfate is considered a promising treatment for osteoarthritis of the knee. It is also most often used to treat osteoarthritis of the finger, hip joints, low back, and facial joints. Clinical trials suggest that chondroitin may have significant effects when compared to placebo.

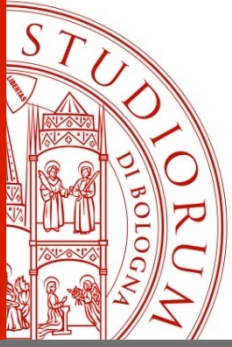


A= Strong scientific evidence for this use

Absolute treatment effects (change from baseline) for pain and function: a meta-analysis of 54 trials including 16427 patients

Treatment	Pain (SMD)	Pain (WOMAC 0-10)	Function (SMD)	Function (WOMAC 0-10)
Celecoxib	-1.09 (-1.23, -0.96)	-2.73 (-3.08, -2.40)	-0.94 (-1.06, -0.82)	-1.97 (-2.23, -1.72)
Glucosamine	-0.85 (-1.05, -0.65)	-2.13 (-2.63, -1.63)	-0.56 (-0.78, -0.35)	-1.18 (-1.64, -0.74)
Chondroitin	-1.02 (-1.31, -0.74)	-2.55 (-3.28, -1.85)	-0.87 (-1.19, -0.54)	-1.83 (-2.50, -1.13)
glucosamine + chondroitin	-1.00 (-1.66, -0.34)	-2.50 (-4.15, -0.85)	-1.66 (-2.45, -0.86)	-3.49 (-5.15, -1.81)

Zeng C et al. Sci Rep. 2015;5:16827.



Comparisons of trials and results

Glucosamine/chondroitin Arthritis Intervention Trial (GAIT) (2010)

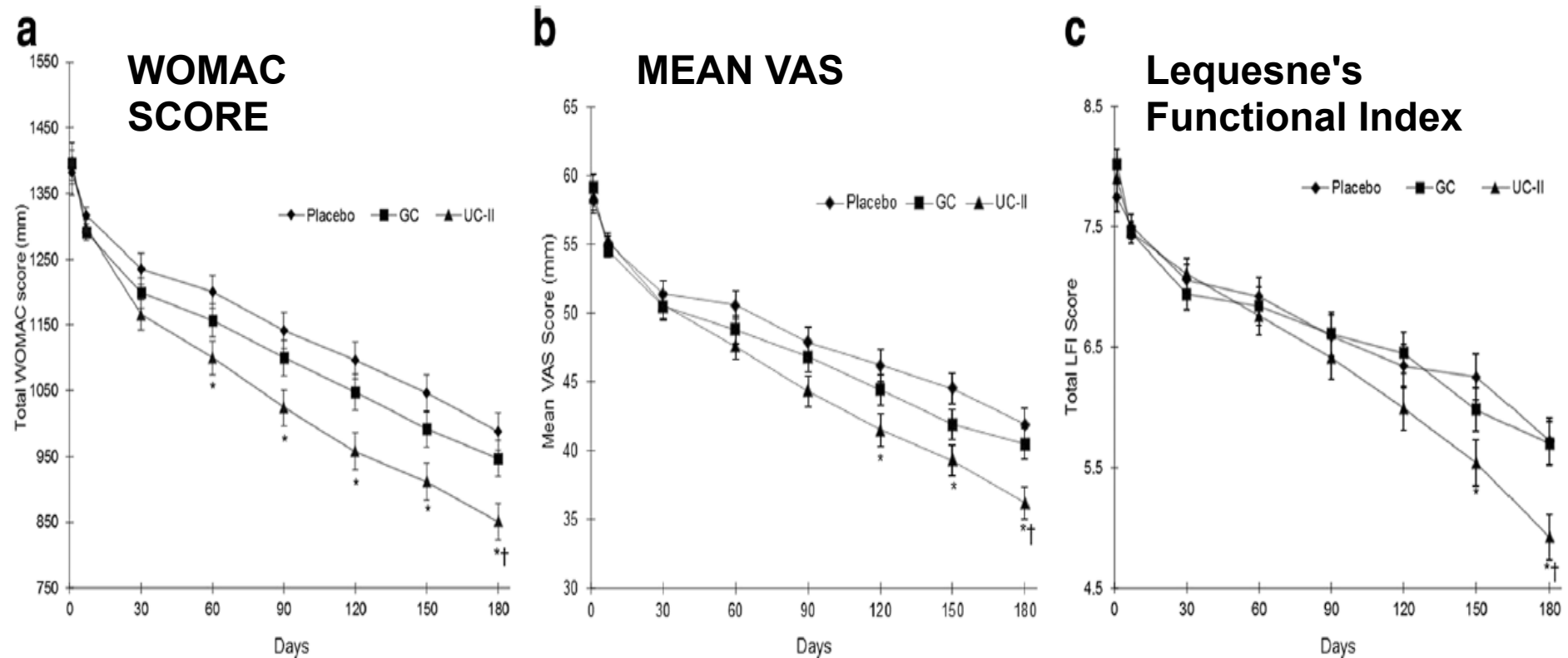
- 662 subjects, Rx follow-up: 2 years
- Over 2 years, no treatment achieved a clinically important difference in WOMAC pain or function as compared with placebo. However, glucosamine and celecoxib showed beneficial but not significant trends.
- Use of Glucosamine hydrochloride in advanced OA stage, t.i.d.

Long Term Evaluation of Glucosamine Sulfate Study (LEGS) (2014)

- 605 subjects, Rx follow-up: 2 years
- No significant differences were found in the amount of joint space narrowing in people taking glucosamine sulphate or chondroitin alone, compared with placebo, u.i.d.
- However, people taking the combination of glucosamine and chondroitin had about half the amount of joint space narrowing compared with those taking placebo (a difference of 0.10 mm, $p=0.046$).

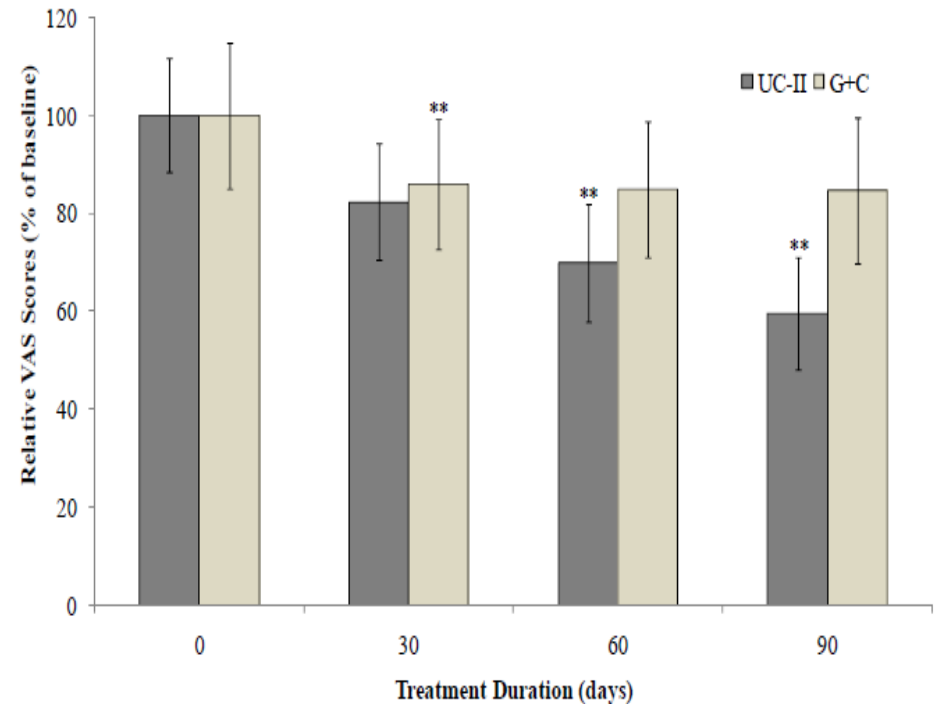
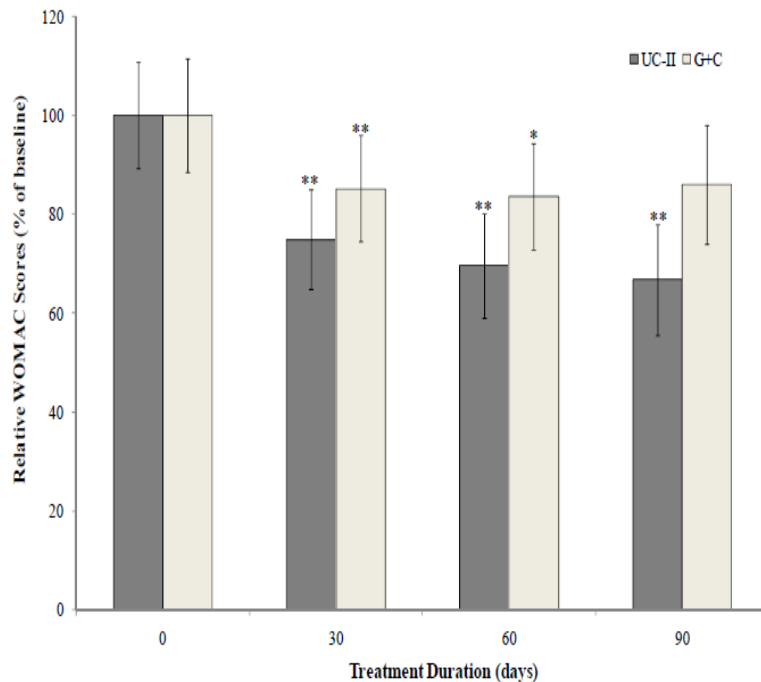
Efficacy of an undenatured type II collagen supplement in modulating knee osteoarthritis symptoms: a multicenter RCT

N.: 199; Placebo vs. Gluco/Condro (1500/1200 mg) vs. Collagen II (40 mg)



Lugo et al. Nutrition Journal (2016) 15:14

Efficacy of undenatured type II collagen in the treatment of osteoarthritis of the knee: an RCT

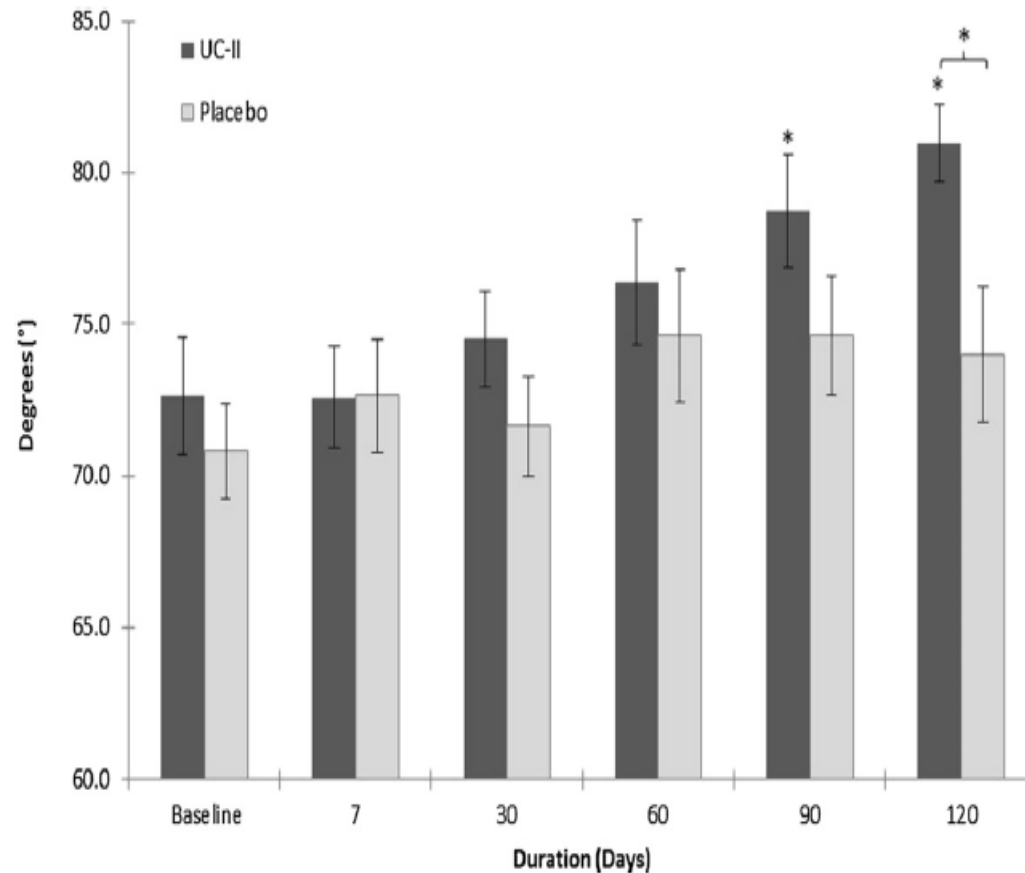


Int. J. Med. Sci. 2009, 6

Undenatured type II collagen (UC-II®) for joint support: an RCT in healthy volunteers

**Knee
extension
as
measured
by
goniometry**

***Lugo et al. J
Int Soc
Sports Nutr
2013;10:48***

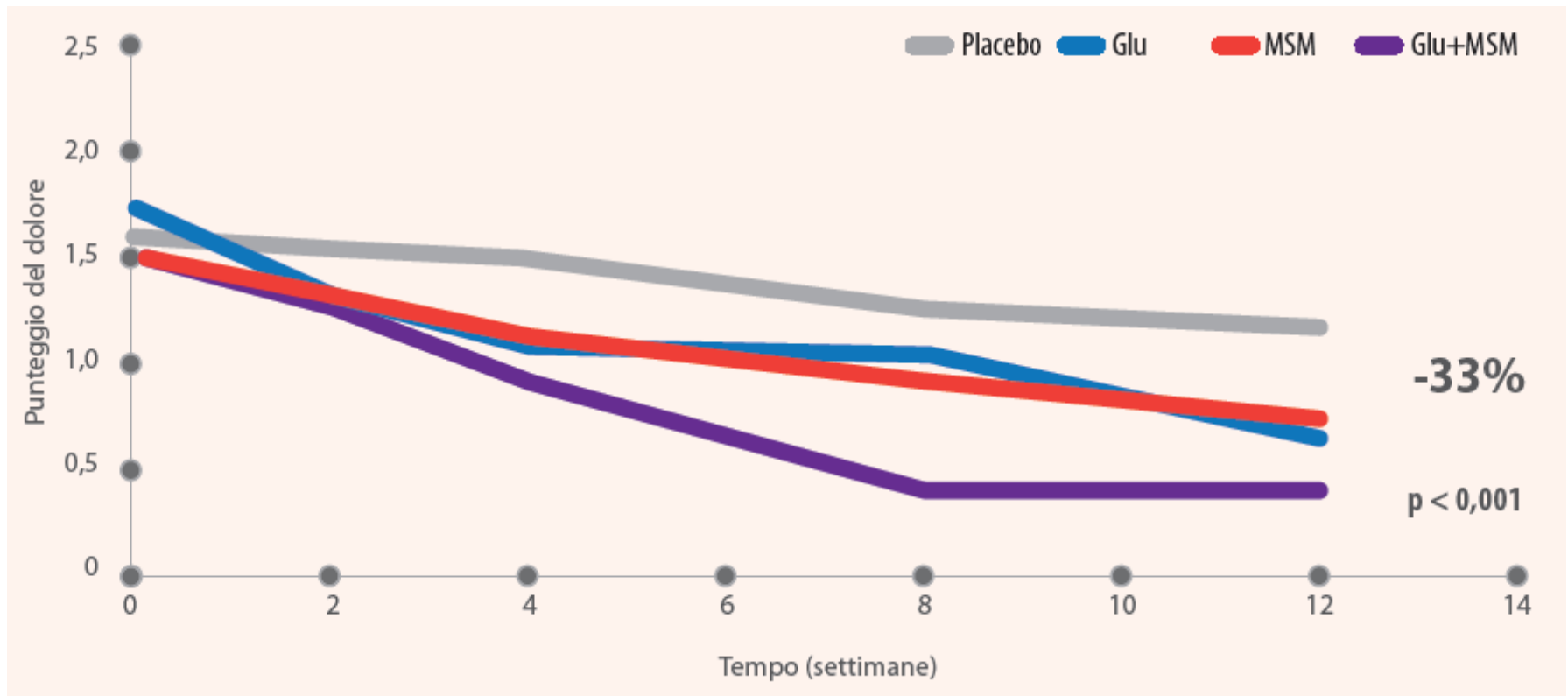


Effetto del MSM sull'artrosi del ginocchio

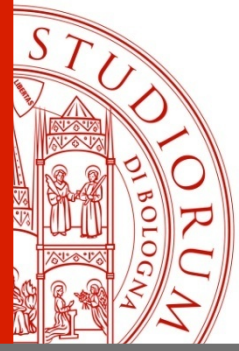
	MSM (n = 25)			Placebo (n = 25)				Significance for between group differences at follow-ups	
	6 weeks	12 weeks	Difference 0-12 wk [CI]	6 weeks	12 weeks	Difference 0-12 wk [CI]	Between group difference [CI]	0-6 wks	0-12 wks
WOMAC									
Pain	35.5 ± 26.1	34.0 ± 24.5	-9.0 ± 24.0 [-18.9, 0.9]	47.1 ± 26.6	49.4 ± 20.8	3.5 ± 19.3 [-4.5, 11.5]	12.4 [0.0, 24.8]	0.20	0.05*
Stiffness	39.2 ± 31.0	36.0 ± 26.2	-11.7 ± 30.7 [-24.3, 1.0]	52.9 ± 30.4	58.5 ± 24.2	15.5 ± 35.8 [0.7, 30.3]	27.2 [8.2, 46.2]	0.03*	0.01*
Function	36.6 ± 23.7	33.1 ± 23.1	-7.7 ± 19.3 [-15.8, 0.3]	46.2 ± 25.1	54.3 ± 21.1	6.9 ± 17.0 [0.1, 13.9]	14.6 [4.3, 25.0]	0.51	0.01*
Total	36.6 ± 23.9	33.3 ± 22.5	-8.4 ± 17.8 [-15.8, -1.1]	47.2 ± 24.5	53.5 ± 20.3	6.5 ± 17.0 [0.5, 13.5]	15.0 [5.1, 24.9]	0.26	0.00*
ALF	36.5 ± 16.6	36.9 ± 20.7	-6.8 ± 10.3 [-11.0, -2.5]	32.2 ± 10.6	33.9 ± 10.9	0.8 ± 4.9 [-1.2, 2.8]	7.6 [2.9, 12.2]	0.02*	0.00*
SF-36	59.8 ± 19.7	62.2 ± 20.3	8.1 ± 21.8 [-0.8, 17.1]	61.1 ± 16.2	54.5 ± 15.4	-3.4 ± 14.6 [-9.5, 2.6]	-11.6 [-22.1, -1.0]	0.52	0.03*
VAS	3.30 ± 2.8	3.61 ± 2.9	-0.2 ± 3.2 [-1.5, 1.1]	5.22 ± 2.9	5.16 ± 2.22	0.6 ± 2.7 [-0.6, 1.7]	0.7 [-0.9, 2.4]	0.18	0.38

BMC Complement Altern Med. 2011 Jun 27;11:50.

Studio condotto in 118 pazienti con OA del ginocchio lieve-moderata randomizzati alla supplementazione 3 volte/die, con: - glucosamina 500 mg - MSM 500 mg - glucosamina + MSM - placebo

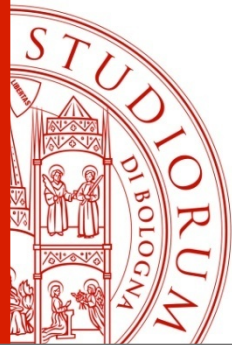


Usha PR et al. Clin Drug Invest 2004;24:353-363



Attenzione ai falsi amici

- **Gli «omega 3» sono antinfiammatori solo per dosaggi molto alti e spesso più per applicazione topica che per ingestione**
- **L'artiglio del diavolo funziona come un antinfiammatorio standard ed ha gli stessi effetti collaterali !!!**
- **Uno studio non fa primavera**

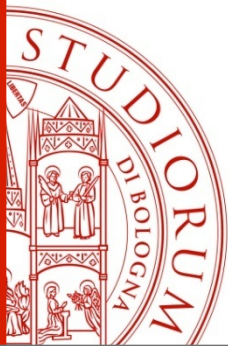


Effetto dell'acido ialuronico per os sul dolore percepito nell'artrosi del ginocchio: uno studio clinico

	<u>HA</u> (n = 21)		Placebo (n = 19)	
	Baseline	3 months	Baseline	3 months
VAS	6.75 ± 0.18 ^a	4.06 ± 0.53 ^{b*}	6.18 ± 0.21	5.84 ± 0.50
WOMAC pain	8.81 ± 0.67 ^a	5.75 ± 0.90 ^{b*}	8.05 ± 0.77	8.16 ± 0.73
WOMAC total	40.29 ± 2.55 ^a	27.62 ± 4.38 ^{b*}	40.53 ± 3.40	39.58 ± 3.97

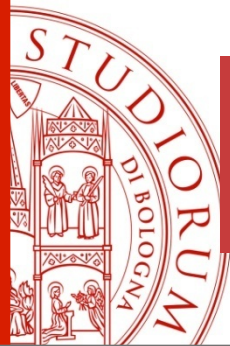
Ca. – 30% !!!

Rheumatol Int. 2015;35(1):43-52.



Vantaggi dell'approccio nutraceutico

- Usualmente buon profilo di safety
- Rarissime controindicazioni (pregressa intolleranza)
- Rarissime interazioni con terapia farmacologica
- Gradito dal paziente
- Multi-target
- Potenzialmente efficaci (se molecole, forme farmaceutiche, durata del trattamento e dosaggi corretti)



La conclusione irriverente

**Il dietologo mi ha
detto di eliminare il
pane, quindi da oggi
la Nutella me la
spalmo direttamente
sulla lingua.**