

Why do my joints hurt and will anything help them?

Philip Conaghan MBBS PhD FRACP FRCP
Director, NIHR Leeds Biomedical Research Centre
Professor of Musculoskeletal Medicine, University of Leeds

NIHR | Leeds Biomedical
Research Centre

Leeds Institute of Rheumatic
& Musculoskeletal Medicine 
UNIVERSITY OF LEEDS

1

About me

Who am I?

- A rheumatologist
- A clinical researcher
- Someone with osteoarthritis!

2

This talk

- What is arthritis?
- How is the diagnosis made?
- Where does joint pain come from?
- How is arthritis treated?
- What osteoarthritis research do we do in Leeds?

3

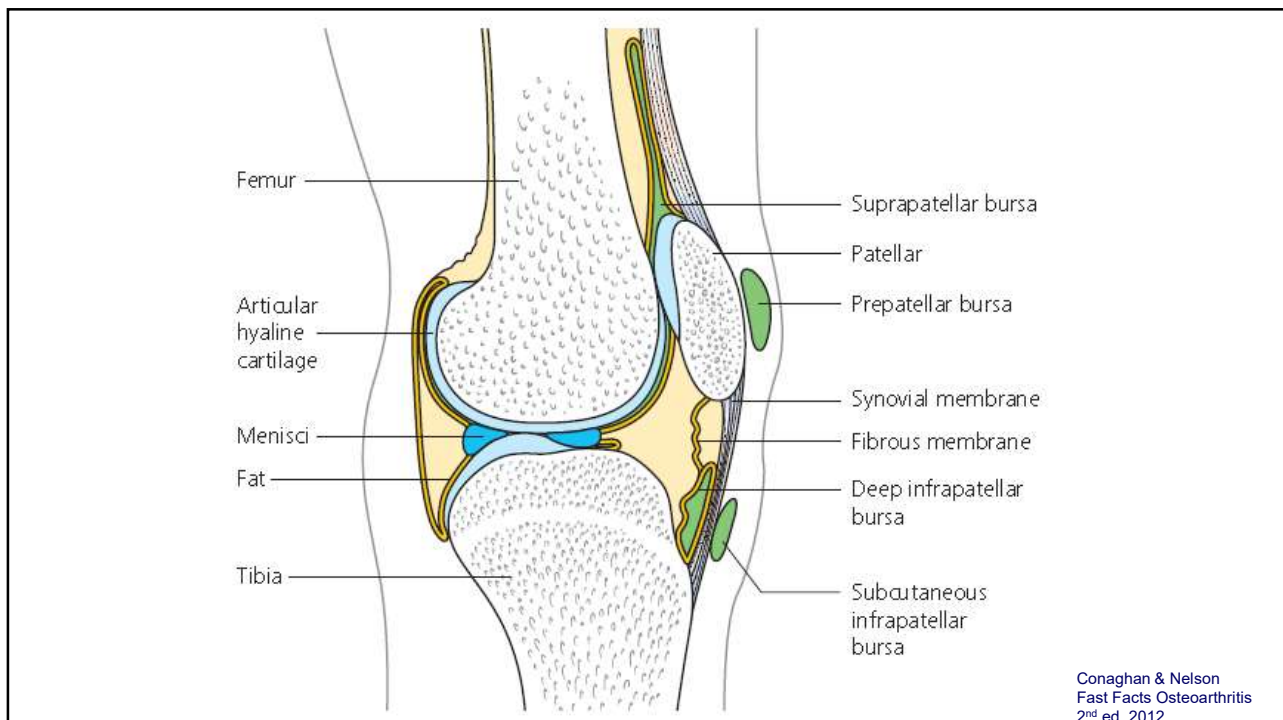
What is arthritis?

4

A Simple Classification of Arthritis

- >100 conditions involving joints, immune system and other organs
- Primary mechanical origin eg OA
- Primary inflammatory origin eg RA

5



6

Types of Arthritis or Rheumatic Conditions

- Mechanical problems
 - Back pain
 - Osteoarthritis (OA)
 - Tendon problems
 - Osteoporosis
- Inflammatory arthritis
 - Gout
 - Rheumatoid arthritis (RA)
 - Polymyalgia rheumatica
 - Ankylosing spondylitis (AS)
 - Connective tissue diseases eg SLE

7

Burden of OA: Arthritis Care OA Nation 2012 Survey

- On-line survey, random, self-reported OA, 2001 respondents, 56% women, mean age 65 years
- Significant difficulty reported with daily activities:
 - stairs (64%), gardening (57%), getting out of a chair (48%)
- 50% had reduced/stopped walking and exercise
- 15% had retired early, by average of 7.8 years
- 86% of working age reported work lives affected
- Average increased cost p.a. per person due to OA: £500

Conaghan et al.
Clin Rheumatol 2014

8

Impact of Arthritis

- Personal
 - Pain, stiffness, fatigue
 - Flat mood, poor sleep, lack of aerobic fitness
 - Reduced activity and 'diminishing circle of life'
- Families/carers
- Societies
 - 20-25% of GP consultations
 - Massive numbers of joint replacements
 - 1-2% of Gross Domestic Product

9

Why do we get arthritis?

- Genetics
- Environmental
 - Joint injury
 - Muscle weakness
 - Occupation (eg weight bearing, kneeling)
 - Pre-existing joint abnormality
 - Obesity
 - Smoking

More than one factor may apply to a person or a given joint in a person

10

How is the diagnosis made?

11

Making a Diagnosis

Your story

- Early morning joint stiffness
- Age
- Pattern of joint involvement
- Associated diseases eg psoriasis
- Associated CT features eg photosensitive rash, severe Raynaud's phenomenon
- Examination: joint swelling, psoriasis
- Tests: Blood, Xrays, ultrasound

12

Has modern imaging explained pain?

- Modern imaging has helped us understand the extent of pathology in different arthritis

HOWEVER:

- Lots of people with joint abnormalities on Xrays and MRI have NO PAIN

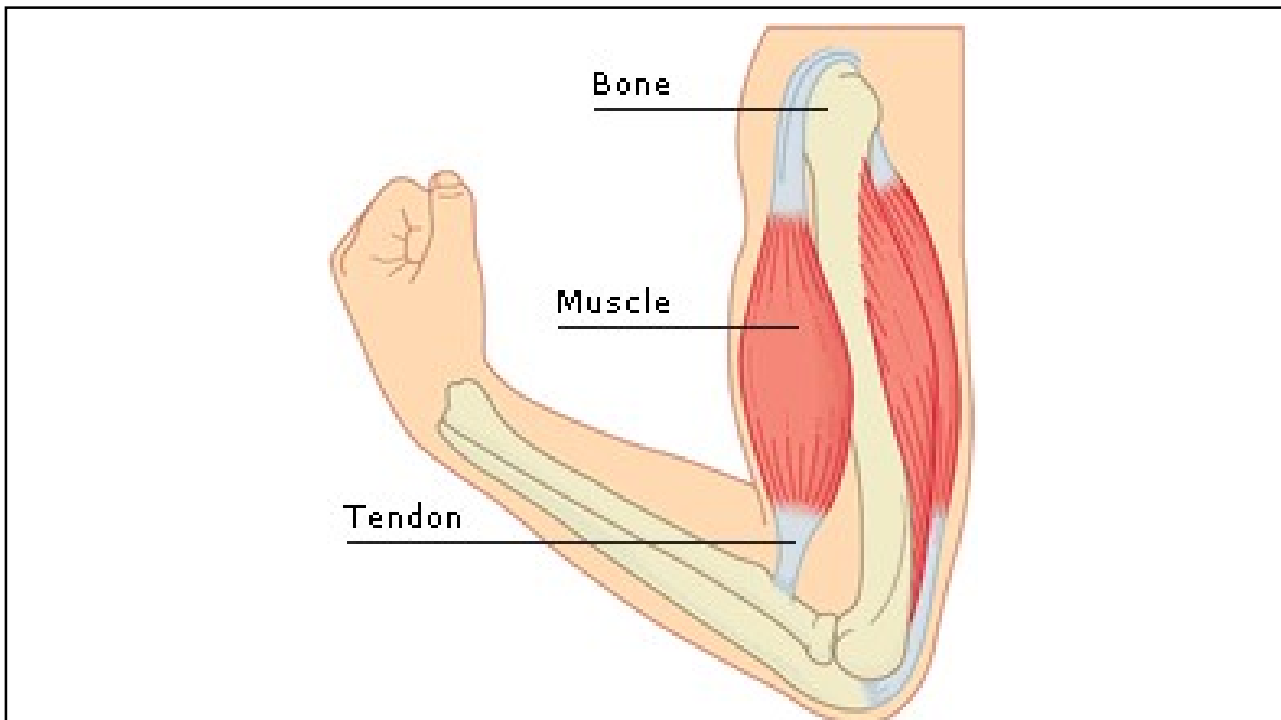
And

- Some people with lots of joint pain have no abnormalities on standard imaging

13

Where does the pain come from?

14



15

Why are joints painful?

Structures inside the joint

- Inflammation in joint lining tissue (synovitis): eg rheumatoid arthritis
- Deforming bone: eg finger joint osteoarthritis

Structures around the joint

- Inflammation or tears in tendons (tendonitis) or shock-absorbing sacks next to joints (bursitis): most shoulder pain
- Inflammation where tendons attach to bone (enthesitis) eg tennis elbow

16

How is arthritis treated?

17

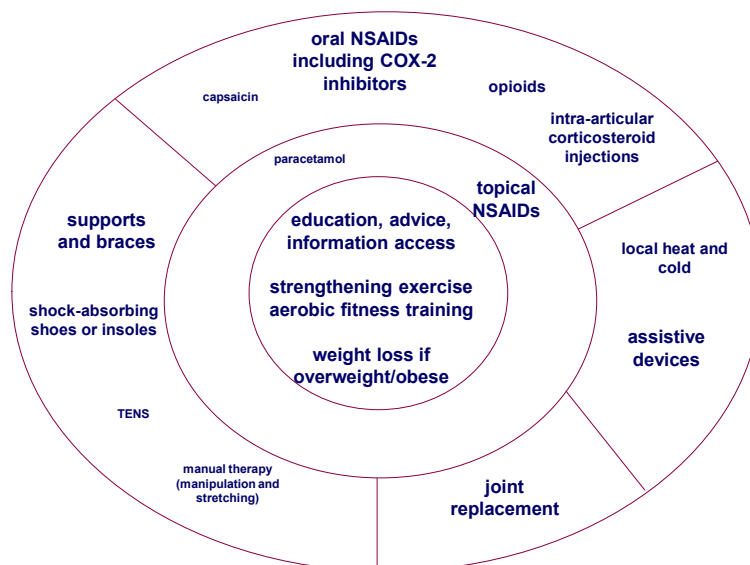
Arthritis Treatments

Combination of:

- Non-drug therapies
 - Muscle strengthening (physiotherapy)
 - Aids and devices
- Drugs (very good for inflammatory arthritis)

18

How is osteoarthritis treated?



Conaghan PG, Dickson J, Grant RL. BMJ 2008

19

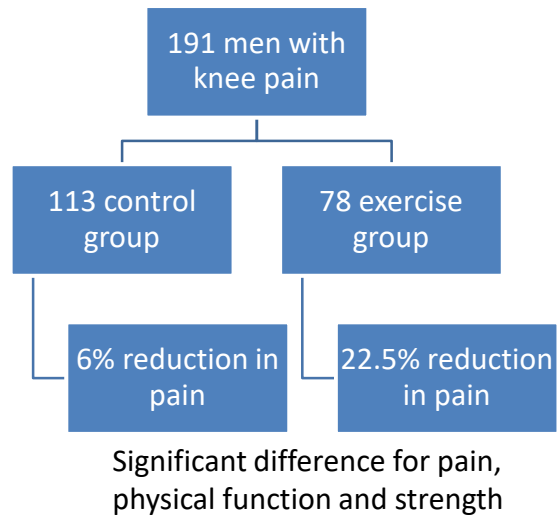
Medication use reported by people with OA: the UK OA Nation 2012 Survey

- Respondents had tried an average of 3 medications
- 50% used their medications every day
- 62% were prescribed oral OA medication, 47% topical therapies, 38% physiotherapy, 28% steroid injections
- OTC use in 25%, 1/3 without doctor's knowledge
- OTC medication was used due to no prescription by GP (26%) or medication not relieving pain (20%)
- **71% reported varying degrees of persistent pain despite taking all prescribed medication**

Conaghan et al.
Clin Rheumatol 2014

20

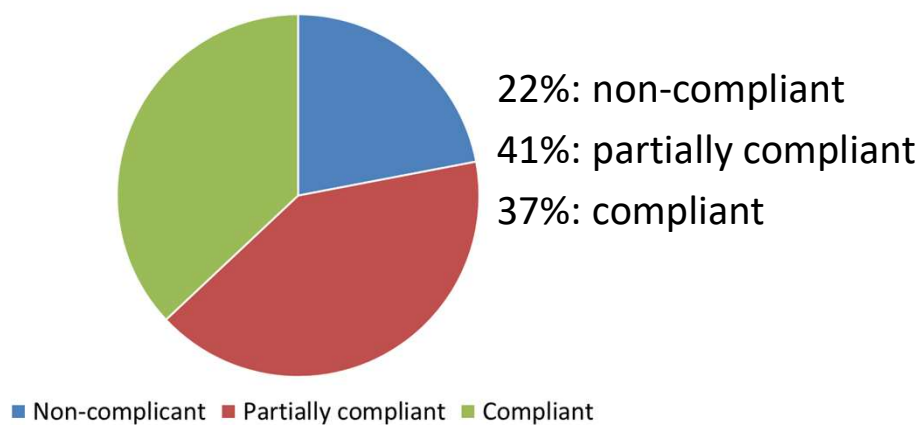
Muscle Strengthening Exercise Helps!



O'Reilly et al. Ann Rheum Dis 1999

21

But....



Sluijs et al. Phys Ther 1993

22

What osteoarthritis research do we do in Leeds?

23

Leeds OA Research

Understanding why we get pain

- MRI using accurate machine learning quantification
- Understanding new biochemical pathways

Developing new therapies

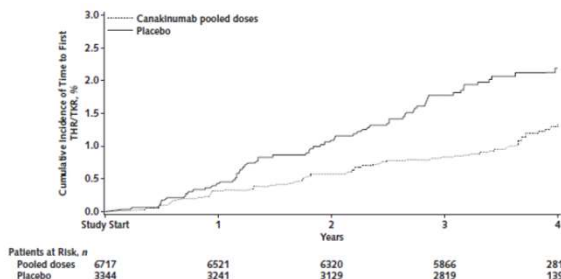
- Digital interventions
- New drug therapies

National and international collaborations & leadership

24

Anti-IL1 mAb (canakinumab) and THR/TKR

Full trial population



Subgroup with baseline OA

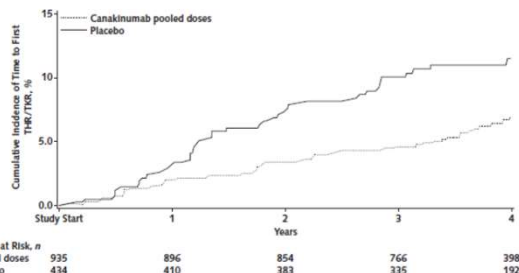


Table 2. Incidence Rates and HRs for the Primary End Point of THR/TKR, According to Randomized Treatment Allocation and Subgroup

Trial Cohort/Subgroup	Placebo	Canakinumab			
		50 mg	150 mg	300 mg	All Doses
Full trial cohort, n	3344	2170	2284	2263	6717
THR/TKR events, n	68	26	25	28	79
Rate per 100 PY	0.54	0.33	0.29	0.33	0.31
HR (95% CI)	1.00	0.60 (0.38-0.95)	0.53 (0.33-0.84)	0.60 (0.38-0.93)	0.58 (0.42-0.80)

Schieker M, Conaghan PG et al. Ann Intern Med 2020

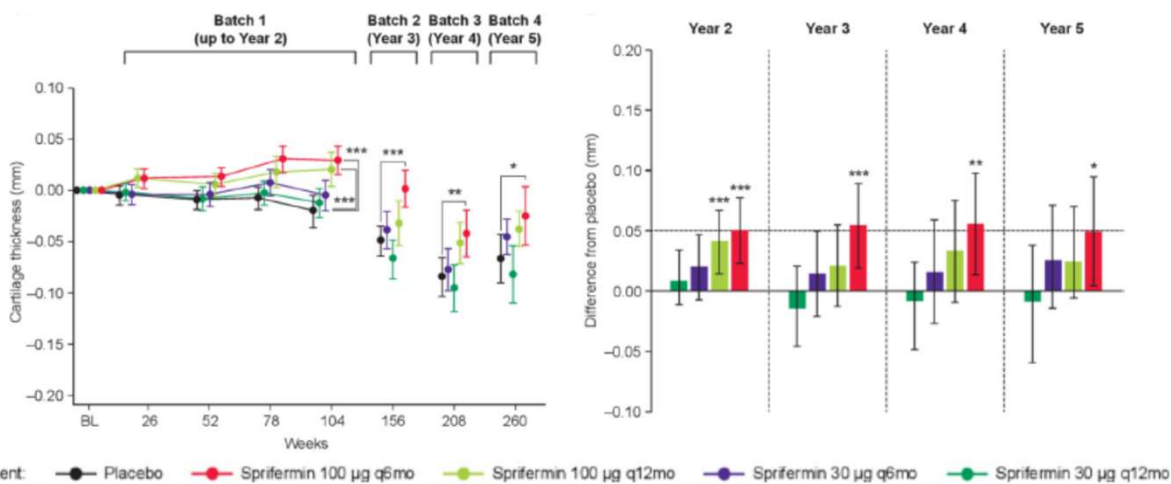
25

Digital-My Arm Pain Programme



26

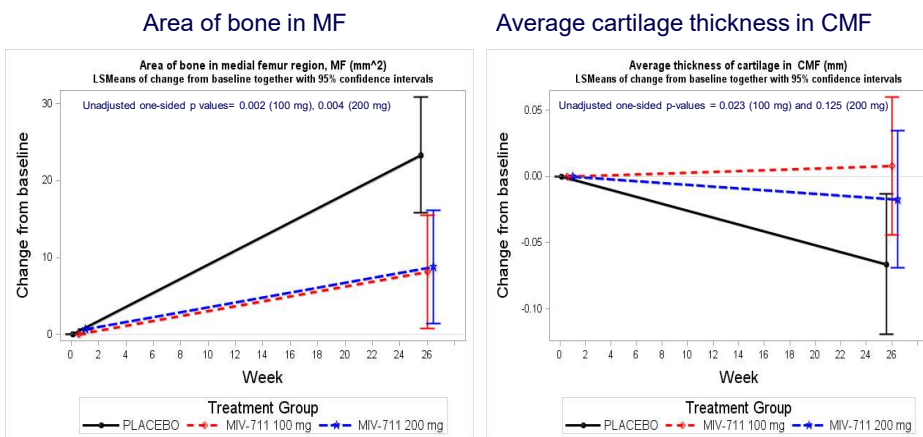
Regrowing cartilage: ReH Fibroblast Growth Factor 18 Ph2 RCT



Eckstein F et al.
Ann Rheum Dis 2021

27

Modifying bone: Cathepsin K inhibitor (MIV-711) Ph2a RCT



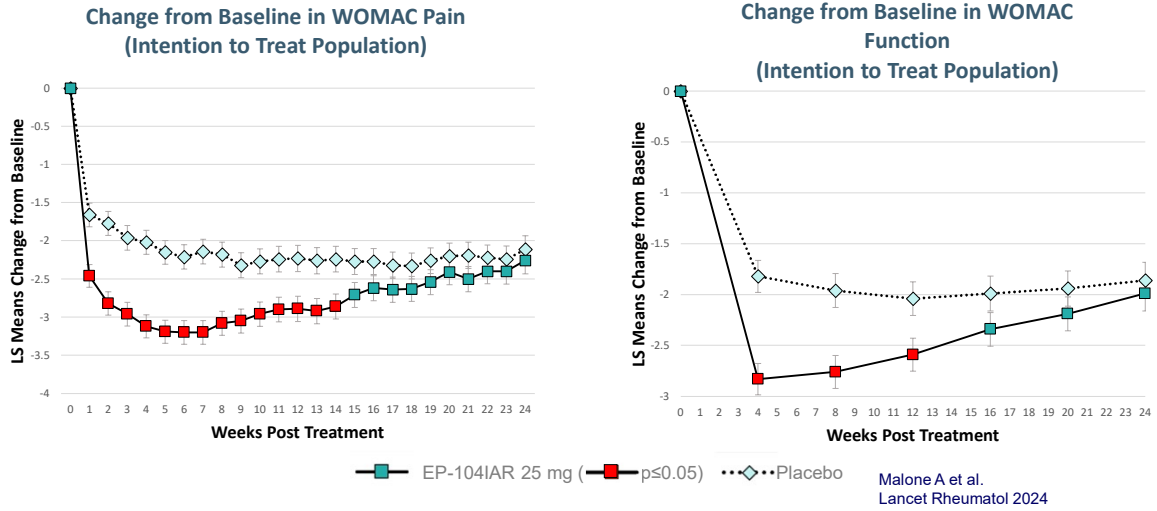
Reduction in bone area
increase for both doses

Trend for reduced cartilage
thickness loss for both doses

Conaghan PG et al.
Ann Intern Med 2020

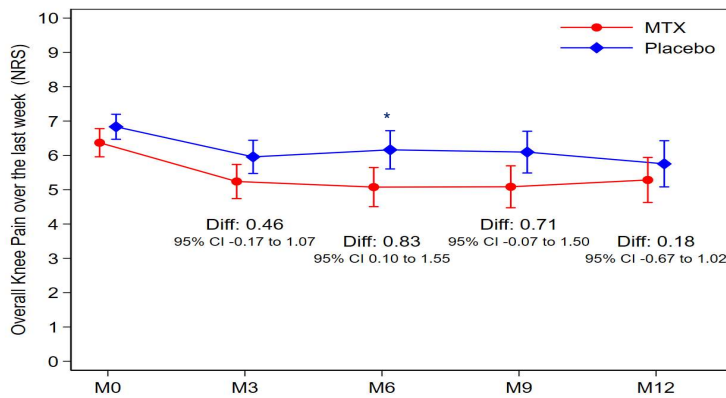
28

Treating inflammation: RCT of prolonged action steroid injections



29

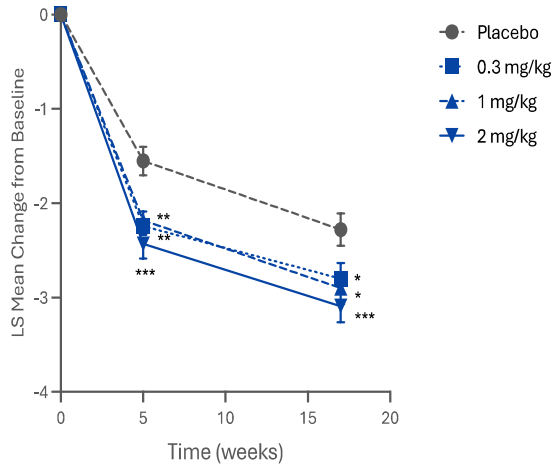
Treating inflammation: RCT of Methotrexate in Knee OA (PROMOTE)



Kingsbury SR et al. Ann Intern Med 2024

30

Treating nerve signaling: NT3 modulation with Levi-04 Ph2 RCT



Conaghan PG et al.
Arthritis Rheumatol 2024 [abst]

31

Final Thoughts

32

Overview of painful joints

- Many different types of joint problems
- People can have more than 1 type
- Most are mechanical in nature (worse with use) and respond to muscle strengthening
- We badly need new therapies for osteoarthritis

33

My thanks to

- Many patients who worked with us
- Many staff
- Our academic and industry collaborators
- Our funders, especially NIHR and Versus Arthritis

34

My thanks to

- Many patients who worked with us
- Many staff
- Our academic and industry collaborators
- Our funders, especially NIHR and Versus Arthritis
- And to YOU!