

# Osteoartritis, puesta al día.

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Unidad de Reumatología, Clínica Alemana de Santiago

# Potenciales Conflictos de Interés.

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Asistencia a Cursos o Congresos  
Consultorías, Conferencista  
Protocolos de Investigación Clínica

- Abbvie
- Bristol Squibb Myers
- Glaxo Smith Kline
- Janssen
- Merck Sharp & Dhome
- Novartis
- Pfizer
- Roche
- Sanofi

# Temario.

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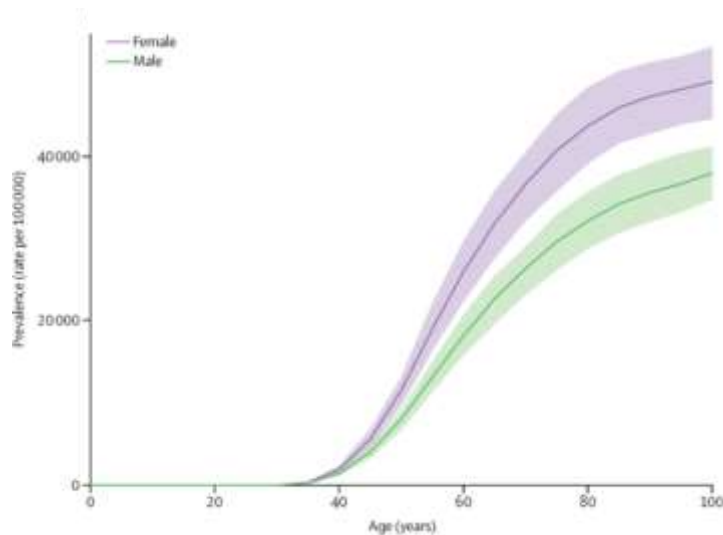
- Epidemiología
- Patogenia
- Manejo

# Temario.

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- **Epidemiología**
- Patogenia
- Manejo

Prevalencia global de OA por sexo y edad 2020.



## Estimación de Prevalencia OA 2020, 204 países.

Mayores de 30 años

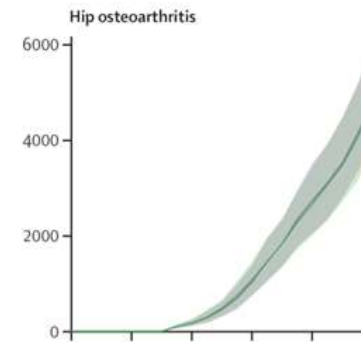
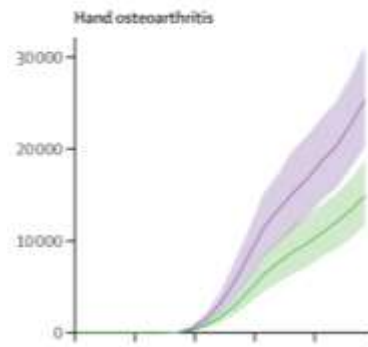
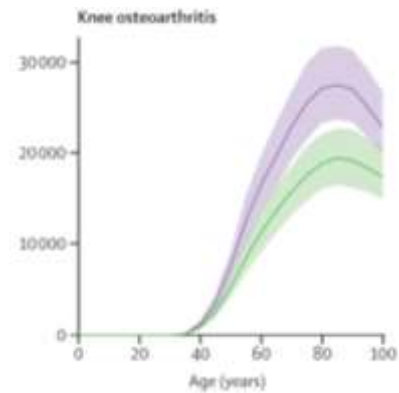
OA sintomática, confirmada Rx en 42 países

Severidad por índice WOMAC

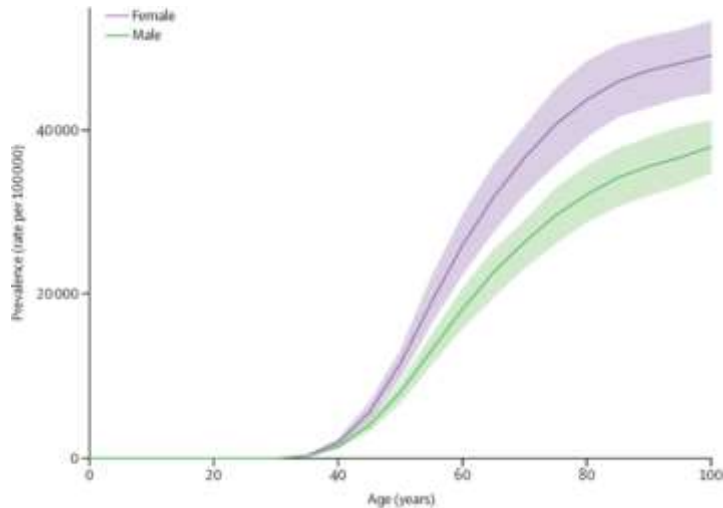
- Inicia a los 40 años / > edad
- 7.6% población mundial (95% UI 6.8-8.4)
- 595 millones personas (95% UI 535-656)
- Mujeres 8.059/100.000 (95% UI 7252-8868)
- Hombres 5.780/100.000 (95% UI 5218-6342)
- 255/100.000 (119-557) YLDs
- 14° causa YLDs / 7° causa YLDs > 70 años

Prevalencia estandarizada por edad y sitio anatómico/100.000 personas.

Knee osteoarthritis		Hand osteoarthritis		Hip osteoarthritis	
Number of prevalent cases (95% UI)	Age-standardised prevalence rate per 100 000 (95% UI)	Number of prevalent cases (95% UI)	Age-standardised prevalence rate per 100 000 (95% UI)	Number of prevalent cases (95% UI)	Age-standardised prevalence rate per 100 000 (95% UI)
368 000 000 (328 000 000–420 000 000)	4307·4 (3844·5–4913·3)	189 000 000 (146 000 000–238 000 000)	2226·1 (1719·7–2802·8)	35 300 000 (26 500 000–45 100 000)	417·7 (314·7–532·7)



### Prevalencia global de OA por sexo y edad 2020.



### Estimación de Prevalencia OA: 1990 > 2020 > 2050

#### Compara prevalencia 1990 > 2020

- OA Global +132%
- YLDs + 9.5%

#### Proyección 2020 > 2050

- 642 (95% UI 574-722) millones personas
- OA Rodilla + 78.6% (95% UI 59-90)
- OA Cadera + 74.9% (95% UI 59-90)
- OA Mano + 48.6% (95% UI 58-105)



Fernando Botero (1932- 2023)

## Estimación de Prevalencia OA 2020, 204 países

### Factores de Riesgo para OA ...

#### Influencia IMC > 25

- 1990 19.1% (-1.3 - 30.2)
- 2020 20.4% (-1.7 - 36.6)
  
- Hombres 19.3% (-1.7 - 37.7)
- Mujeres 21.1% (-1.8 - 37.7)
  
- **LATAM sur 27.9% (-2.4 - 47.7)**

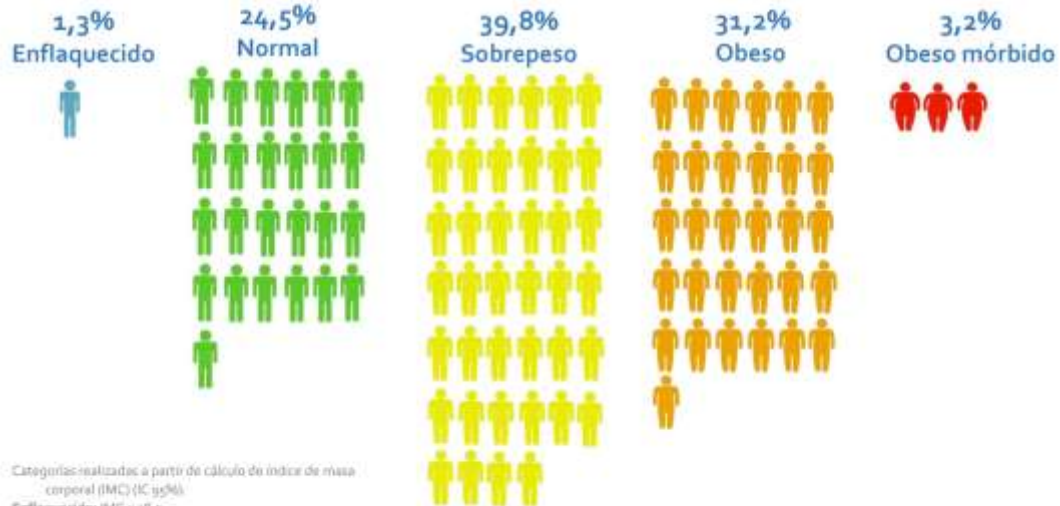


## ESTADO NUTRICIONAL



Encuesta  
Nacional de  
Salud  
2016-2017

### Estado nutricional, prevalencia total país. ENS 2016-17



Categorías realizadas a partir de cálculo de índice de masa corporal (IMC) (IC 95%).

- Enflaquecido: IMC < 18,5
- Normal: IMC 18,5-24,9
- Sobrepeso: IMC 25-29,9
- Obesidad: IMC 30-39,9
- Obesidad mórbida: IMC ≥ 40

**Sobrepeso + Obesidad: 74.2%**



Prevalencia estandarizada por edad y sitio anatómico/100.000 personas.

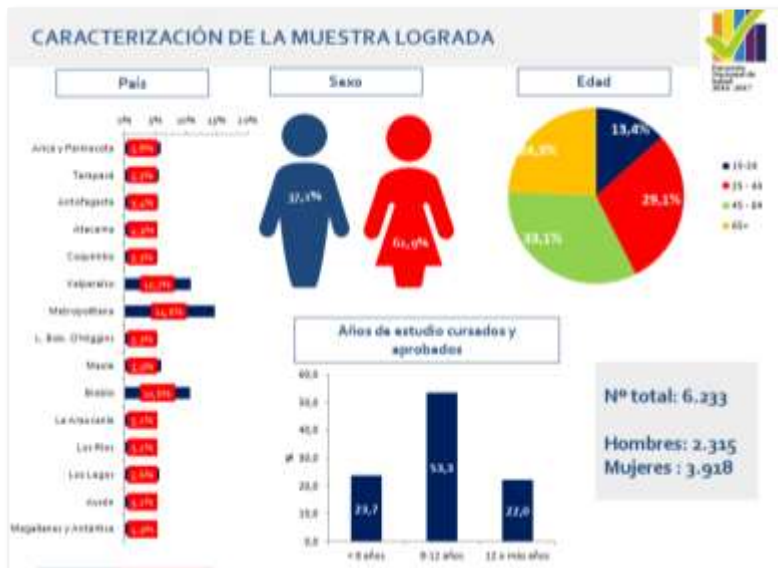
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Chile	1 160 000 (1 020 000–1 310 000)	4715·6 (4150·9–5302·0)	594 000 (454 000–747 000)	2395·9 (1844·6–2997·5)	177 000 (134 000–228 000)	716·6 (542·6–920·2)
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**+9.5%**

**+72%**





## Población de Chile 2017:

General	17.574.003
> 15 años	14.050.253

## Autorreporte OA

OA Rodilla	5.7%	800.864
OA Cadera	3.1%	435.558

Garantías Explícitas en Salud (GES-AUGE)

Casos GES (AUGE) acumulados a diciembre de 2022

Contiene los casos GES (AUGE) acumulados a diciembre del año 2022.

**Número de Casos Acumulados  
Jul 2005 a Sept 2023**

12. Artrosis de Cadera Severa que requiere Prótesis, 2005	57.567
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41. Tratamiento médico en personas de 55 años y más con artrosis de cadera y/o rodilla, leve o moderada, 2008	1.014.862
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1.072.429

(Estimación por GBD 1.337.000)

(Estimación por ENS 1.236.422)

Garantías Explícitas en Salud (GES-AUGE)

## GES y Artrosis.

### Prestaciones a 09/2023

### Garantías Vencidas 09/2022

Problema de Salud 12. GES 2005	Fonasa	Isapres	Total
Artrosis de Cadera Severa que requiere Prótesis	51.335	4.232	1824
Problema de Salud 41. GES 2008	Fonasa	Isapres	
Tratamiento médico en personas de 55 años y más con artrosis de cadera y/o rodilla, leve o moderada.	976.390	38.472	312

## Autorreporte de Artrosis y Alteración de la Capacidad, ENS 2016-2017.

	Prevalencia (%)	Alteración de la Capacidad Prevalencia (%)			
		Ninguna	Leve	Moderada	Severa
<b>Autorreporte de Artrosis de Rodilla</b>	5.7%	1.8%	17%	<b>31.5%</b>	<b>49.7%</b>
<b>Autorreporte de Artrosis de Cadera</b>	3.1%	1.1%	18.7%	<b>26.9%</b>	<b>53.4%</b>

## OARSI White Paper- OA as a Serious Disease



# Temario.

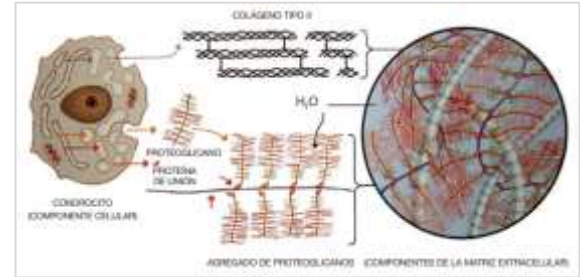
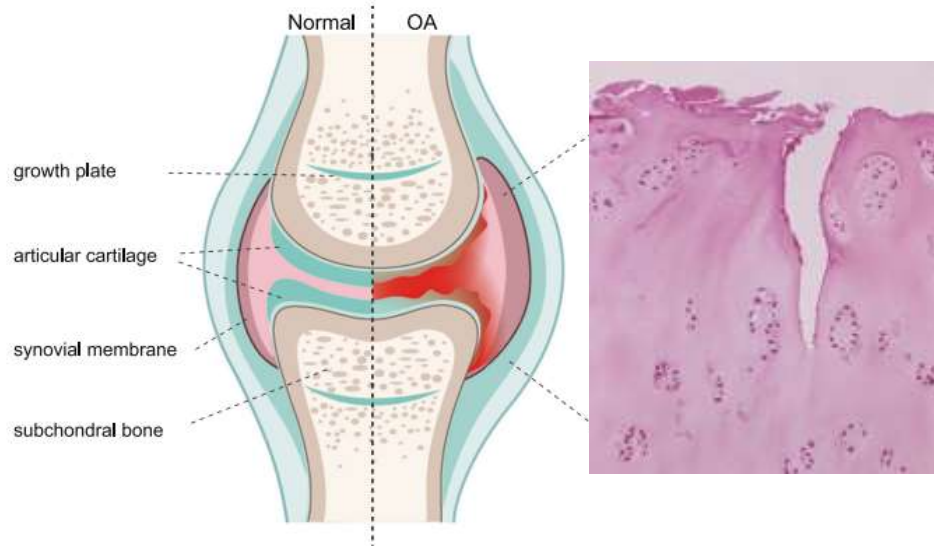
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- Epidemiología
- **Patogenia**
- Manejo



# “Uso y Desgaste”

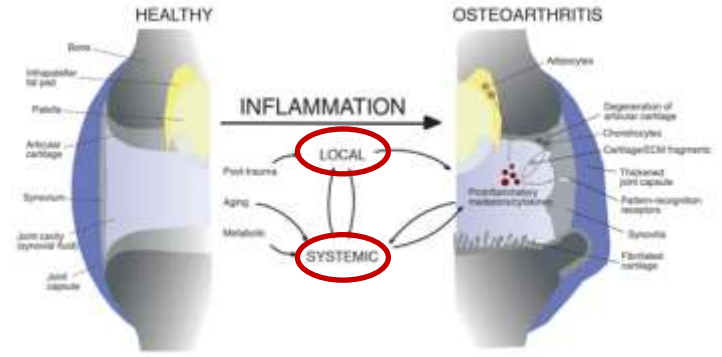
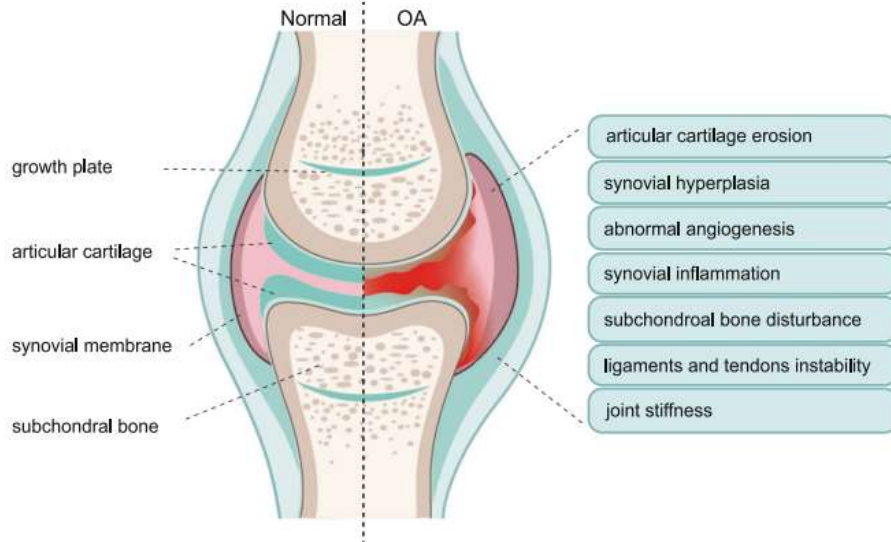
## Artrosis





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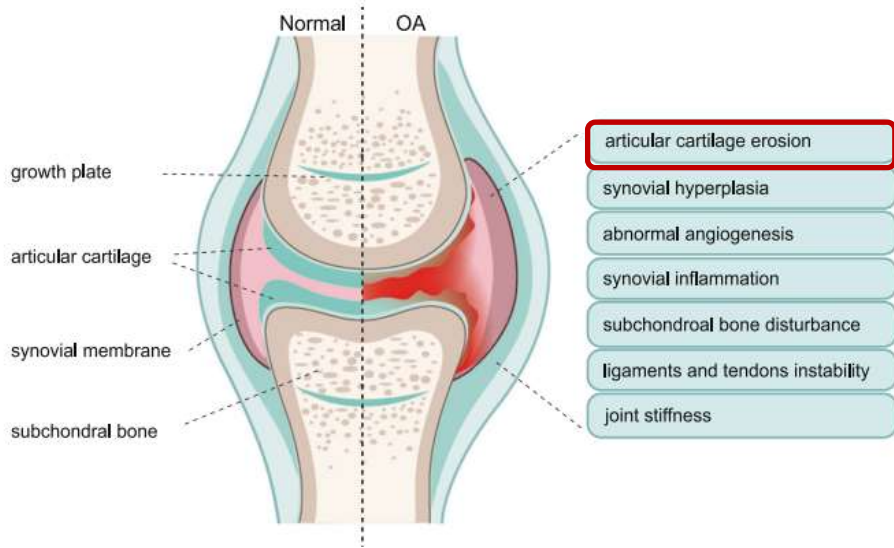
# Osteoarthritis: pathogenic signaling pathways and therapeutic targets





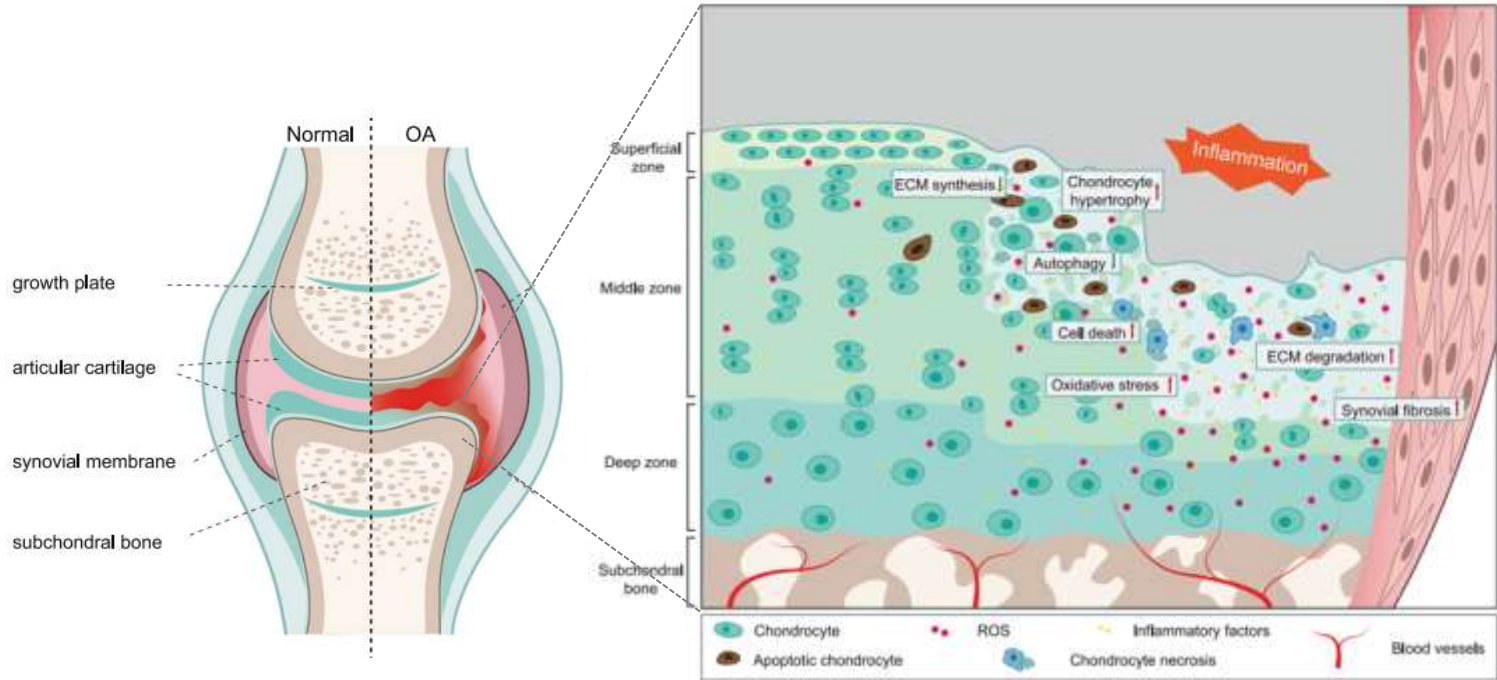
REVIEW ARTICLE OPEN

# Osteoarthritis: pathogenic signaling pathways and therapeutic targets





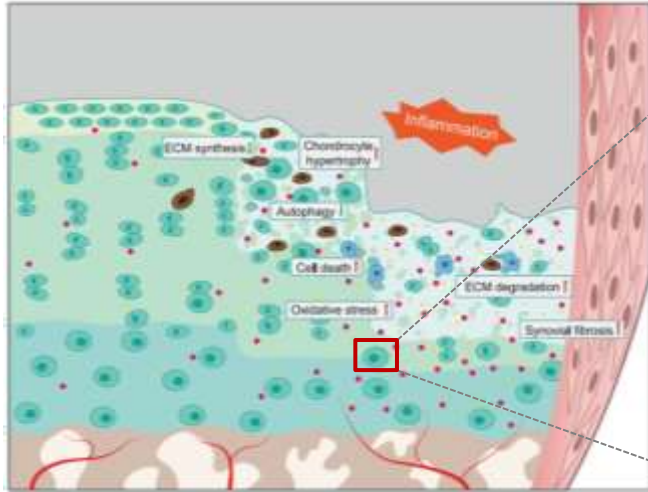
## Estrés Oxidativo, Inflamación y Apoptosis



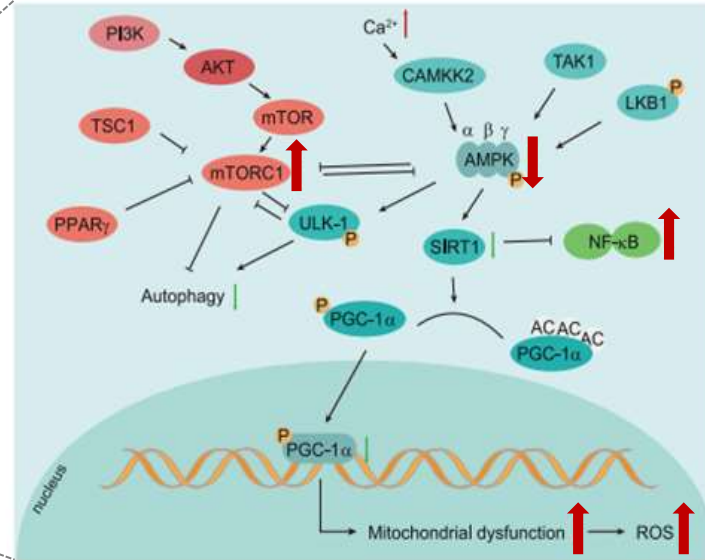


REVIEW ARTICLE OPEN

# Osteoarthritis: pathogenic signaling pathways and therapeutic targets



## Estrés Oxidativo y Disfunción Mitocondrial



## REVIEW



### **Is osteoarthritis a mitochondrial disease? What is the evidence**

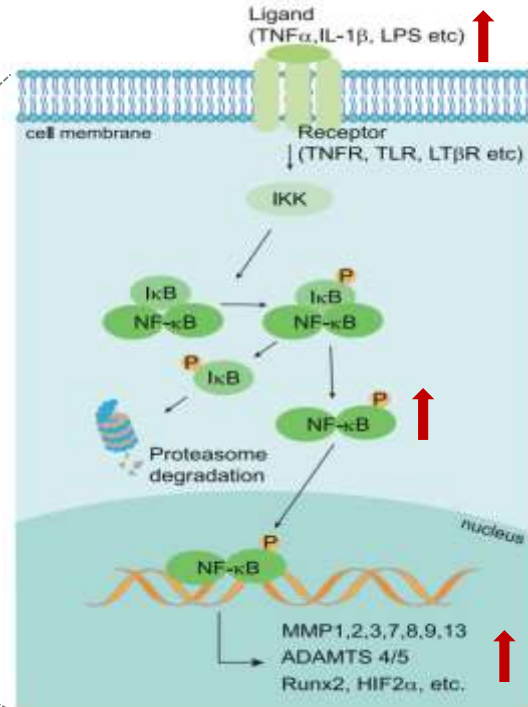
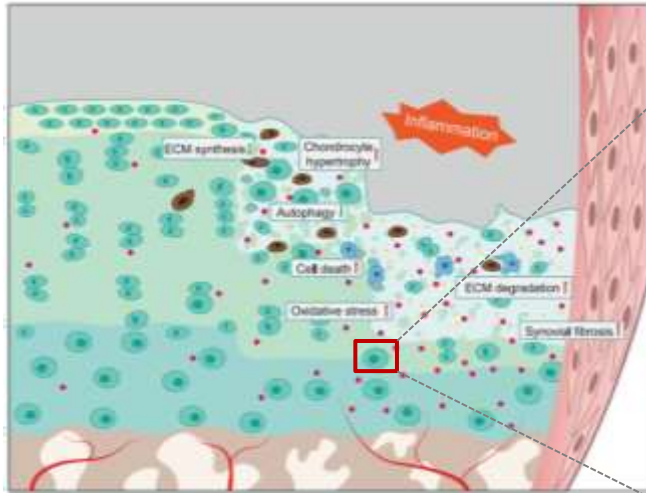




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Osteoarthritis: pathogenic signaling pathways and therapeutic targets

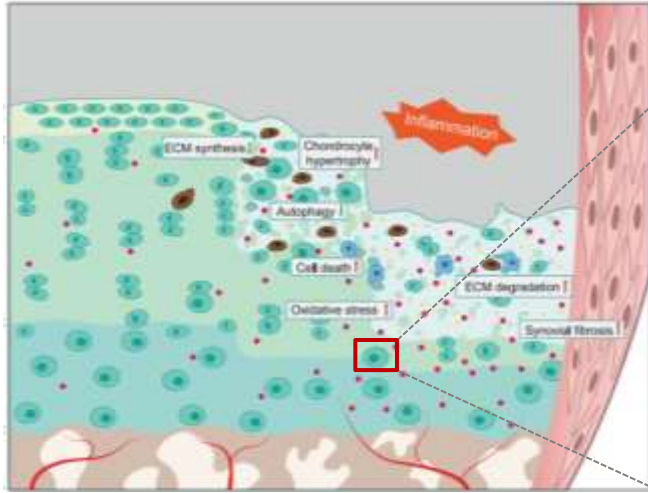
## CKs Proinflammatory > Metaloproteinasas



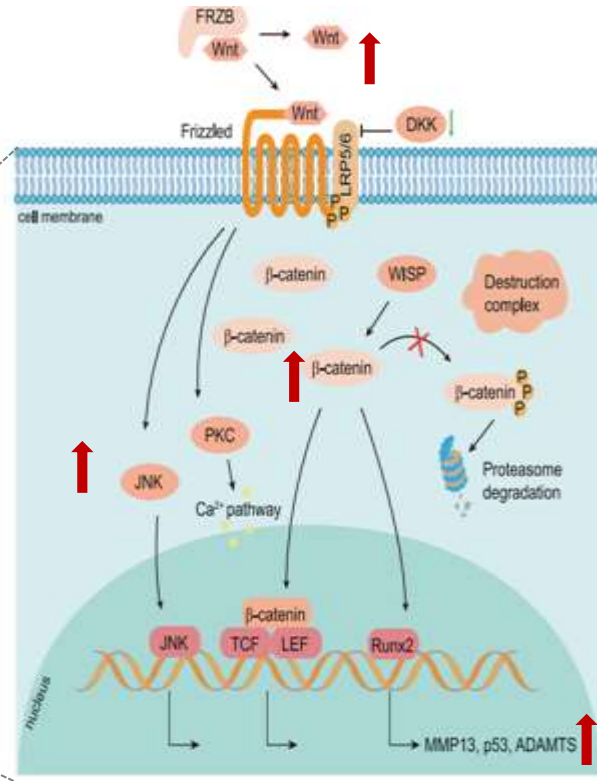


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Osteoarthritis: pathogenic signaling pathways and therapeutic targets



## Señal *Wnt* > Metaloproteinasas



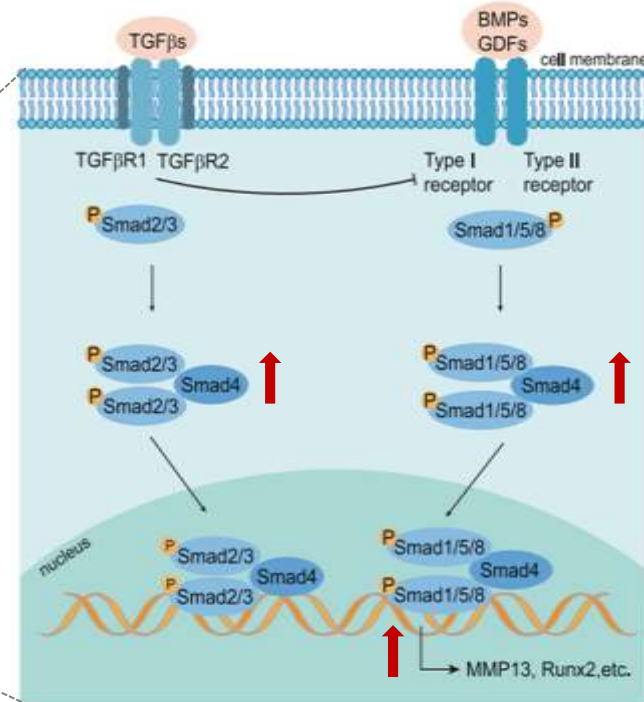
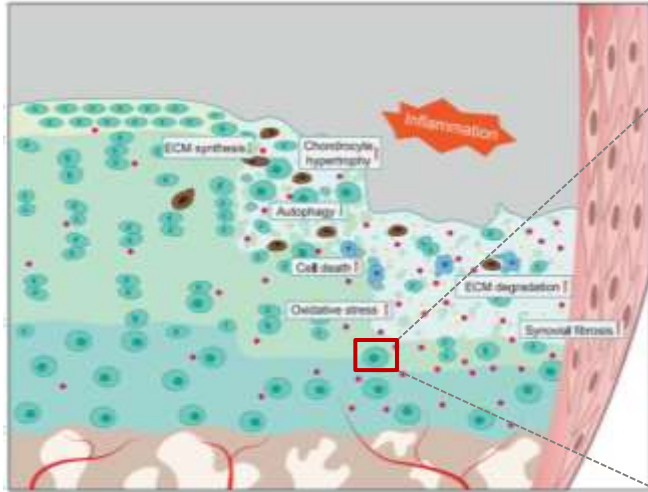




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Osteoarthritis: pathogenic signaling pathways and therapeutic targets

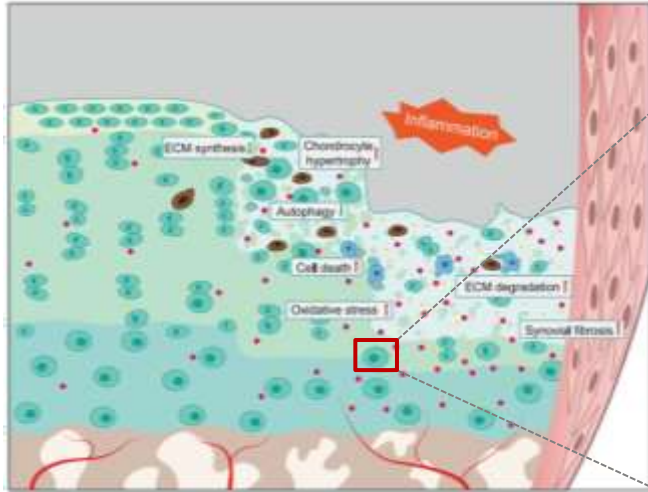
## TGF- $\beta$ y BMPs > Smad > Runx-2 Metaloproteinasas



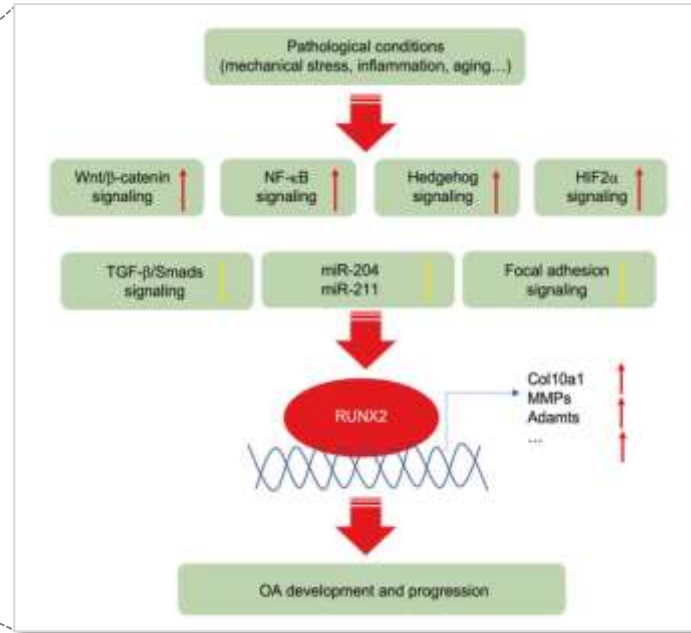


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# Osteoarthritis: pathogenic signaling pathways and therapeutic targets



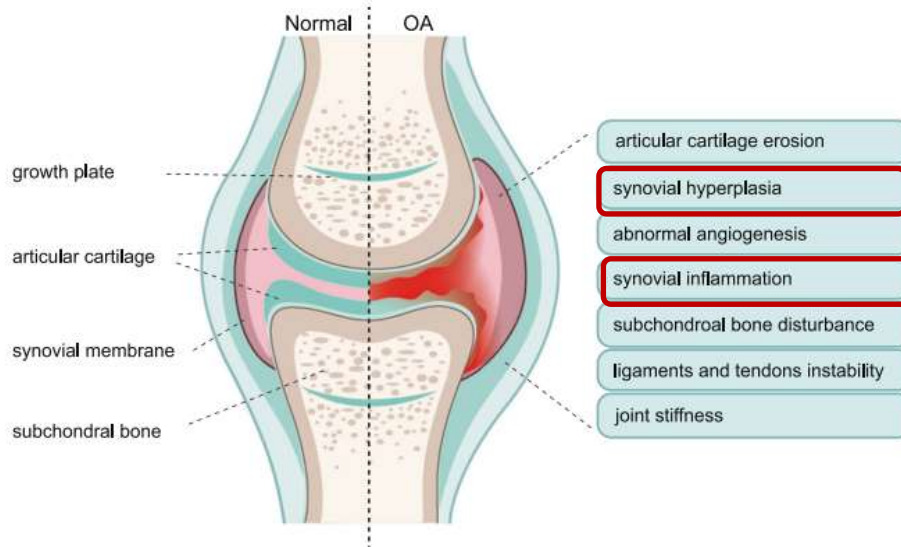
## Múltiples Vías > Daño Tisular





REVIEW ARTICLE **OPEN**

# Osteoarthritis: pathogenic signaling pathways and therapeutic targets

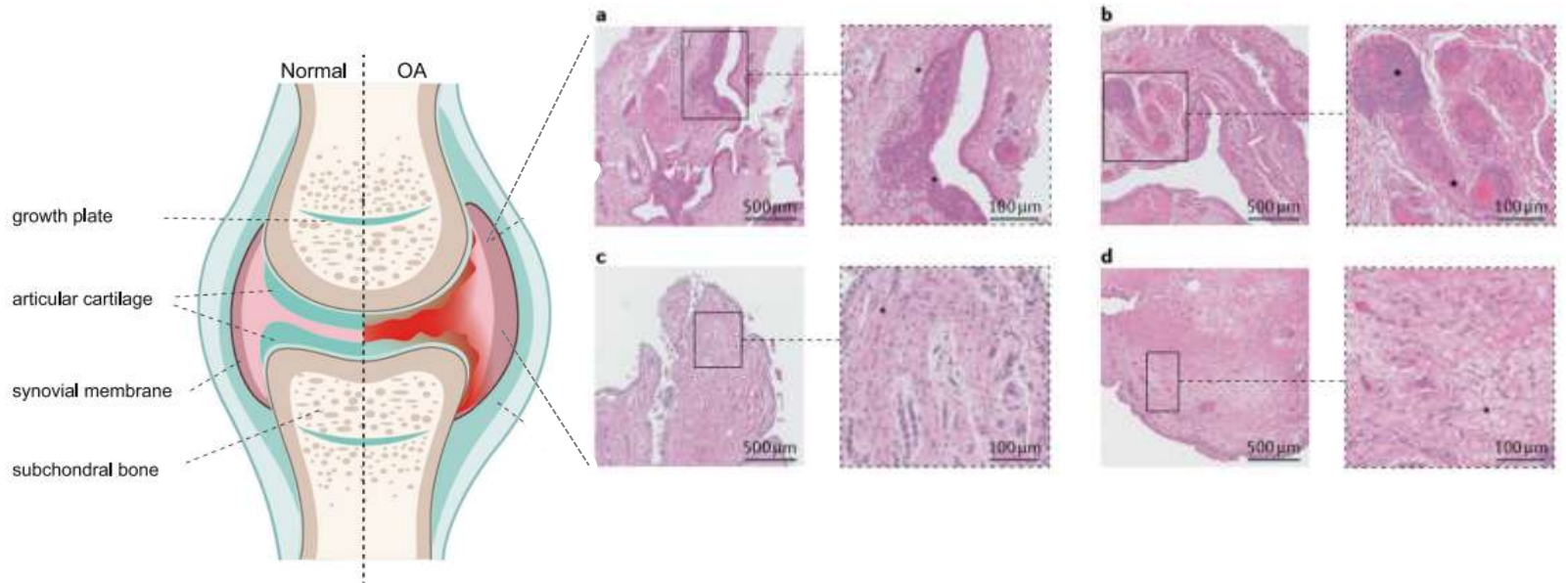




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# Osteoarthritis: pathogenic signaling pathways and therapeutic targets

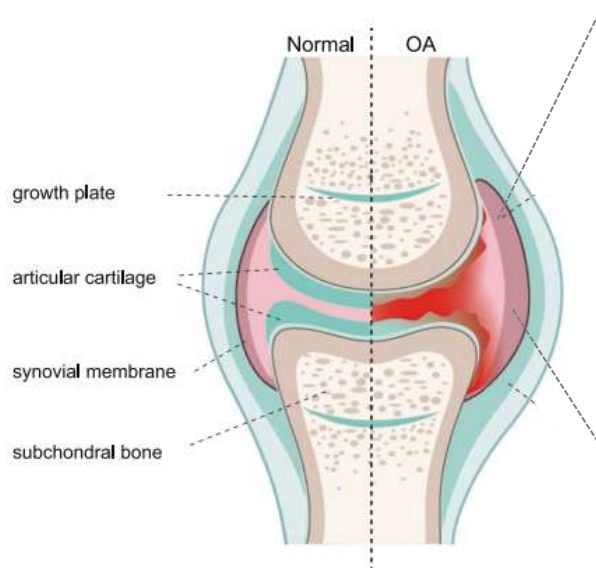
## Sinovitis > Daño Tisular





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Osteoarthritis: pathogenic signaling pathways and therapeutic targets



## Factores de Riesgo de Sinovitis

### Trauma

- Meniscus and ligament injuries
- Intra-articular fractures

### Mechanical loading

- Shear stress and compression
- Induces inflammatory mediators (e.g. NOS, IL-6 and IL-8)



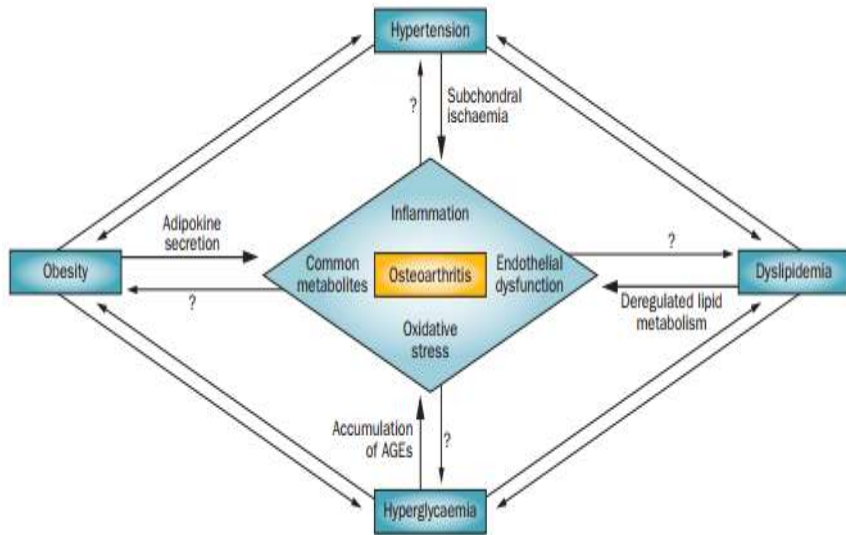
### Comorbidities

- Obesity
- Type 2 diabetes mellitus

### Diet and gut microbiome

- Diet might shape the gut microbiome
- Microbial dysbiosis
- Changes in intestinal permeability
- Metabolic endotoxaemia (systemic LPS) correlates with activated synovial macrophages

## Metabolic syndrome meets osteoarthritis



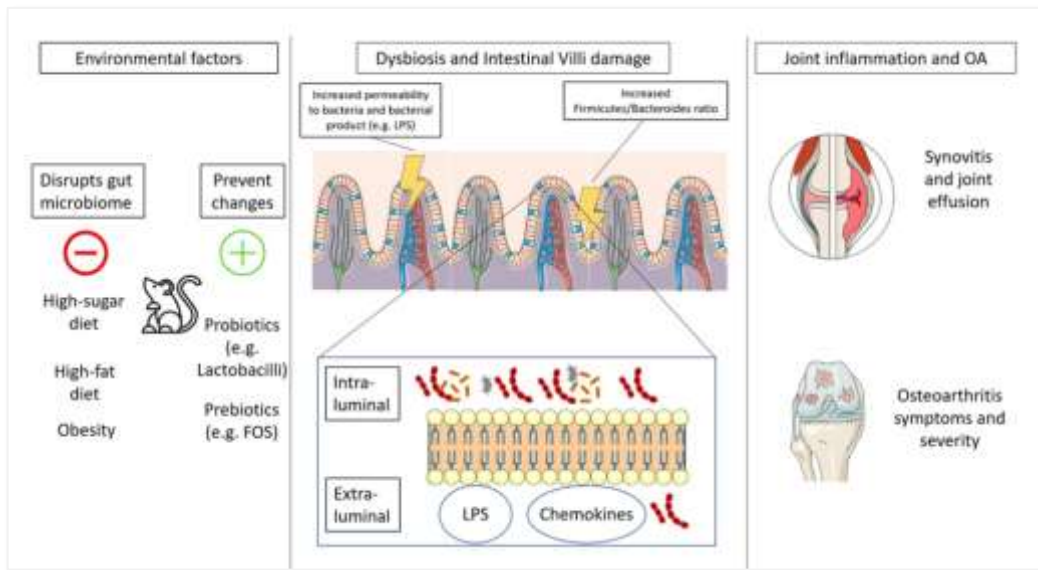
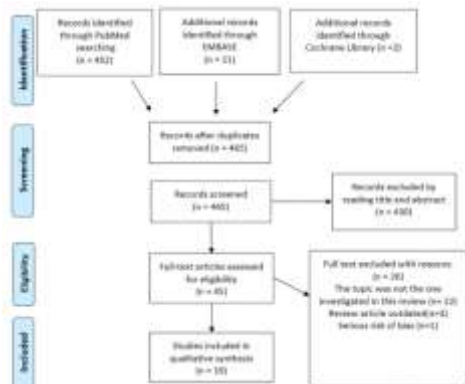
## Obesity, Metabolic Syndrome, and Osteoarthritis—An Updated Review

- Leptina
- Adiponectina
- Visfatina
- Resistina
- Quimerina
- Lipocalina-2
- Apelina
- Serpina



- IGF-1
- TGB- $\beta$
- PGE2
- MMPs
- IL-1  $\beta$
- IL-6
- TNF $\alpha$

# The relation between the gut microbiome and osteoarthritis: A systematic review of literature



## The Potential Role of Probiotics in the Management of Osteoarthritis Pain: Current Status and Future Prospects

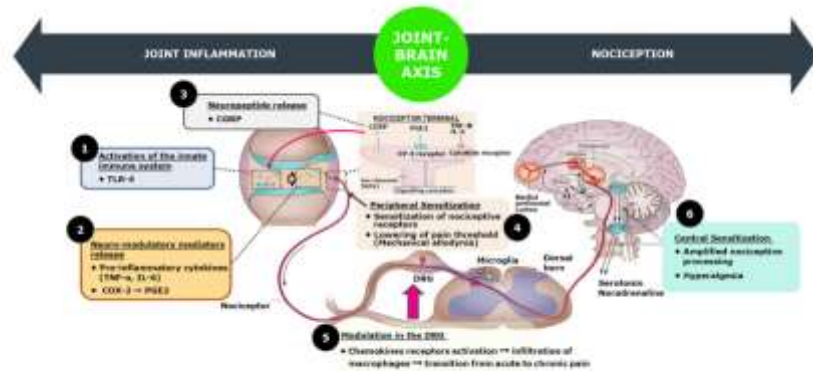


Fig. 2 Joint brain axis illustrating both peripheral and central processes leading to the OA pain experience.

- Sensibilización periférica
- Sensibilización central

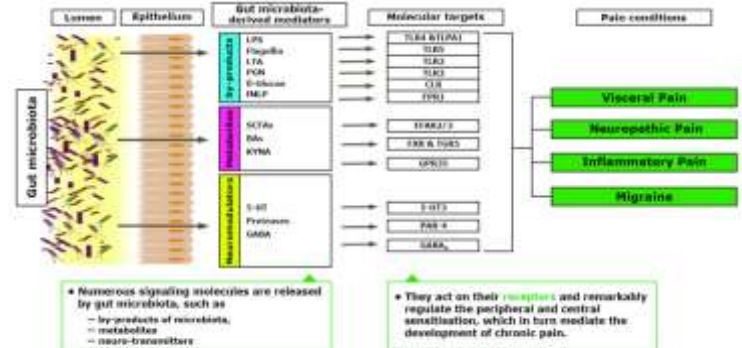


Fig. 3 Effect of gastrointestinal microbiota on peripheral sensitization triggering chronic pain



# Temario.

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- Epidemiología
- Patogenia
- **Manejo**

The current state of the osteoarthritis drug development pipeline: a comprehensive narrative review of the present challenges and future opportunities

- No farmacológico
- Sintomático
- DMOADs

**Table 3.** Practical understanding of current EMA or FDA guidance on DMOAD.

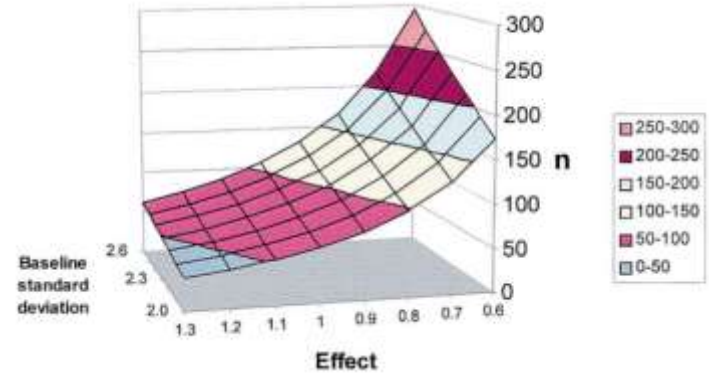
Structure improvement	• VAS • WOMAC • AIMS	Symptom improvement
Radiographic indicator (JSN)	• HAQ-DI	Pain indicator
MRI indicator (cartilage volume and thickness)	• KOOS	Function indicator
Non-cartilage indicator (BML, synovitis, and effusion)	• OKS	Delay of surgical intervention
To obtain approval, both conditions must be met.		
BML, bone marrow lesion; DMOAD, disease-modifying osteoarthritis drugs; EMA, European Medicines Agency; FDA, US Food and Drug Administration; JSN, joint space narrowing; MRI, magnetic resonance imaging.	• IKDC • LAI	
	• OARSI	
	• SF-36	

# Smallest Detectable and Minimal Clinically Important Differences of Rehabilitation Intervention With Their Implications for Required Sample Sizes Using WOMAC and SF-36 Quality of Life Measurement Instruments in Patients With Osteoarthritis of the Lower Extremities

Table 3. Smallest detectable difference (SDD) and sample sizes (n) given the data of a pilot study (Tables 1 and 2)\*

Given the ...	n of pilot study, SD (baseline)		ES	SRM	MCID for worsening,	MCID for improvement,
	1a	2			SD (baseline)	SD (baseline)
Using formula†	1a	2	3	4	5	6
Results in	SDD	n per treatment arm	n total	n total	n total	n total
<b>WOMAC (n = 122)</b>						
Pain	0.81	187	66	80	142	142
Stiffness	0.96	>1000	765	431	216	216
Function	0.78	325	100	43	167	167
Global	0.73	297	100	42	133	133
<b>SF-36 (n = 116)</b>						
Bodily pain	6.1	40	39	83	71	71
Physical function	7.6	>1000	197	230	612	612
PCS	2.8	173	94	233	233	233

\* SD (baseline) = standard deviation of baseline scores (x prior standard deviation); ES = effect size; SRM = standardized response mean; MCID = assessed (clinically important) difference; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; SF-36 = Medical Outcomes Study 36-item Short-Form; PCS = physical component summary; ES = Mean (effect) ÷ SD (baseline); SRM = mean (effect) ÷ SD (effect).  
† Formulas in Methods section.

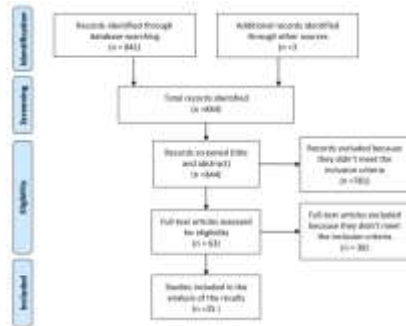
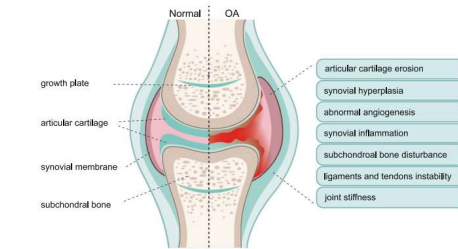


## WOMAC y SF36

- **SSD** Diferencia Mínima Detectable
- **MCID** Diferencia Mínima Clínicamente Importante: **12%**
- **SZ** Tamaño de Muestra Mínimo: **N = 300**



# Identification of clinical phenotypes in knee osteoarthritis: a systematic review of the literature



24 estudios 6/72 fenotipos.

## Fenotipos Clínicos en Artrosis de Rodilla

1. Dolor crónico con sensibilización central
2. Predominante daño de hueso y cartílago
3. Sobrecarga mecánica
4. Inflamatorio
5. Síndrome metabólico
6. Enfermedad articular mínima

## Latest insights in disease-modifying osteoarthritis drugs development

Ther Adv Musculoskelet Dis  
2023, Vol. 15: 1-24  
DOI: 10.1177/  
1759720231161828

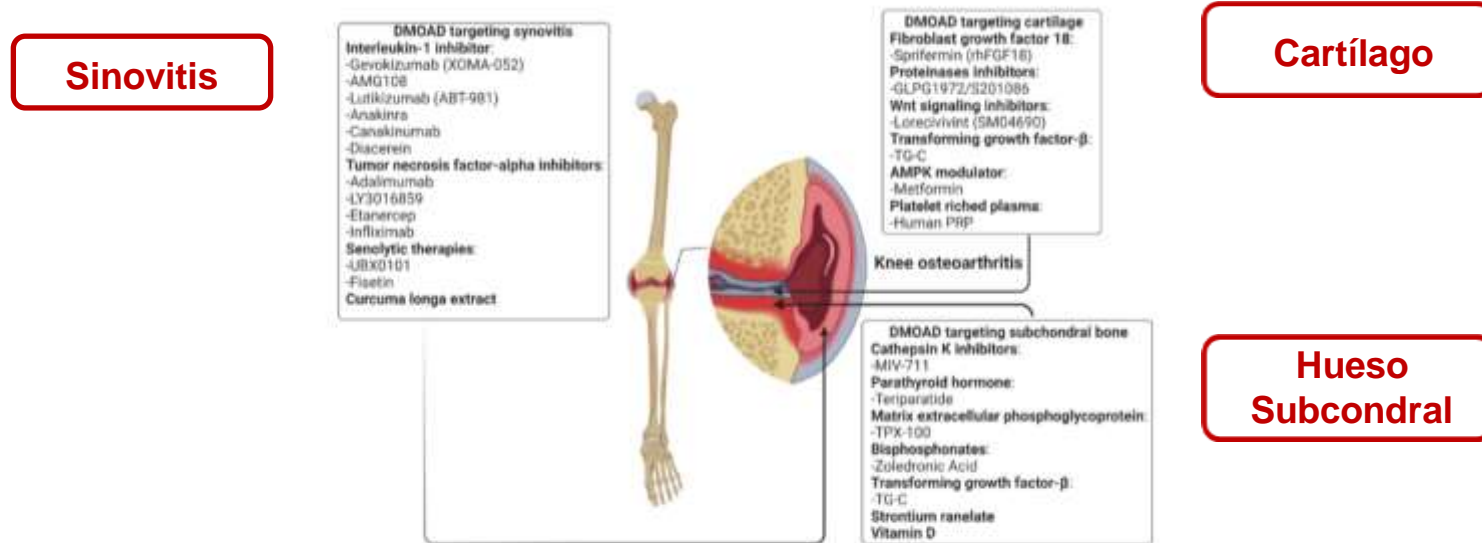
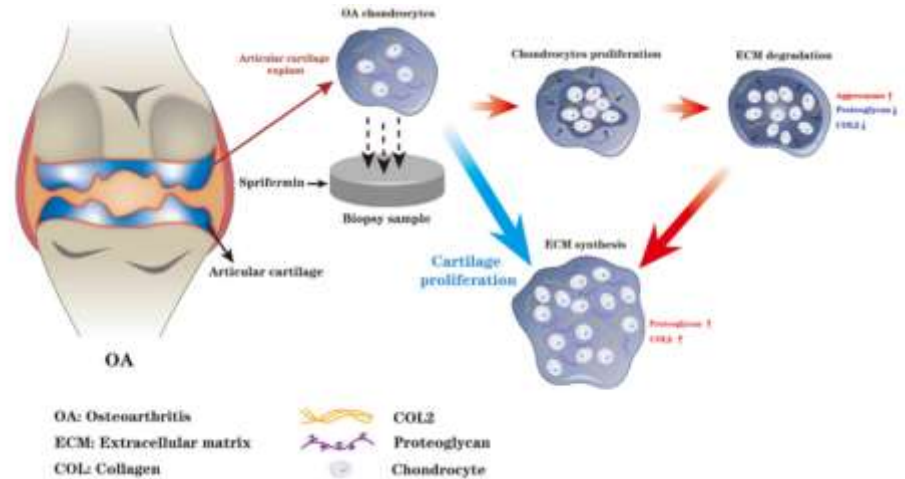
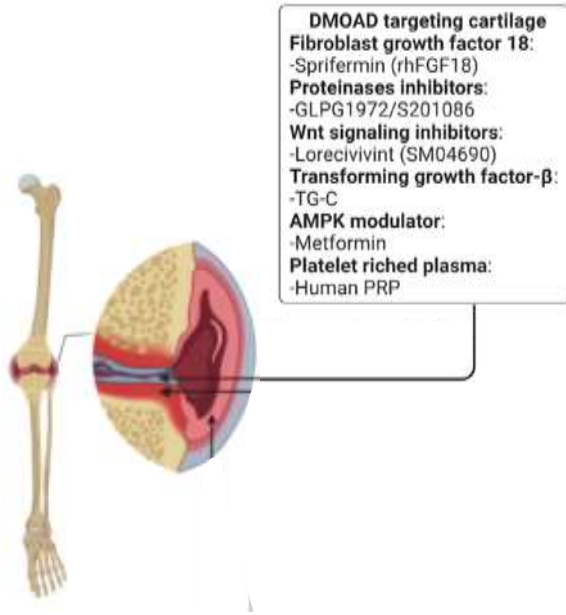


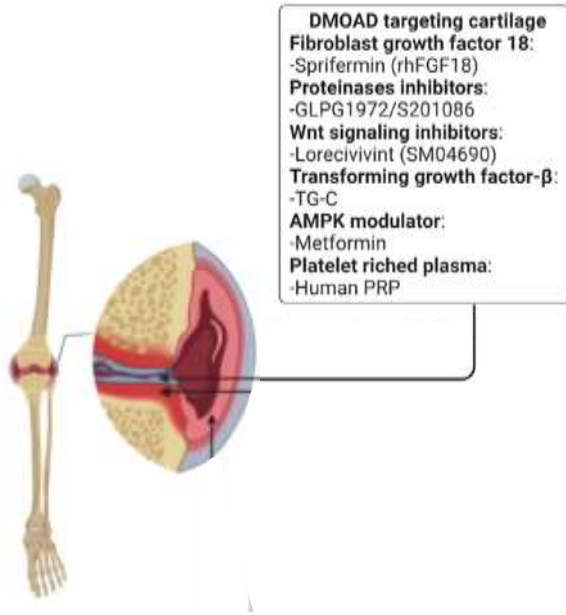
Figure 1. Potential pharmacological therapies for OA.

# Cartílago

## Factor de Crecimiento de Fibroblastos 18 (FGF18)



## Cartílago



## Factor de Crecimiento de Fibroblastos 18 (FGF18)

### FGF18 recombinante humano / Sprifermin

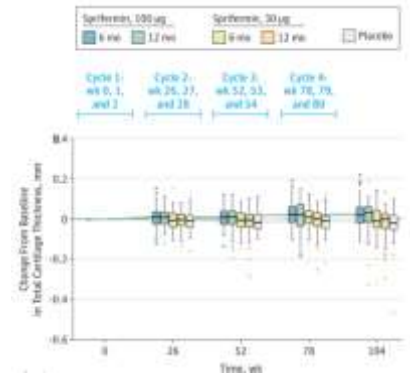
Proliferación de Condrocitos y  $< / >$  Matriz Extracelular

- NCT 00911469. Fase 1
- NCT 01033994. Fase 2
- NCT 01919164. Fase 3

### Estudio FORWARD

Fase 2. RTC 549 pac. 30-100 mcg IA, c/6-12 m x 2 años

- Grosor cartílago FT/RNM.  
100 mcg c/6 m  $> 0.05$  mm \*  
100 mcg c/12 m  $> 0.04$  mm \*
- **WOMAC** n.s.
- **CL: Significado clínico incierto**



## Cartílago

## Inhibición de Proteinasas

### Inhibición MMP-13

#### PG-116800

- NCT 00041756. Fase 2: Toxicidad

#### BAY 12-9566

- RCT Fase 2: Mejora *turnover* proteoglicanos

### Inhibición ADAMTSs

#### GLPG 1972/S201086

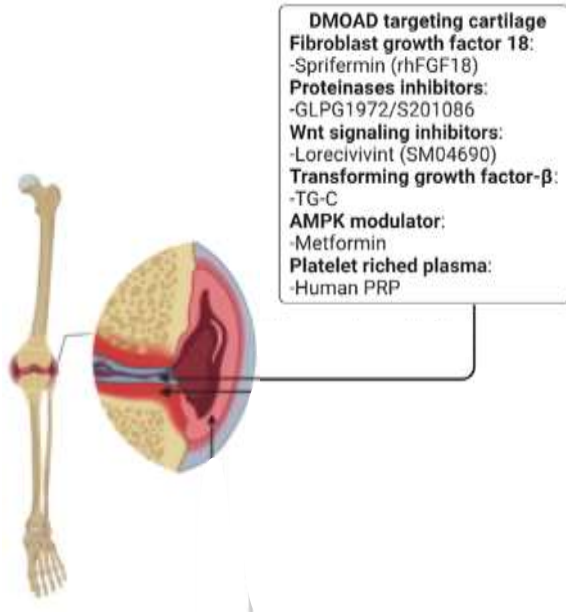
- NCT 03595618. Fase 2, completado 2020 ?

#### AG523

- NCT 00427687. Fase 1 ...Suspendido
- NCT 00454298. Fase 1 ...Suspendido

#### M6495 / Ac Mb

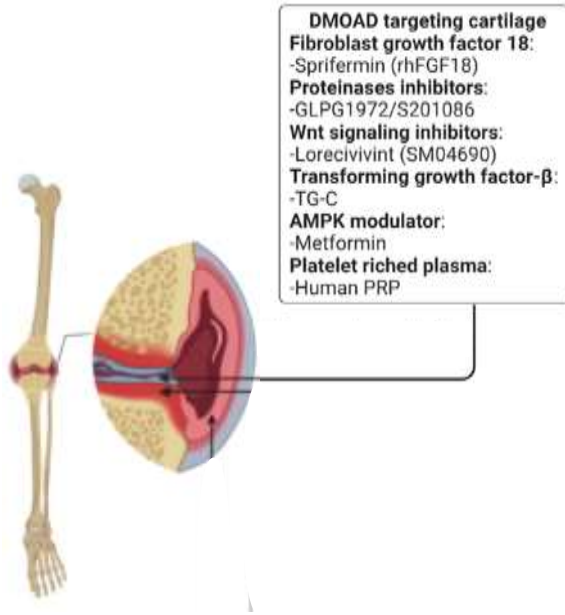
- NCT 03583346. Fase 1 ... ?





## Cartílago

## Inhibición de Señal *Wnt*



### Lorecivivint

Inhibición transcripcional de *Wnt*

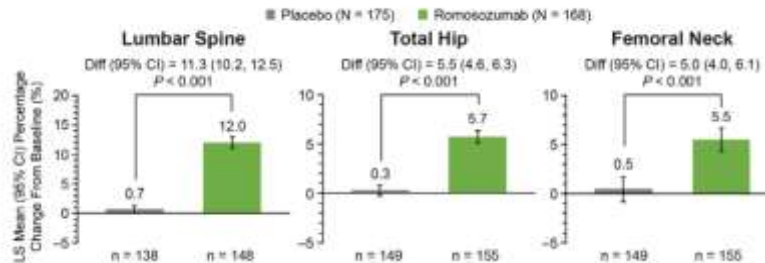
(LOR SM 04690)

- NCT 02095548 Fase 2. 2015 \*
- NCT 02536833 Fase 2. 2017 n.s.
- NCT 03122860 Fase 2. 2021 \*
- NCT 03928184 Fase 3. 2021 ... ?

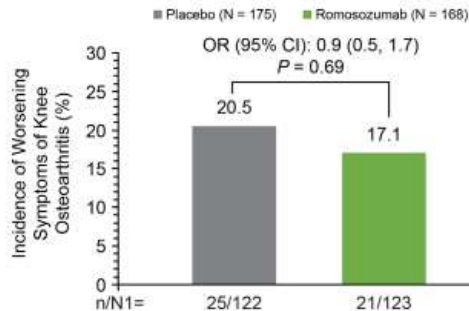
## Effect of Romosozumab Treatment in Postmenopausal Women With Osteoporosis and Knee Osteoarthritis: Results From a Substudy of a Phase 3 Clinical Trial

## Inhibición de Señal *Wnt*

A FRAME Overall Study



B FRAME Osteoarthritis Substudy



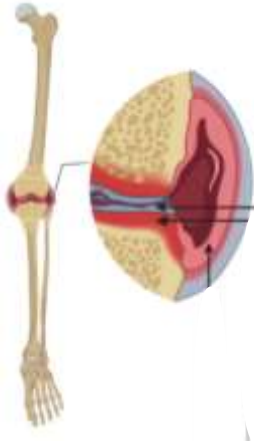
## Cartílago

## Modulación AMPK

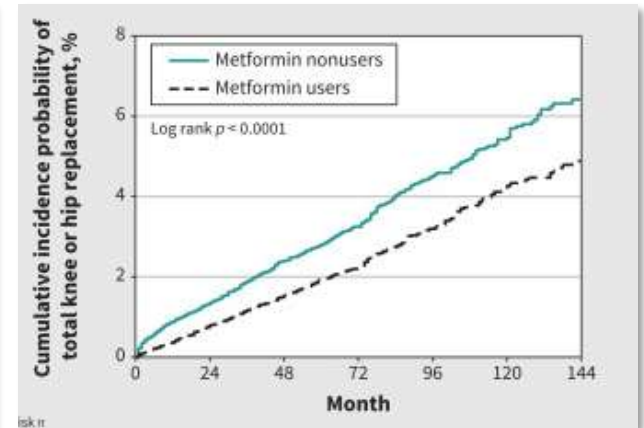
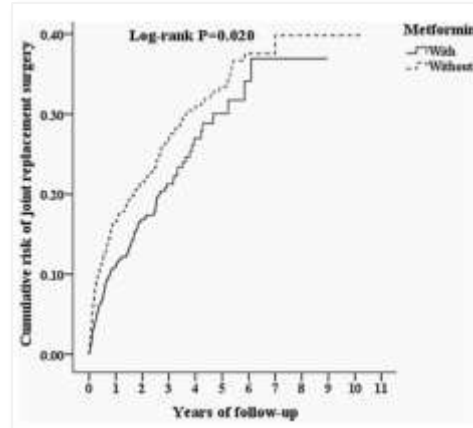
### Metformina

#### Activación AMP - Protein Kinasa

**DMOAD targeting cartilage**  
**Fibroblast growth factor 18:**  
 -Sprifermin (rhFGF18)  
**Proteinases inhibitors:**  
 -GLPG1972/S201086  
**Wnt signaling inhibitors:**  
 -Lorecivint (SM04690)  
**Transforming growth factor-β:**  
 -TG-C  
**AMPK modulator:**  
 -Metformin  
**Platelet rich plasma:**  
 -Human PRP



- **RCT Pacientes OA y DM2.** MTF+COX2i v/s PBO x10 años  
 N = 968. PTC/PTR HR 0.742 (95% CI 0.60-0.92) p = 0.005
- **RCT Pacientes DM2 y OA.** MFT v/s PBO x4 años  
 N = 40.694. PTC/PTR HR 0.70 (95% CI 0.60-0.81) P = 0.0001



## Cartílago

## Plasma Rico en Plaquetas (hPRP).

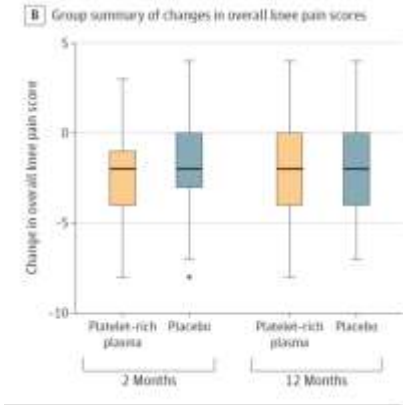
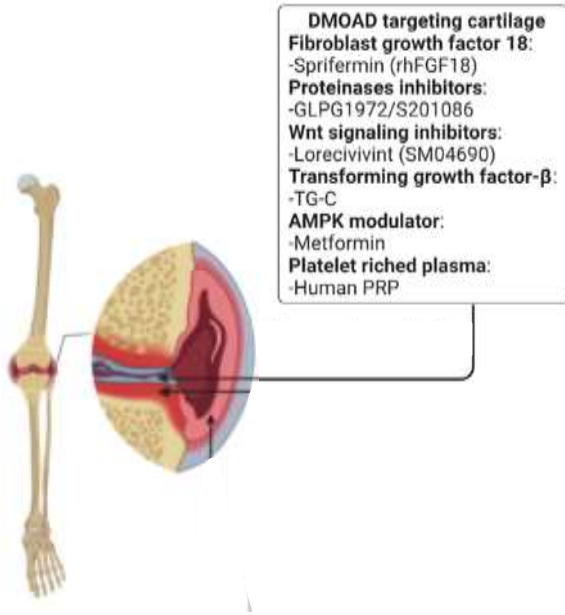
### hPRP

Factores de crecimiento y citocinas gránulos  $\alpha$ PLQ

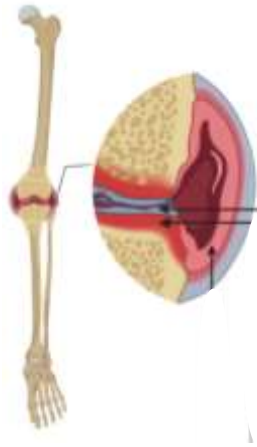
**RESTORE / Australia. hPRP Comercial, Regen Lab.**  
**ACTRN 12617000853347**

- RTC N = 288, KOA KL 2-3, 62 años, IA x3. 12m

- Dolor y Grosor RNM: n.s.
- 29/31 Objetivos 2°: n.s.



## Cartílago



**DMOAD targeting cartilage**  
**Fibroblast growth factor 18:**  
-Sprifermin (rhFGF18)  
**Proteinases inhibitors:**  
-GLPG1972/S201086  
**Wnt signaling inhibitors:**  
-Lorecivint (SM04690)  
**Transforming growth factor- $\beta$ :**  
-TG-C  
**AMPK modulator:**  
-Metformin  
**Platelet riched plasma:**  
-Human PRP

## Plasma Rico en Plaquetas (hPRP).

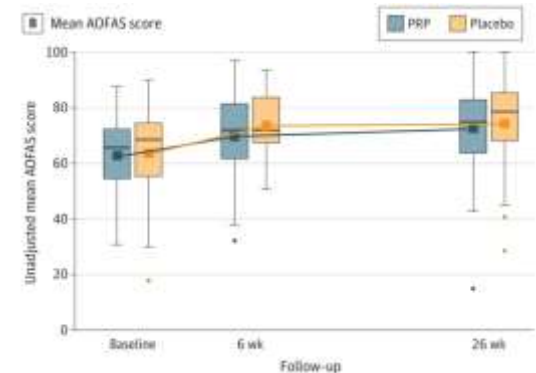
### hPRP

Factores de crecimiento y citocinas gránulos  $\alpha$ PLQ

### PRISMA / Holanda. hPRP Comercial, Arthrex NTR 7261

- RTC N = 100, OA Tibiotalar, 55 años, IA x2.

- **Dolor y Función: n.s.**



## Sinovitis

# DMOAD Dirigidos a la Sinovitis

## Diacereína

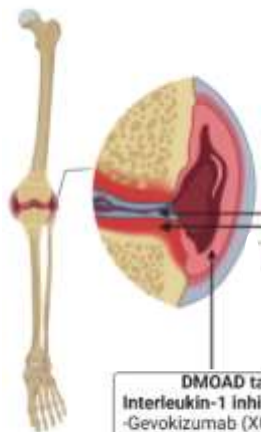
Inhibición de IL-1

### Cochrane Database of Systematic Reviews

10/40 RCT. 2.210 px. OA, 59 años.

### Conclusiones:

- Evidencia de baja calidad
- Pequeño beneficio en dolor
- Pequeño beneficio en espacio cadera, no en rodilla
- EA frecuente: diarrea



**DMOAD targeting synovitis**

**Interleukin-1 inhibitor:**

- Gevokizumab (XOMA-052)
- AMG108
- Lutikizumab (ABT-981)
- Anakinra
- Canakinumab
- Diacerein

**Tumor necrosis factor-alpha inhibitors:**

- Adalimumab
- LY3016859
- Etanercept
- Infliximab

**Senolytic therapies:**

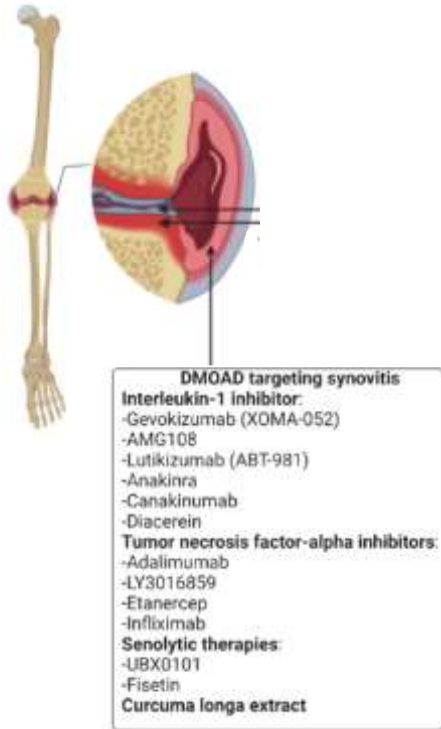
- UBX0101
- Fisetin

**Curcuma longa extract**

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo	Diacerein				
<b>Pain overall visual analogue scale for pain</b> Scale from: 0 to 100 Follow-up: three to 36 months	Mean pain overall visual analogue scale for pain in control groups was <b>43 mm</b>	Mean pain overall visual analogue scale for pain in the intervention groups was <b>8.65 points lower</b> (15.62 to 1.68 lower)		1,283 (six studies)	<b>low</b> 1.2	NNT6 6 (4 to 30) <sup>5</sup> Absolute risk difference -9% (-16% to -2%) Relative percentage change -19% (-34% to -4%)

## Sinovitis

## DMOAD Dirigidos a la Sinovitis



### Inhibición de IL-1

#### Gevokizumab

- NCT01683396. Fase 2
- NCT01882491. Fase 2

#### AMG 108

- NCT 00110942. Fase 2

#### Lutikizumab

- NCT02087904. Fase 2
- NCT02384538

#### Anakinra

- NCT00110916. Fase 2

#### Canakinumab

- NCT01160822. Fase 2

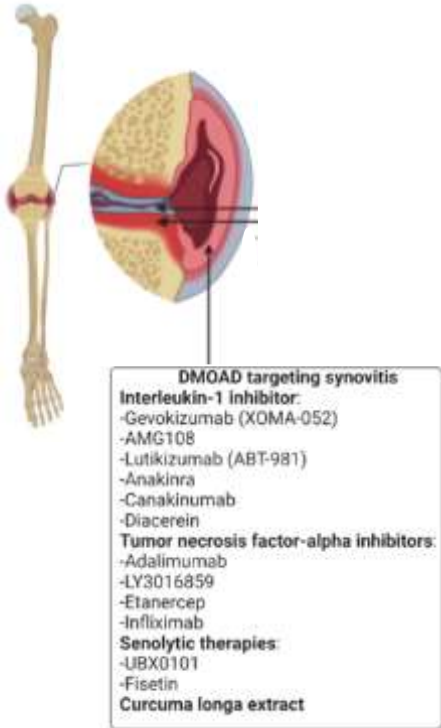
#### Diacereína

- NCT02688400. Fase 3

n.s.

## Sinovitis

## DMOAD Dirigidos a la Sinovitis



### Inhibición de TNF- $\alpha$

#### Adalimumab

- NCT 00296894. Fase 2
- ACTRN 126162000791831. Fase 2

#### Etanercept

- NTR 1192. Fase 2

#### Infliximab

- NCT 001144143. Fase 4

n.s.

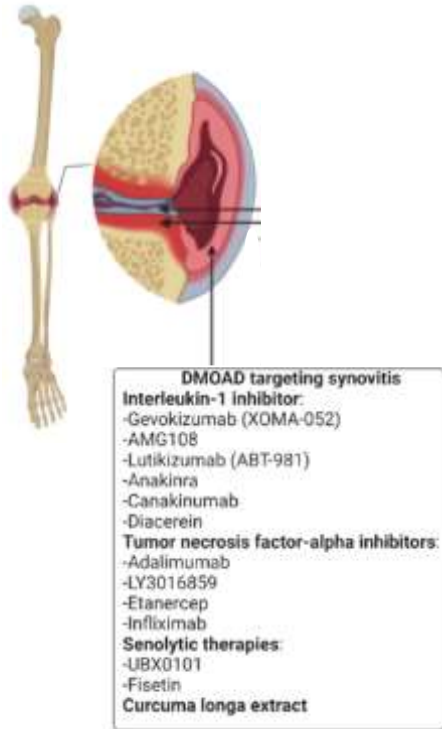


## Sinovitis

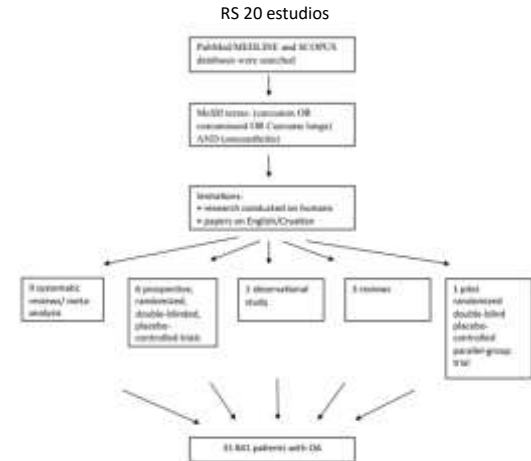
## DMOAD Dirigidos a la Sinovitis

### Cúrcuma longa L. / Curcumina / Tumeric

Bloqueo NF-KB en condrocitos



- NCT 02409381. Fase 4
- NCT 04500210. Fase 3
- NCT 00792818. Fase 3
- NCT 00992004. Fase 2

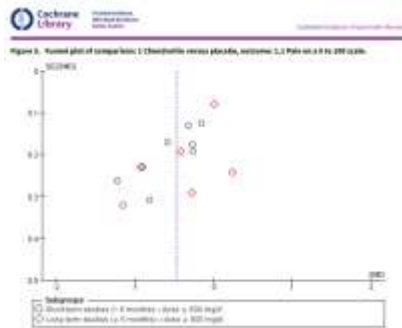


**Conclusión: 1000 – 2000 mg/d ...**



## Chondroitin for osteoarthritis (Review)

43 RCT, N = 9.110, CS v/s PBO, KOA, 3a.



### Authors' conclusions:

A review of randomized trials of mostly low quality reveals that chondroitin (alone or in combination with glucosamine) was better than placebo in improving pain in participants with osteoarthritis in short-term studies.

### Chondroitin versus placebo for osteoarthritis

**Patient or population:** patients with osteoarthritis

**Settings:** international inpatient and outpatient clinics, hospitals, and research centers

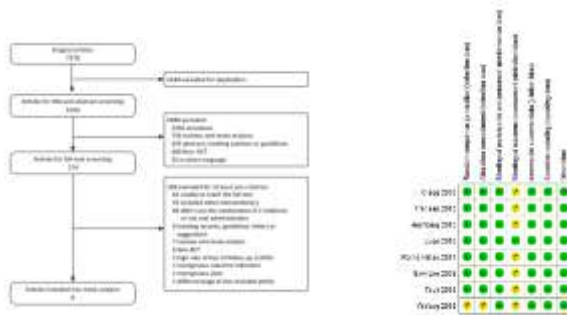
**Intervention:** Chondroitin versus placebo

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of Participants (Studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Chondroitin versus Placebo				
<b>Pain on a 0 to 100 mm scale - Short-term studies (&lt; 6 months)—dose ≥ 800 mg/d</b>	The mean pain on a 0 to 100 scale in the control groups was <b>28 points</b> <sup>§</sup>	The mean pain on a 0 to 100 scale in the intervention groups was <b>10.3 mm lower</b> (14.6 to 5.7 lower)		1077 (8 studies)	⊕⊕⊕⊕ <b>low</b> 1,2	Mean Difference: -10.14 (95% CI -14.58 to -5.71) Absolute risk difference: -10% (95% CI -15% to -6%) Relative risk difference: -38% (95% CI -52% to -20%) NNTB = 5 (95% CI 3 to 8)
<b>Pain on a 0 to 100 scale - Long-term studies (≥ 6 months)—dose ≥ 800 mg/d</b>	The mean pain on a 0 to 100 scale in the control groups was <b>30 points</b>	The mean pain on a 0 to 100 scale in the intervention groups was <b>5 points lower</b> (18 to 0 lower)		985 (6 studies)	⊕⊕⊕⊕ <b>low</b> 1,2	Mean Difference: -5.02 (95% CI -17.68 to -0.34) Absolute risk difference: -9% (95% CI -18% to 0%) Relative risk difference: -30% (95% CI -60% to 0%) NNTB = n/a
<b>WOMAC MCH Pain subscale (reduction in knee pain by 20%) - Long-term studies (≥ 6 months)—dose ≥ 800 mg/d</b>	<b>471 per 1000</b>	<b>526 per 1000</b> (476 to 584)	<b>RR 1.12</b> (1.01 to 1.24)	1234 (2)	⊕⊕⊕⊕ <b>high</b>	Absolute risk difference 6% (3% to 12%) Relative risk difference 12% (1% to 24%) NNTB = 16 (9 to 134)
<b>Composite Measure of Pain, Function and Disability as assessed with Lequesne's index on 0 to 24 scale (lower indicates less pain and disability) - Short-term studies (&lt; 6 months)—dose ≥ 800 mg/d</b>	The mean Lequesne's index on 0 to 24 scale in the control groups was <b>7.4 points</b>	The mean Lequesne's index on 0 to 24 scale in the intervention groups was <b>1.98 lower</b> (2.79 to 1.17 lower)		903 (7 studies)	⊕⊕⊕⊕ <b>moderate</b> 4	SMD: -0.57 (95% CI -0.84 to -0.30) Absolute risk difference: -9% (95% CI -12% to -6%) Relative risk difference: -18% (95% CI -29% to -10%) NNTB=2 (95% CI 2, 3)
<b>Radiographic Outcome: Reduction in Minimum Joint Space Width (JSW) in mm - Long-term studies (≥ 6 months)—dose ≥ 800 mg/d</b>	The mean reduction in JSW in the control group was <b>6.3 mm</b>	The mean reduction in JSW in the intervention groups was <b>0.18 mm lower</b> (0.06 to 0.30 lower)		822 (2 studies)	⊕⊕⊕⊕ <b>high</b>	Absolute risk difference not calculable because no range is provided for this measure Relative risk difference: 4.7% (95% CI 1.6% to 7.8%) NNTB = 7 (95% CI 5 to 13)



# Efficacy and safety of the combination of glucosamine and chondroitin for knee osteoarthritis: a systematic review and meta-analysis

8/214 RCT, N=3793, KOA, WOMAC.  
GS+CS v/s PBO, GS, CS, AINES



\* MCID - 6.98 (95% CI 22,3-1.8) p=0.02

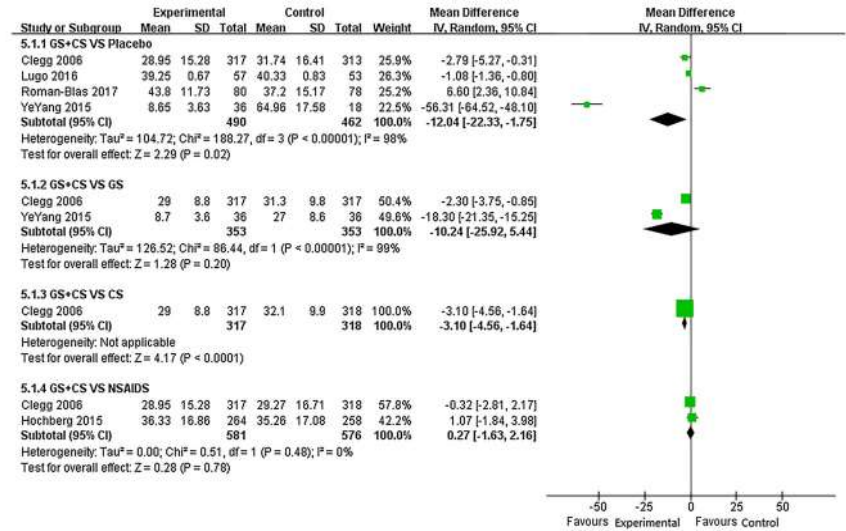


Fig. 3 GS glucosamine, CS chondroitin, SD standard difference. 95% CI 95% confidence interval. Green squares and lines stands for mean difference and 95% CI of each group. Rhombus stands for 95% CI of each groups of comparison

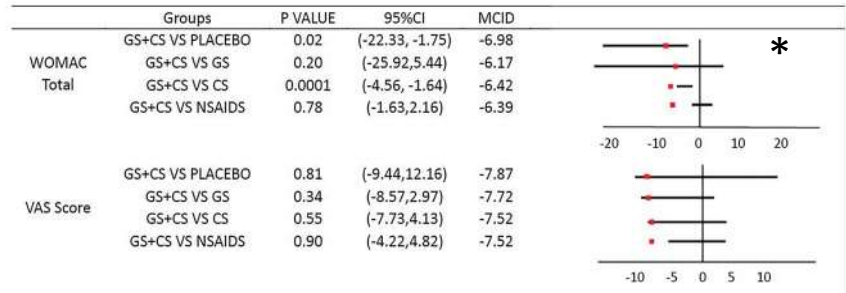


Fig.4 MCID minimum clinically important differences. Red squares stands for MCID. Black lines stands for 95% CI

¿ Dr. ...y el extracto de palta y soya sirve ?



¿ Dr. ... y el colágeno sirve ?



¿ ... y si probamos con hidroxiclороquina?



¿ ... y si probamos con colchicina?



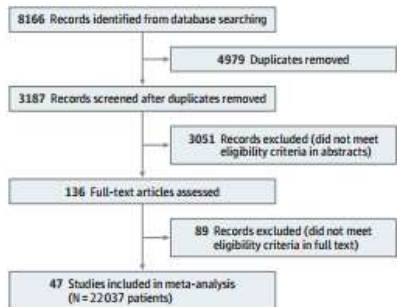


# Association of Pharmacological Treatments With Long-term Pain Control in Patients With Knee Osteoarthritis

## A Systematic Review and Meta-analysis

47 RCT, 37 Rx > 12 meses, N = 22.037

Figure 1. Flow Diagram of Study Identification, Screening, Eligibility Assessment, and Inclusion

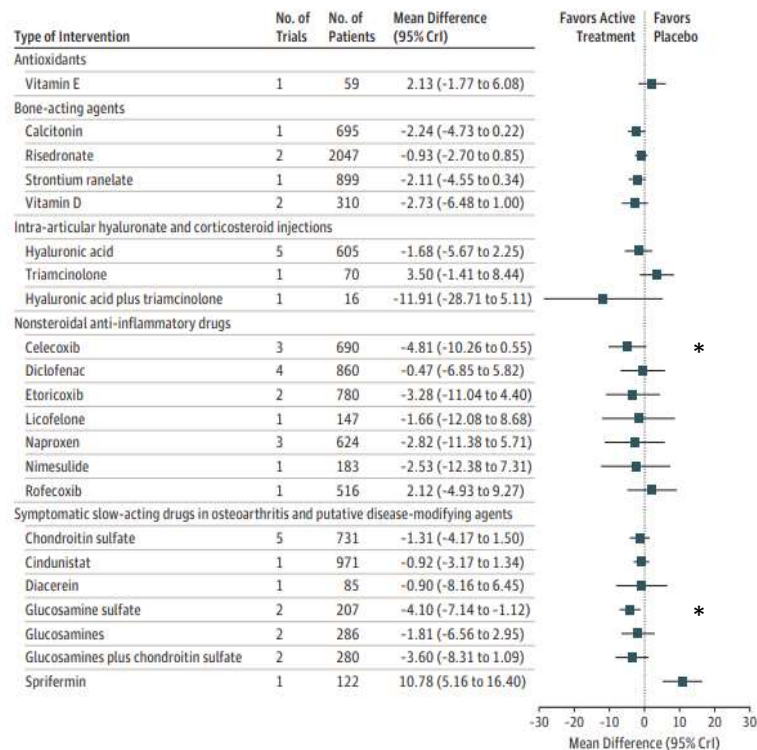


**CONCLUSIONS:** In this systematic review and network meta-analysis of patients with knee osteoarthritis and at least 12 months of follow-up, there was uncertainty around the estimates of effect size for change in pain

Box. Pharmacological Interventions Eligible for Inclusion in the Network Meta-analysis by Therapeutic Class

- Analgesics**
  - Acetaminophen (paracetamol)
- Antioxidants**
  - Vitamin E
- Bone-Acting Agents**
  - Calcitonin
  - Risedronate
  - Strontium ranelate
  - Vitamin D
  - Zoledronic acid
- Intra-Articular Injection Medications**
  - Hyaluronic acid
  - Betamethasone
  - Methylprednisolone
  - Triamcinolone
  - Hyaluronic acid plus betamethasone
  - Hyaluronic acid plus methylprednisolone
  - Hyaluronic acid plus triamcinolone
- Nonsteroidal Anti-inflammatory Drugs**
  - Celecoxib
  - Diclofenac
  - Etoricoxib
  - Etiopirinate
  - Etoxicol
  - Indomethacin
  - Licofelone
  - Naproxen
  - Nimesulide
  - Rofecoxib
  - Tiaprofenic acid
- Symptomatic Slow-Acting Drugs in Osteoarthritis**
  - Chondroitin sulfate
  - Diacerin
  - Glucosamine sulfate (prescription product only)
  - Glucosamines (glucosamine hydrochloride with or without sodium sulfate)
  - Glucosamines plus chondroitin sulfate
- Putative Disease-Modifying Agents**
  - Chondroitin
  - Doxycycline
  - Matrix metalloproteinase inhibitors
  - Sprifermin

Figure 3. Forest Plot for the Estimates of Long-term Treatment Effects of Interventions on Knee Pain That Excluded Trials at High Risk of Bias



## Osteoarthritis and Cartilage



OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis



2019

Recommendation

2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis

2018

Recommendation

2018 update of the EULAR recommendations for the management of hand osteoarthritis

2018

Recommendation

EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis

2013

Bannuru R. Osteoarthritis Cartilage. 2019; 27: 1578-1589.

Fernandes L. Ann Rheum Dis. 2013;72: 1125-1135.

Rausch A. Ann Rheum Dis. 2018; 7: 1251-1260.

Kloppenburg M. Ann Rheum Dis. 2019 Jan; 78: 16-24.

## 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee

Físicas  
Psicosocial

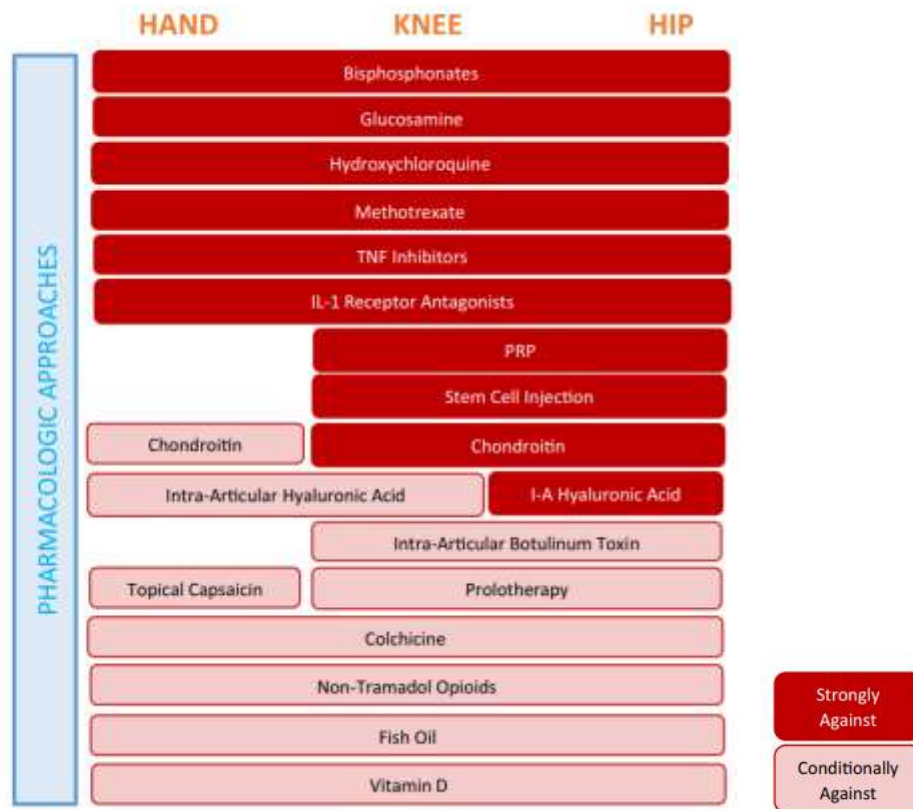
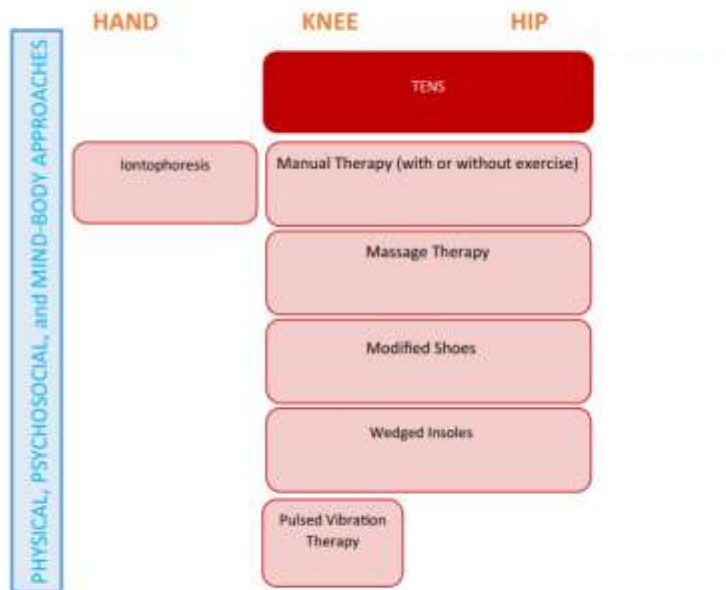
Farmacológicas

	HAND	KNEE	HIP
PHYSICAL, PSYCHOSOCIAL, and MIND-BODY APPROACHES	Exercise*		
	Self-Efficacy and Self-Management Programs		
		Weight Loss	
		Tai Chi	
		Cane	
	1 <sup>st</sup> CMC Orthosis	TF Knee Brace**	
	Heat, Therapeutic Cooling		
	Cognitive Behavioral Therapy		
	Acupuncture		
	Kinesiotaping		
		Balance Training	
	Other Hand Orthoses***	PF Knee Brace**	
	Paraffin	Yoga	
		RFA	
PHARMACOLOGIC APPROACHES	Oral NSAIDs		
	Topical NSAIDs	Topical NSAIDs	
	I-A Steroids	I-A Steroids (Imaging-Guidance for Hip)	
	Acetaminophen		
	Tramadol		
	Duloxetine		
	Chondroitin	Topical Capsaicin	

Strongly recommended

Conditionally recommended

## 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee



RHEUMATOLOGY REGISTRIES, BIG DATA, AND THE RHEUMATIC DISEASES

Education, Home Exercise, and Supervised Exercise for People With Hip and Knee Osteoarthritis As Part of a Nationwide Implementation Program: Data From the Better Management of Patients With Osteoarthritis Registry

Better Management of Patients With Osteoarthritis.  
 BOA Registry, 38.030 px, 12 meses, Suecia.

**Table 3.** Joint pain difference at baseline immediately after treatment and at 12 months after the BOA program, stratified by affected joint and treatment group\*

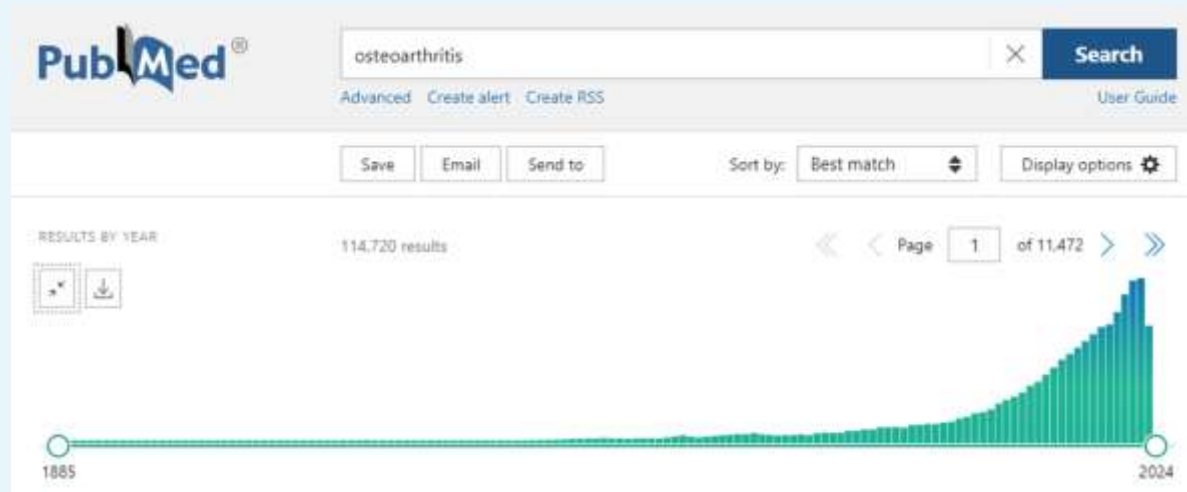
	All participants	ED	HE	SE
Total sample†				
Baseline (ref.)	5.39 (5.32, 5.46)	5.50 (5.30, 5.69)	5.32 (5.29, 5.36)	5.35 (5.32, 5.38)
Difference at baseline				
After treatment	-1.03 (-1.11, -0.95)	-0.91 (-1.15, -0.68)	-1.06 (-1.10, -1.01)	-1.12 (-1.15, -1.08)
12-month follow-up	-0.74 (-0.84, -0.64)	-0.58 (-0.87, -0.30)	-0.82 (-0.87, -0.76)	-0.82 (-0.86, -0.77)
Hip OA‡				
Baseline (ref.)	5.43 (5.37, 5.50)	5.63 (5.30, 5.96)	5.36 (5.29, 5.42)	5.33 (5.28, 5.39)
Difference at baseline				
After treatment	-0.85 (-0.89, -0.80)	-0.84 (-1.25, -0.43)	-0.82 (-0.90, -0.74)	-0.86 (-0.92, -0.80)
12-month follow-up	-0.50 (-0.56, -0.44)	-0.50 (-1.00, -0.20)	-0.48 (-0.57, -0.38)	-0.51 (-0.59, -0.44)
Knee OA‡				
Baseline (ref.)	5.34 (5.28, 5.40)	5.34 (5.11, 5.58)	5.22 (5.18, 5.27)	5.27 (5.23, 5.30)
Difference at baseline				
After treatment	-1.21 (-1.24, -1.17)	-0.95 (-1.25, -0.66)	-1.18 (-1.23, -1.12)	-1.23 (-1.27, 1.19)
12-month follow-up	-0.95 (-0.99, -0.91)	-0.62 (-0.98, -0.26)	-0.97 (-1.03, -0.90)	-0.95 (-1.00, -0.90)

# Conclusiones.

---

- La OA es una enfermedad frecuente, en rápido aumento, y grave
- Sobrepeso y obesidad son condicionantes importantes de OA
- La patogenia es compleja y multifactorial
- Existen diferentes perfiles patogénicos/clínicos de OA
- La estrategia de educación y ejercicio tiene buenos resultados
- Los tratamientos sintomáticos son insuficientes
- Los tratamientos DMOADs en uso poseen un efecto limitado
- Existen varias nuevas terapias, aún en estudio

# Conclusiones.





Gracias ...