Associate Professor Ed Gane

New Zealand Liver Transplant Unit

Auckland

Dr Tracey Kain

Consultant Rheumatologist

Grace Orthopaedic Centre

Tauranga Hospital

Tauranga

Saturday, June 10, 2017

7:00 - 7:55 Abbvie Breakfast Session

1. A Brighter Future for Your Hep C Patients
2. Ankylosing Spondylitis – Don't turn your back on it

Axial Spondyloarthritis: Don’t turn your back on it

Dr Tracey Kain

Rheumatologist

Grace Orthopaedic Centre

Disclosures

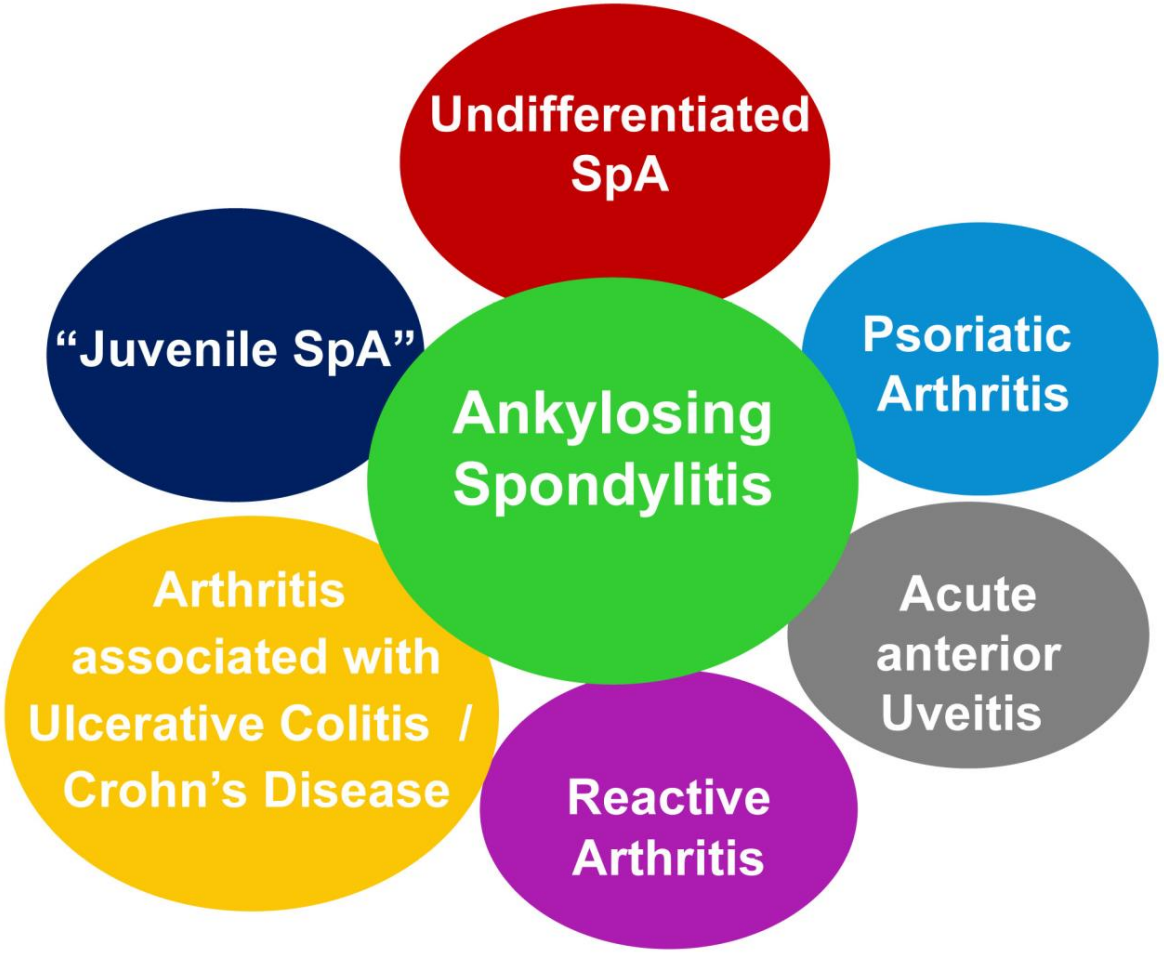
- Today's presentation is sponsored by Abbvie
- I have no actual or potential conflict of interest in relation to this presentation
- Speaker's Bureau: Abbvie (GP meetings)
- Consultant: Abbvie (Don't turn your back on it; Double Whammy), Pfizer (Audit 4)

- The views and opinions expressed in this presentation are those of the presenter and do not necessarily reflect those of Abbvie Ltd. Abbvie Ltd does not endorse the promotion or use of unregistered products or products outside of their registered indications.

The problem with back pain

- Back pain is one of the most common presenting conditions in general practice
- The majority of patients have mechanical back pain
- A minority have different pathology including spondyloarthritis
- It is estimated that one in 20 patients with chronic back pain has spondyloarthritis
- There is little guidance in most general back pain guidelines in how to identify patients who may have spondyloarthritis

Concept of Spondyloarthritis (SpA)



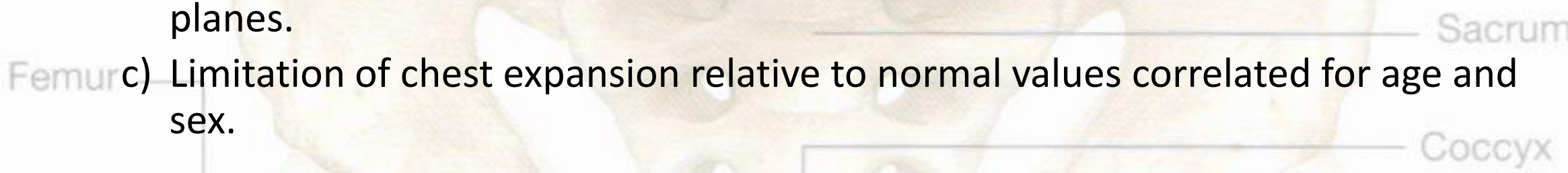
ASAS

Ankylosing spondylitis – 1984 (still the official criteria)

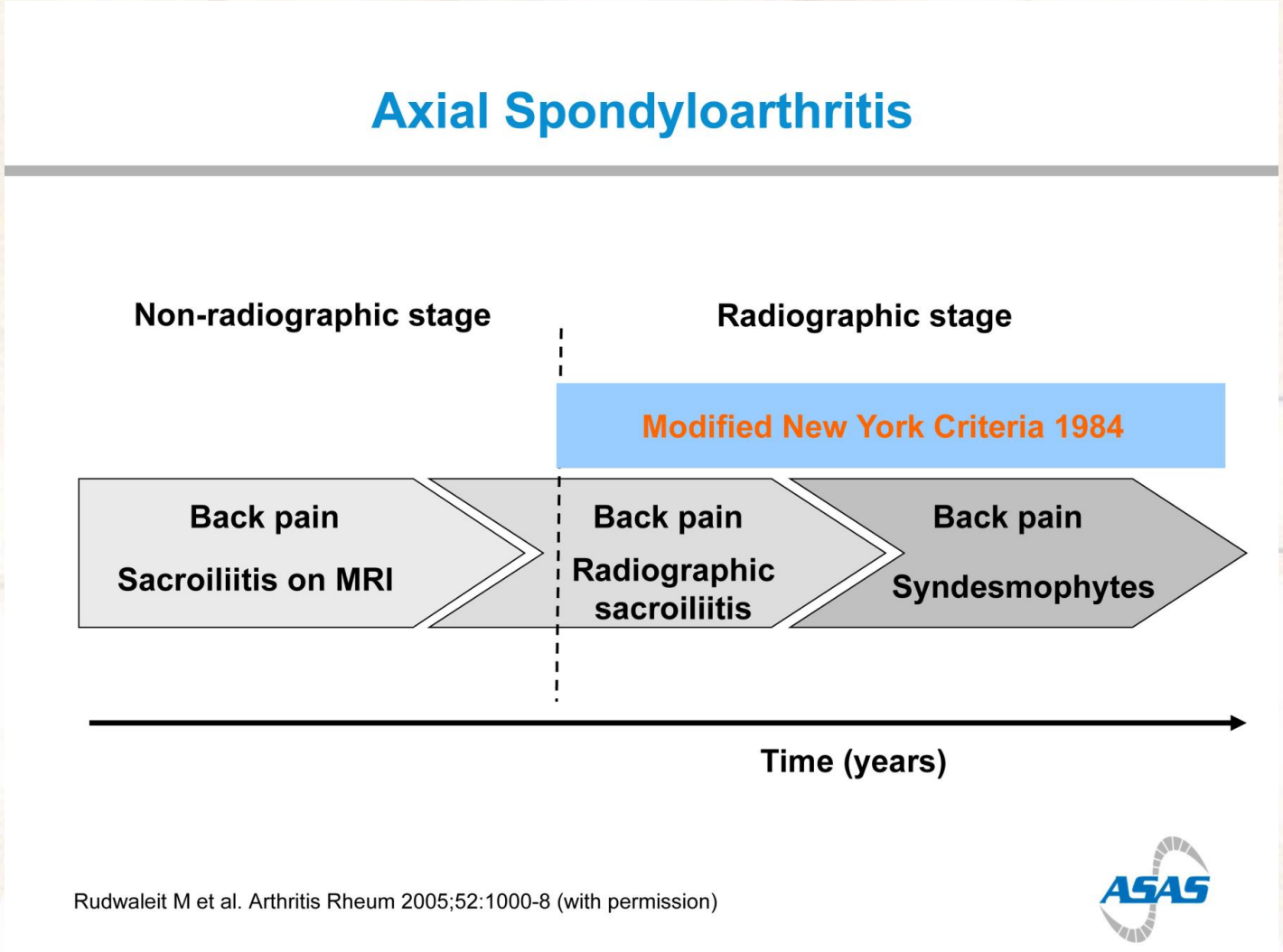
1. **Clinical criteria:**
   a) Low back pain and stiffness for more than 3 months which improves with exercise, but is not relieved by rest.
   b) Limitation of motion of the lumbar spine in both the sagittal and frontal planes.
   c) Limitation of chest expansion relative to normal values correlated for age and sex.

2. **Radiological criteria:**

   Sacroiliitis grade ≥ 2 bilaterally, or grade 3-4 unilaterally



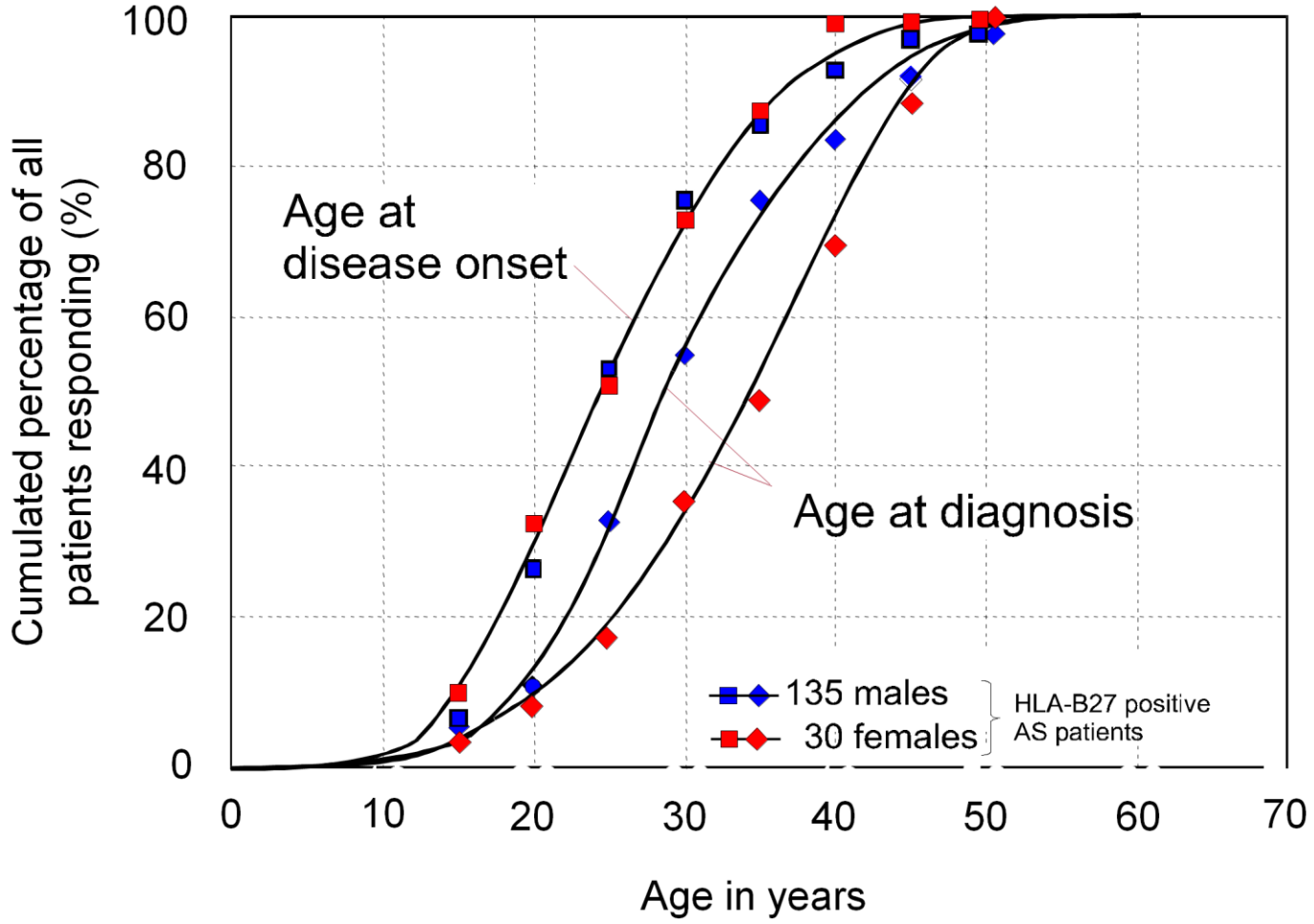
When do x-ray changes occur?



Rudwaleit M et al. Arthritis Rheum 2005;52:1000-8 (with permission)

ASAS

Age at Onset and Time of Ankylosing Spondylitis-Diagnosis



van der Linden SM et al. Arthritis Rheum 1984;27:241-249 (with permission)

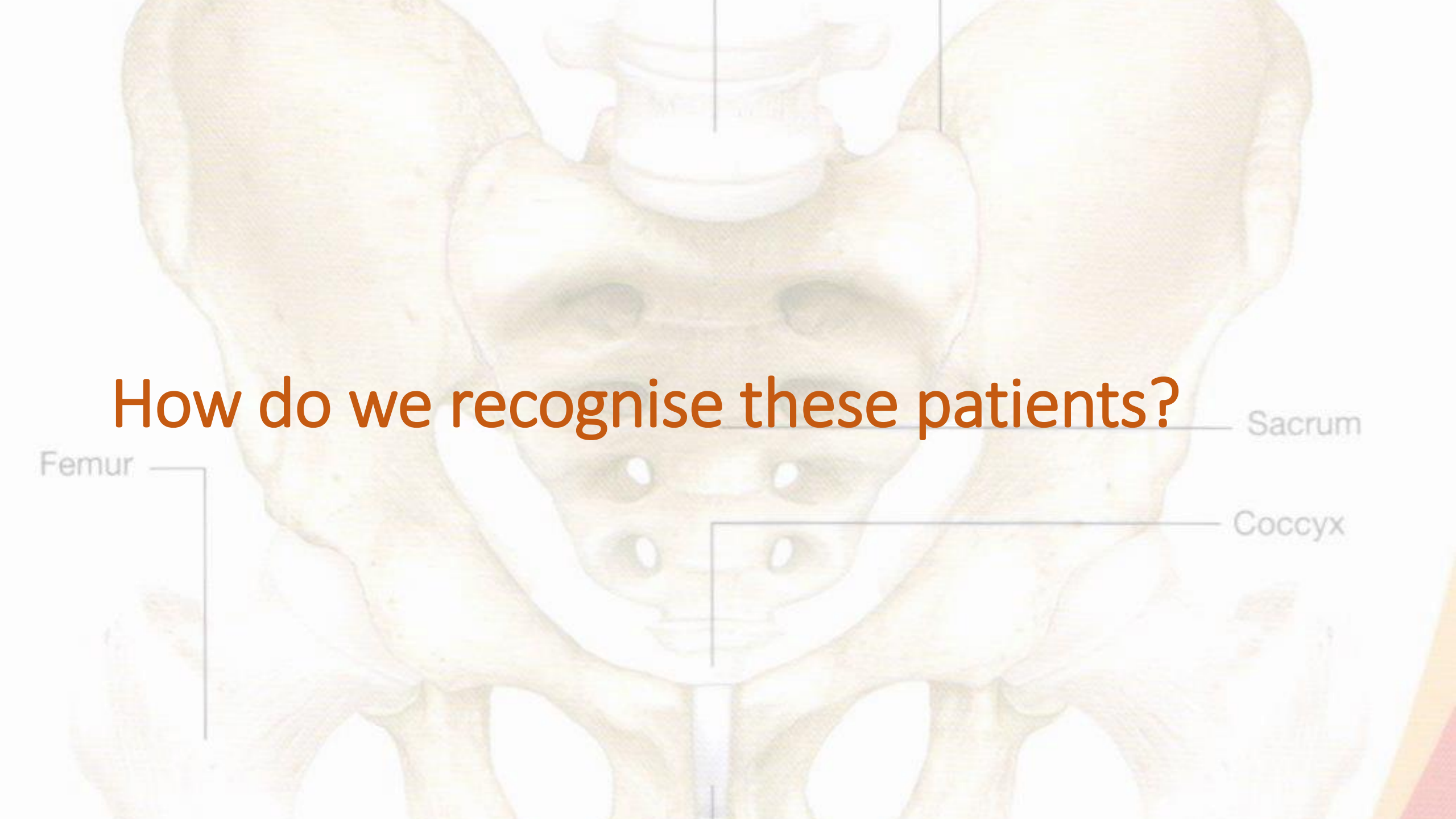
The problem with requiring x-ray changes before being able to diagnose ankylosing spondylitis lead to a new term:

Axial spondyloarthritis

Patients with axial spondyloarthritis who do not have x-ray changes (they may have an abnormal MRI scan) are described as:

Non-radiographic axial spondyloarthritis

How do we recognise these patients?



Bridging the gap…

National Health Committee

Low Back Pain:

A Pathway to Prioritisation

New Zealand Acute Low Back Pain Guide

INCORPORATING THE GUIDE TO ASSESSING PSYCHOSOCIAL YELLOW FLAGS IN ACUTE LOW BACK PAIN

Diagnosis and management of **axial spondyloarthritis** in primary care

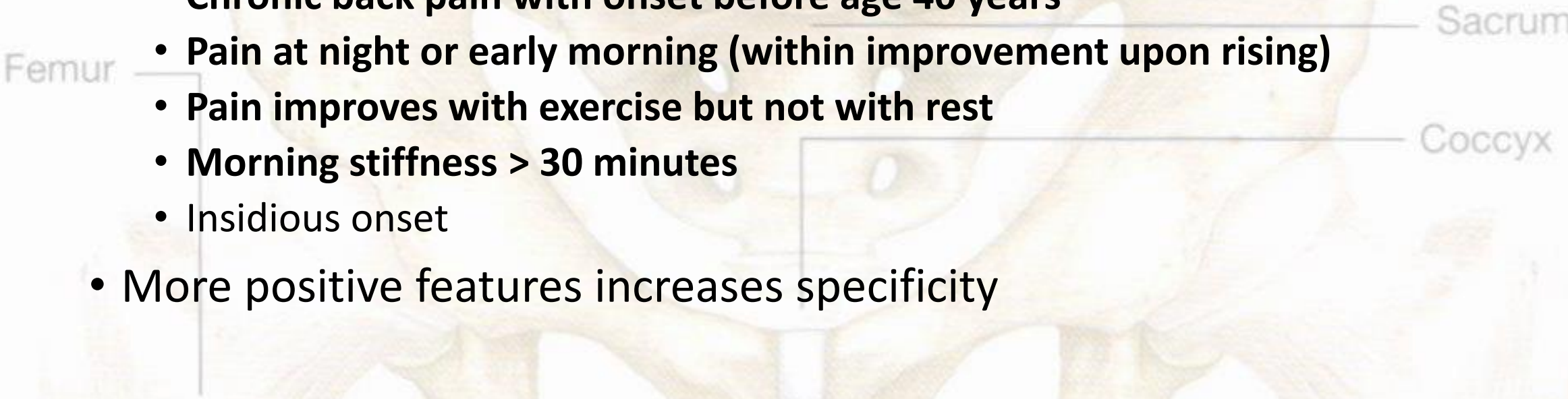
Referral strategies for early diagnosis of axial spondyloarthritis

Screening for spondyloarthritis in GP

- Several studies have looked at screening tools
- No one feature is perfect
- A combination of clinical features is usually required
- Potentially useful tools:
  - **Inflammatory back pain symptoms**
  - **Other clinical features of spondyloarthritis**
  - X-ray/MRI
  - **HLA-B27 testing**

Inflammatory Back Pain

- Most patients with axial spondyloarthritis present with inflammatory back pain features
- These are clinical symptoms of back pain:
  - **Chronic back pain with onset before age 40 years**
  - **Pain at night or early morning (within improvement upon rising)**
  - **Pain improves with exercise but not with rest**
  - **Morning stiffness > 30 minutes**
  - Insidious onset
- More positive features increases specificity

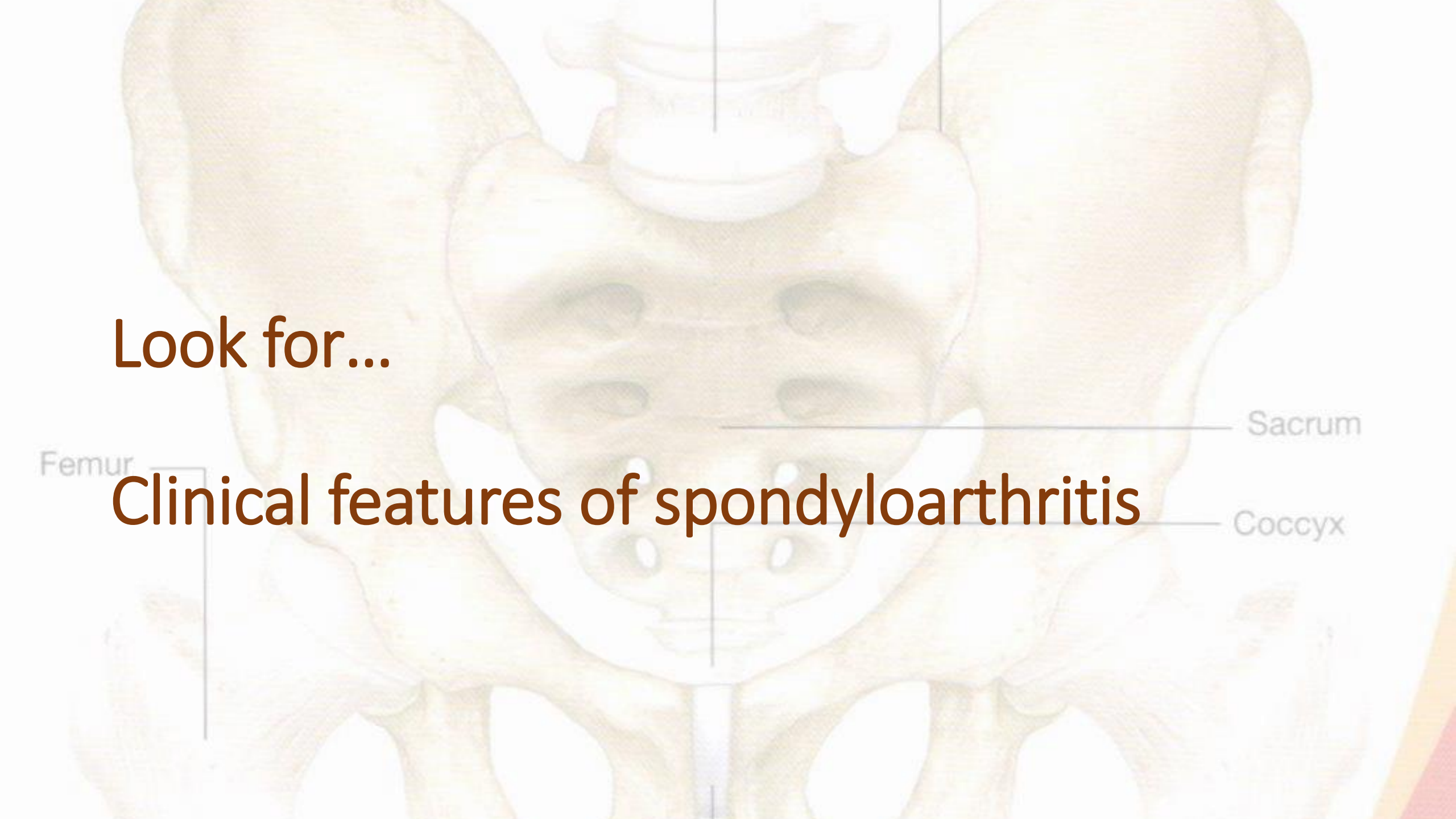


Inflammatory Back Pain (IBP)

- Estimated sensitivity 75% and specificity 76%

- Not all patients with axial spondyloarthritis have inflammatory back pain.
- Axial SpA patients may have typical mechanical back pain…
- 20-25% of all patients with back pain have inflammatory back pain symptoms
- **IBP increases the likelihood of SpA in patients with chronic back pain from 5% baseline to 14% (1 in 7)**

- Useful but not perfect…

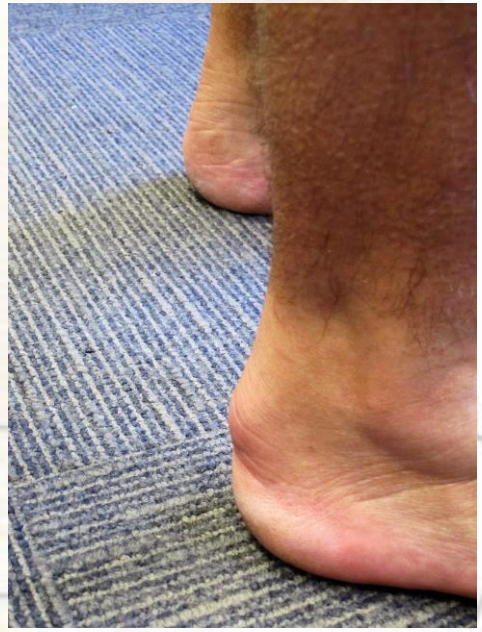


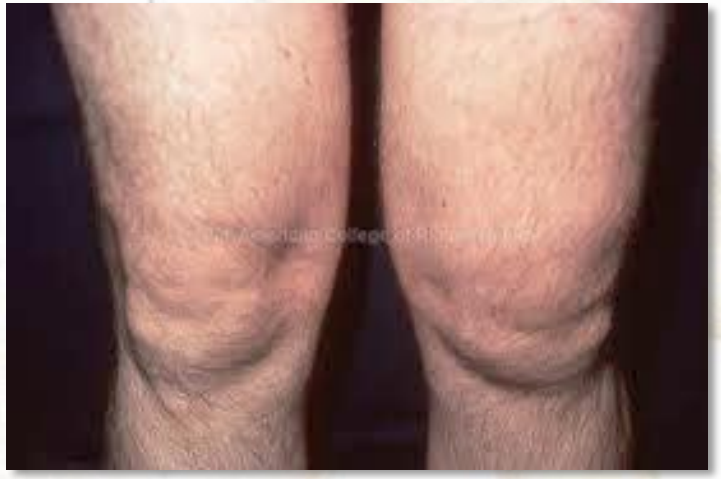
Look for…

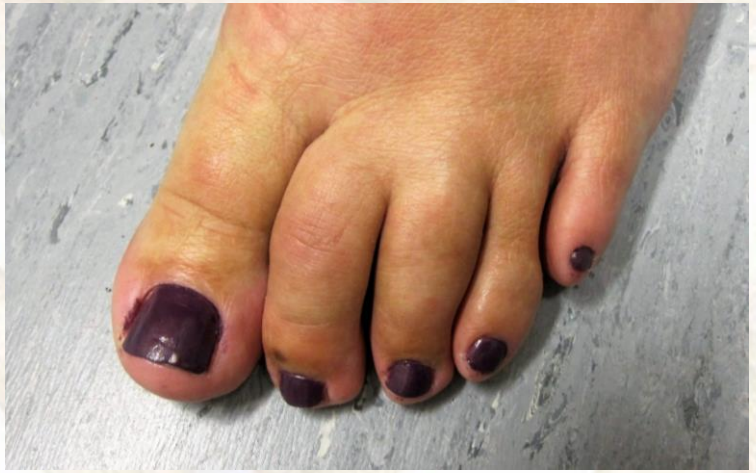
Clinical features of spondyloarthritis

Clinical Features of Spondyloarthritis

- Peripheral inflammatory arthritis
- Dactylitis
- Enthesitis (esp Achilles at heel insertion)
- Good response to NSAIDs

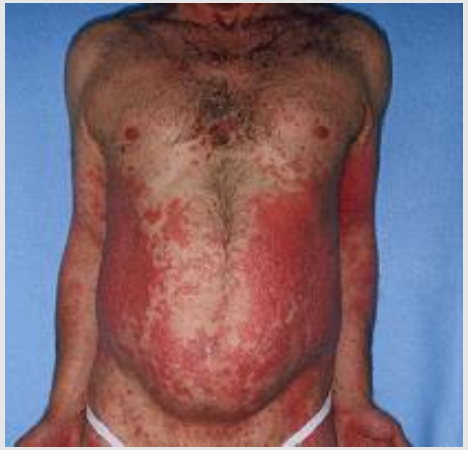


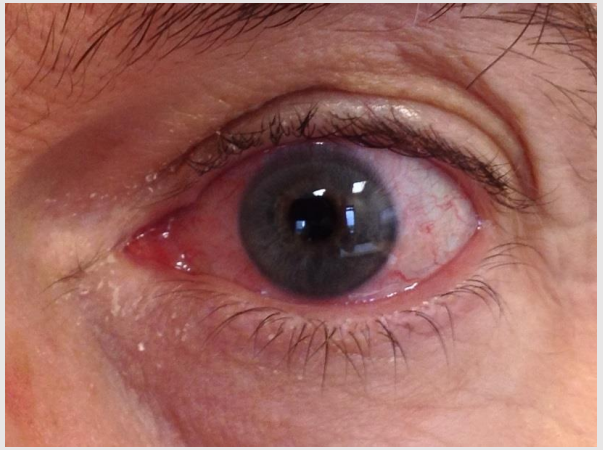




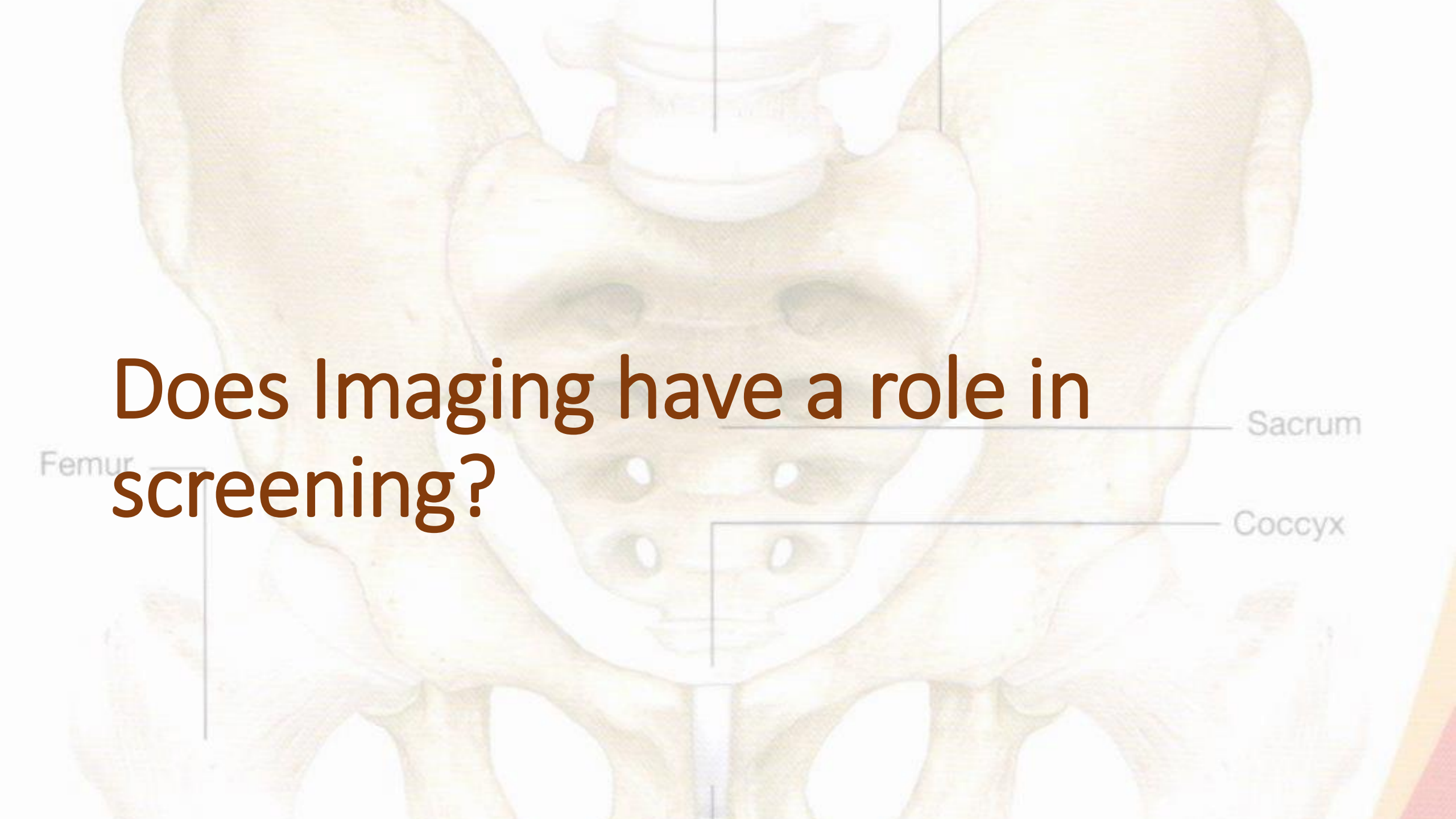
Clinical Features of Spondyloarthritis

- Psoriasis
- Anterior uveitis
- Crohn’s disease/ulcerative colitis
- Family history of spondyloarthritis





Does Imaging have a role in screening?



The role of imaging

- X-ray generally not recommended in non-specific low back pain, low yield
- ?Role in screening for spondyloarthritis?
- More likely to be positive if symptoms have been present several years
- If you do consider x-ray to screen for AS, an **AP pelvis** is the only view needed.

HLA-B27 & CRP testing

- Blood tests also not recommended in general guidelines for back pain
- Useful in screening for SpA – check HLA-B27 and CRP
- HLA-B27 is positive in 85-95% of patients with ankylosing spondylitis, compared to 5-7% of the general population
- Only 40% of patients with axial spondyloarthritis have an elevated CRP – useful if elevated, but a negative test does not exclude SpA

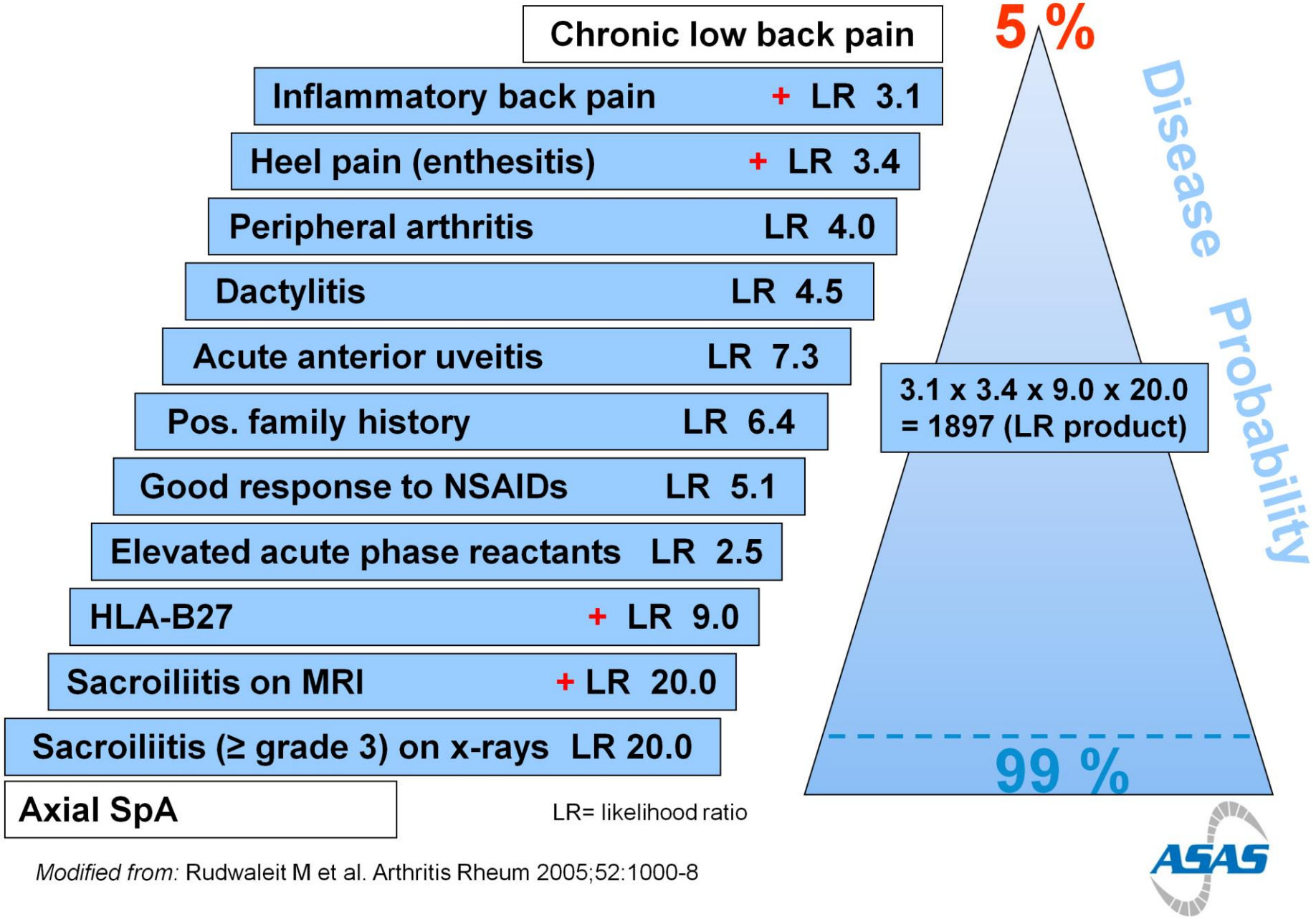
Combining features…

The probability of axial SpA in a patient under age 45 with chronic back:

- 5% of patients aged under 45 years have axial spondyloarthritis
- 14% if patients have inflammatory back pain
- 30% if HLA-B27 positive

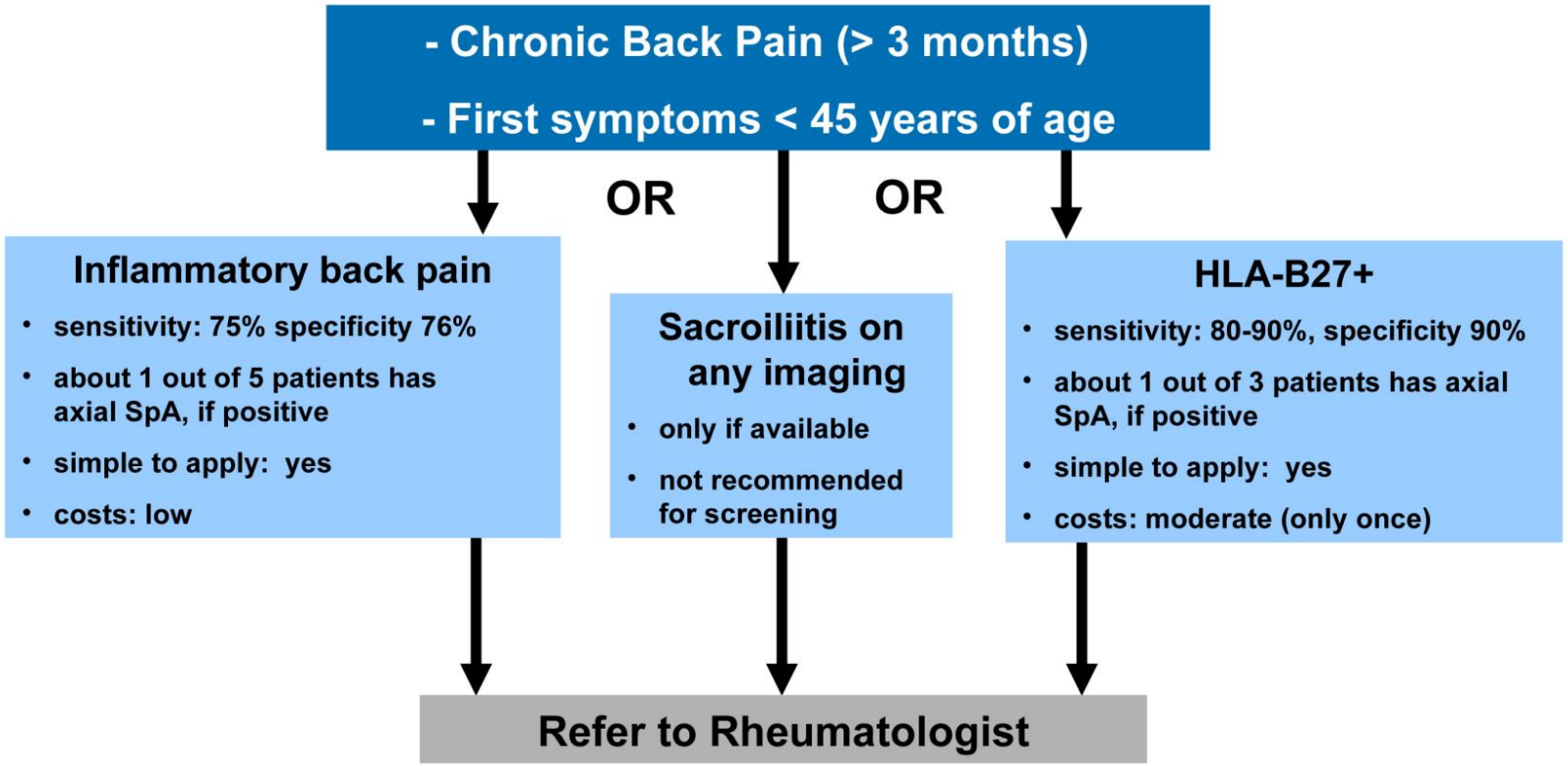
- **60% if patients have inflammatory back pain and are HLA-B27 positive**

Diagnostic Pyramid for Axial Spondyloarthritis



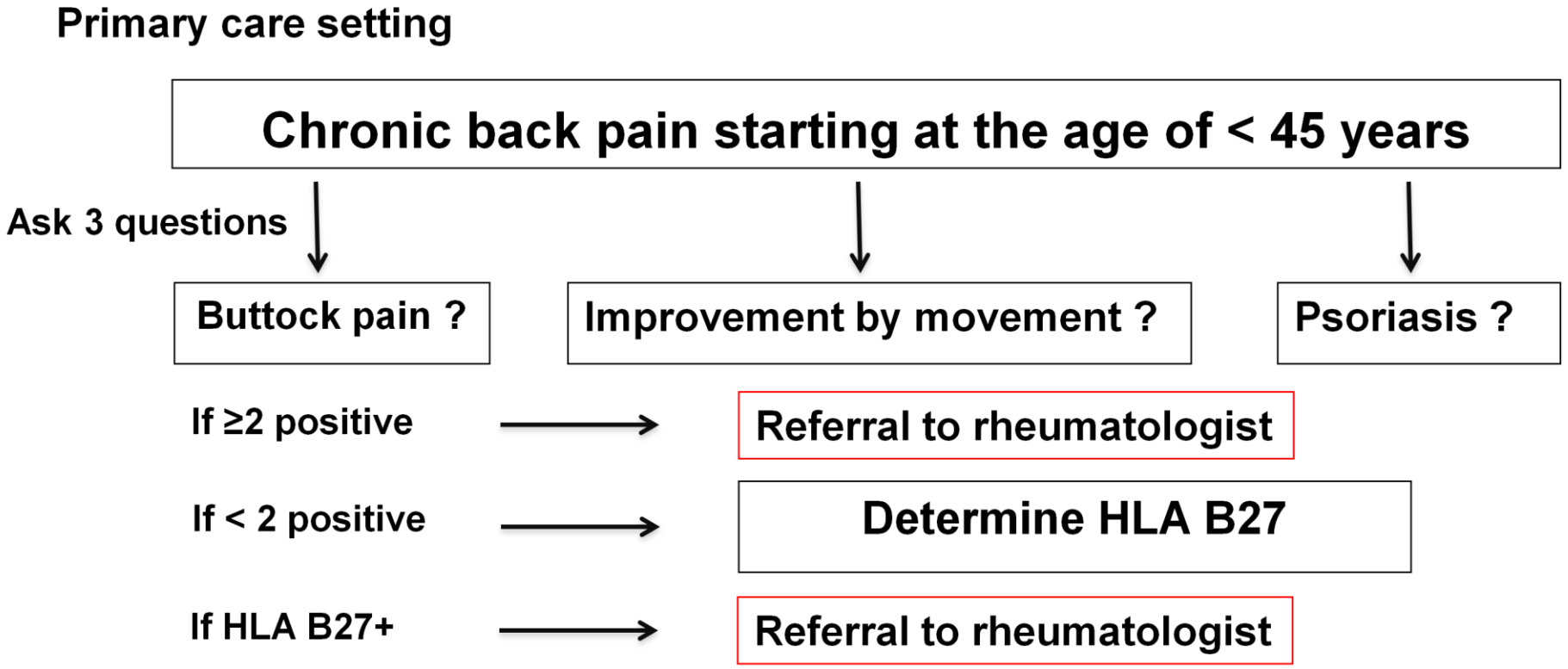
Modified from: Rudwaleit M et al. Arthritis Rheum 2005;52:1000-8

Possible Screening Approach for Axial SpA Among Patients with Chronic Low Back Pain



Adapted from Sieper J et al. Ann Rheum Dis 2005;64:659-63

A Possible 2-Step Referral Strategy



Re-analysis and modelling of the study data based on inclusion of HLA-B27

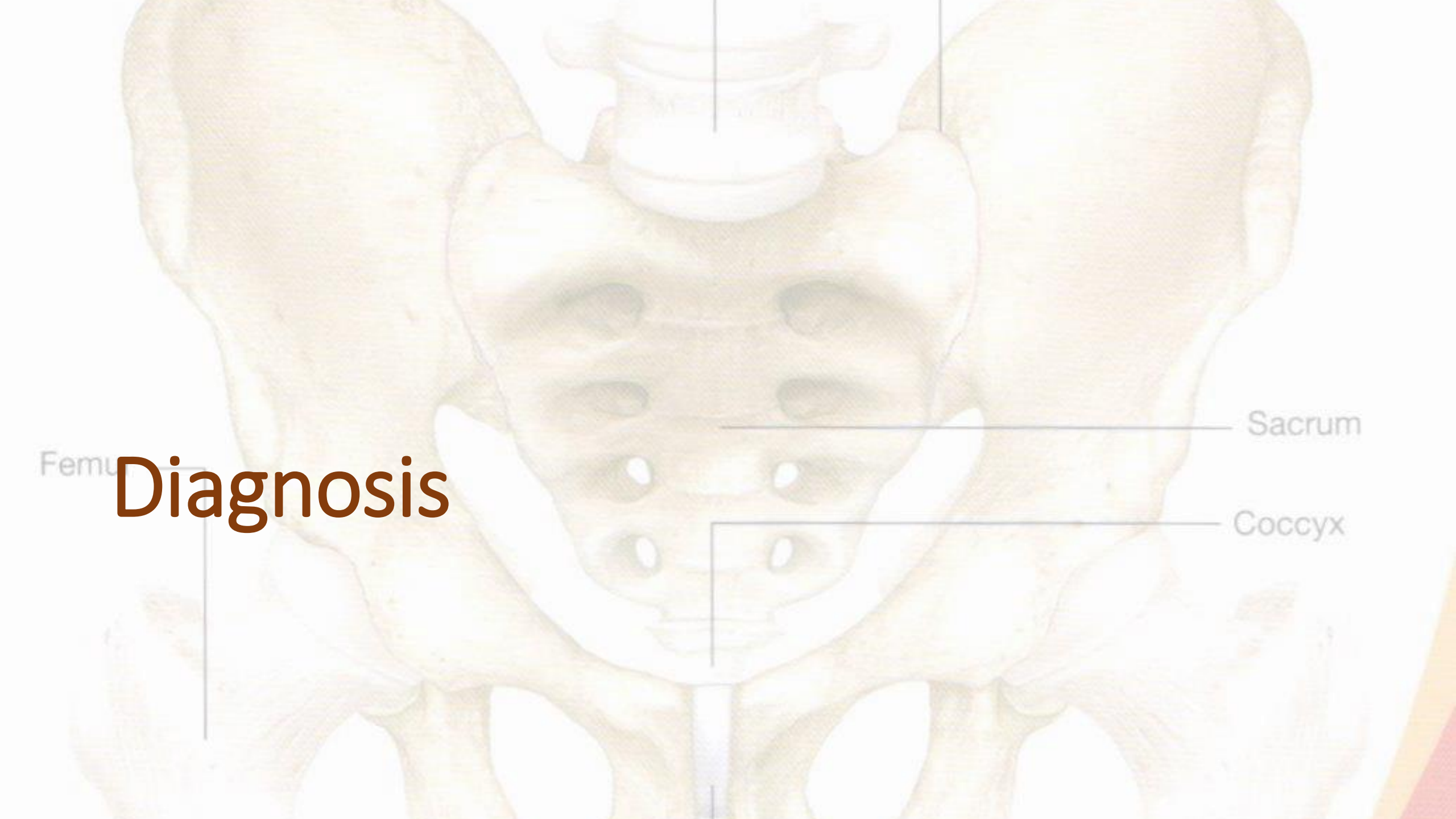
Sensitivity 80.4%
Specificity 75.4%

Braun A et al. Rheumatology (Oxford) 2013;52:1418-24

Perhaps modification of general guidelines?

Screen	Screen for inflammatory back pain symptoms
Consider	Other SpA manifestations, e.g. psoriasis, uveitis, inflammatory bowel disease
Check	HLA-B27 and CRP

Diagnosis



Ankylosing spondylitis – 1984 (still the official criteria)

- **1. Clinical criteria:**

a) Low back pain and stiffness for more than 3 months which improves with exercise, but is not relieved by rest.

b) Limitation of motion of the lumbar spine in both the sagittal and frontal planes.

c) Limitation of chest expansion relative to normal values correlated for age and sex.

2. Radiological criteria:

Sacroiliitis grade ≥ 2 bilaterally, or grade 3-4 unilaterally

ASAS Classification Criteria for Axial Spondyloarthritis (SpA)

In patients with ≥3 months back pain and age at onset <45 years

Sacroiliitis on imaging*

plus

≥1 SpA feature#

OR

HLA-B27

plus

≥2 other SpA features#

#SpA features

- inflammatory back pain
- arthritis
- enthesitis (heel)
- uveitis
- dactylitis
- psoriasis
- Crohn's/colitis
- good response to NSAIDs
- family history for SpA
- HLA-B27
- elevated CRP

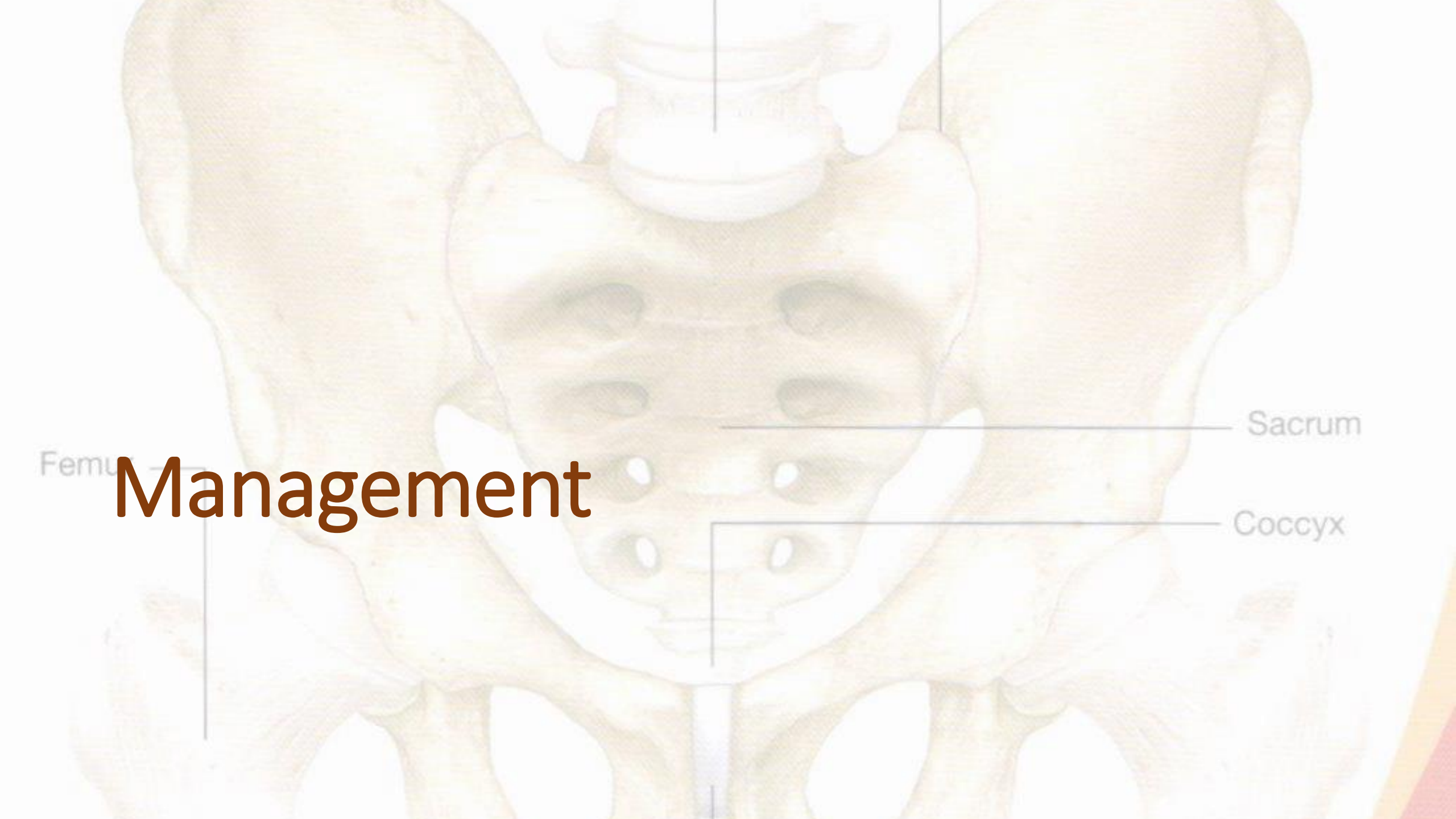
*Sacroiliitis on imaging

- active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA
- definite radiographic sacroiliitis according to mod NY criteria

n=649 patients with back pain;
Sensitivity: 82.9%, Specificity: 84.4%
Imaging alone: Sensitivity: 66.2%, Specificity: 97.3%

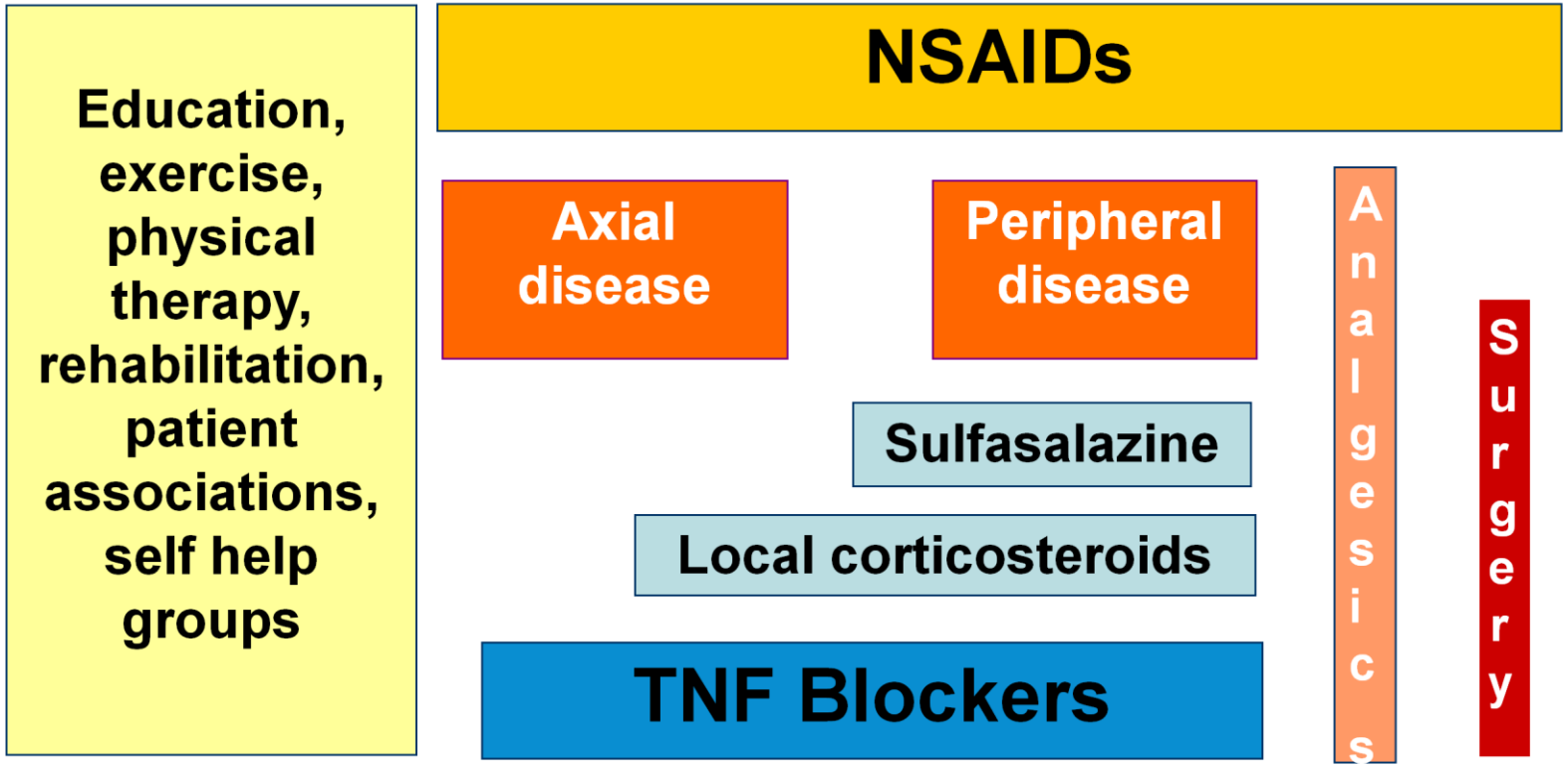
Rudwaleit M et al. Ann Rheum Dis 2009;68:777-783 (with permission)

ASAS



Management

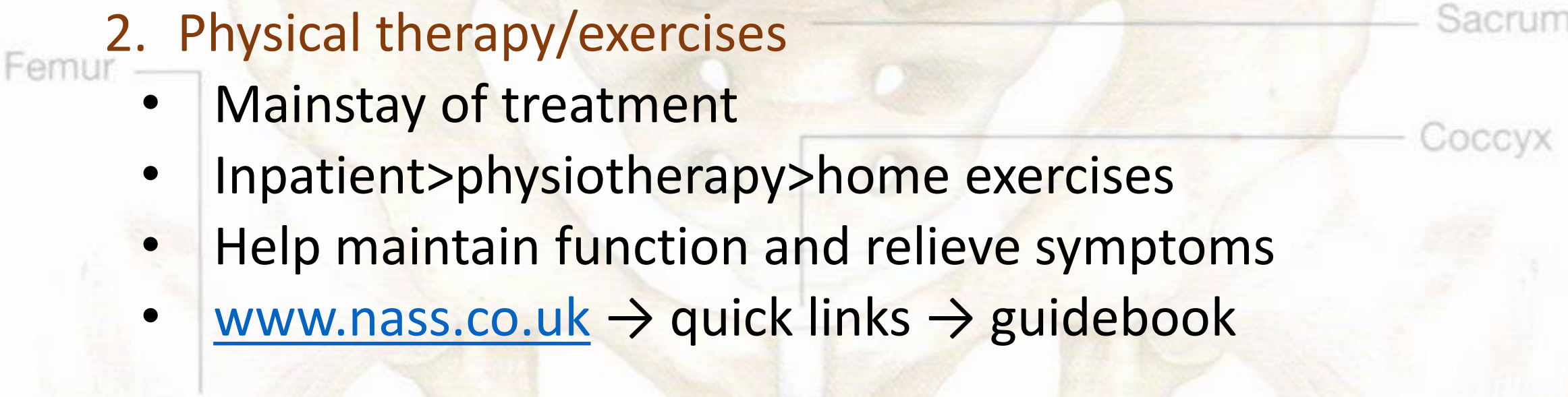
ASAS/EULAR Recommendations for the Management of Ankylosing Spondylitis



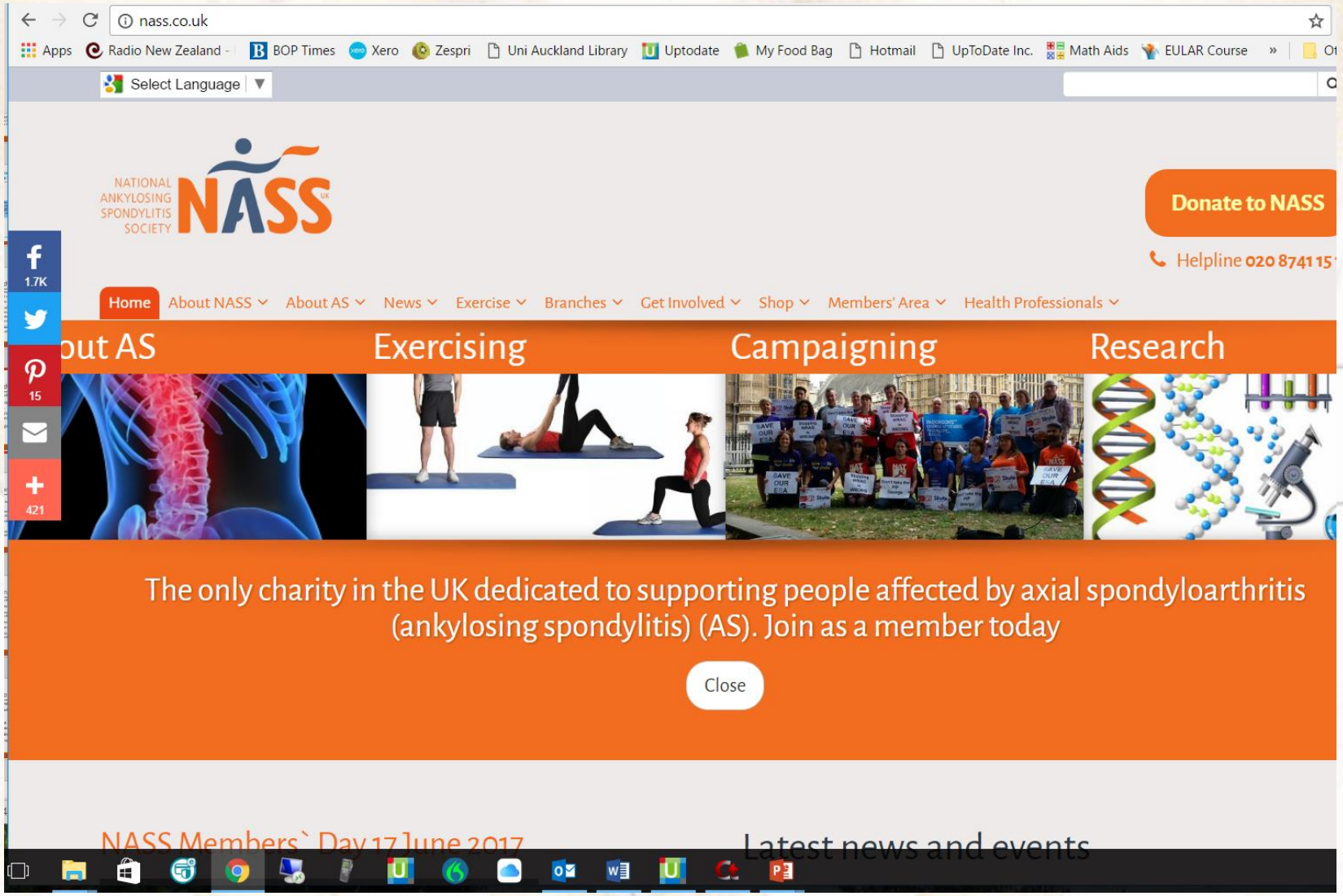
Zochling J et al. Ann Rheum Dis 2006;65:442-52 (with permission)

Spondyloarthritis - Treatment

1. Education/lifestyle factors
   - Quit smoking, patient associations
   - Spine protection – avoid falls (10x risk fracture)
2. Physical therapy/exercises
   - Mainstay of treatment
   - Inpatient>physiotherapy>home exercises
   - Help maintain function and relieve symptoms
   - www.nass.co.uk → quick links → guidebook



www.nass.co.uk

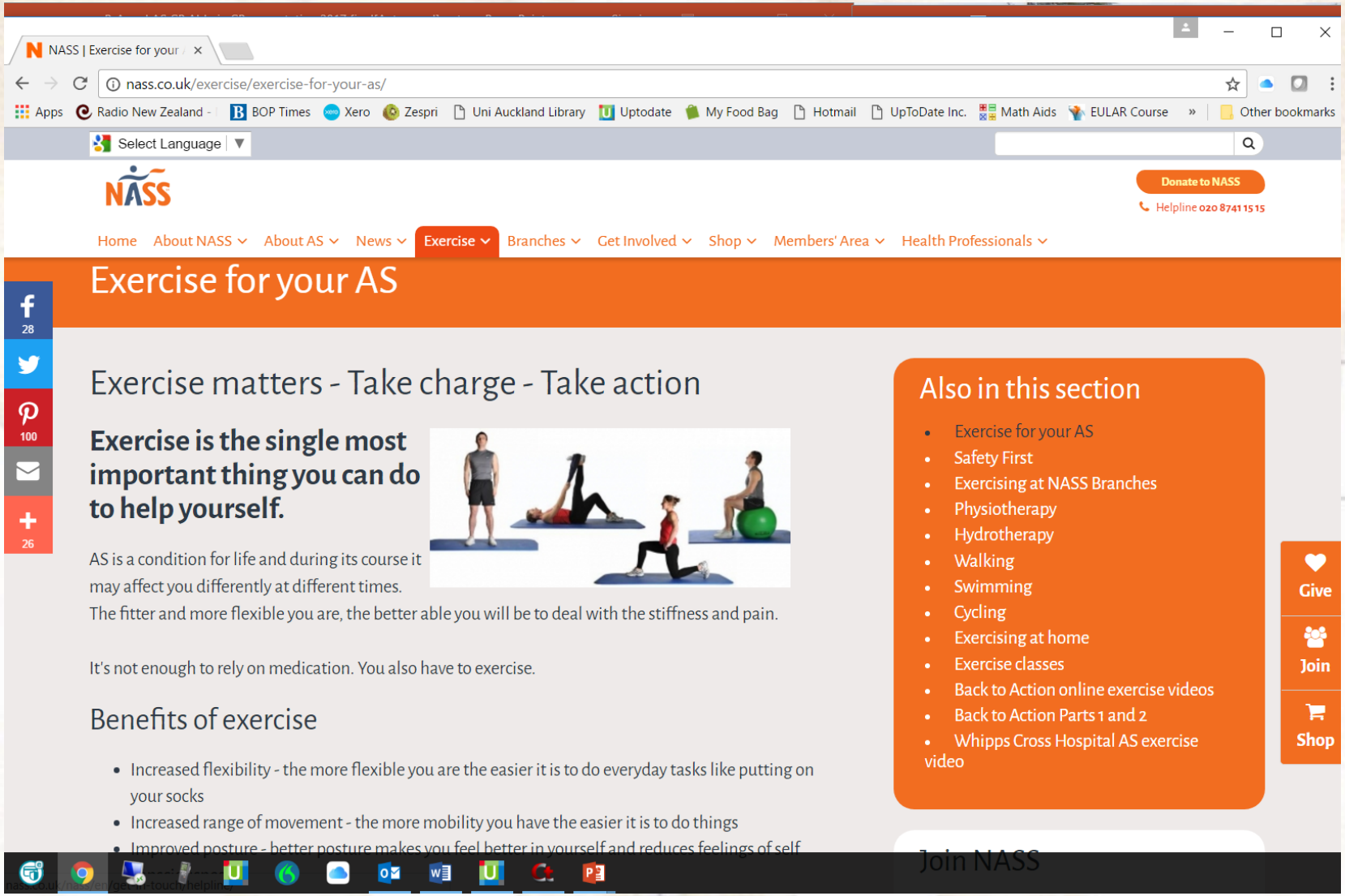


Femur

Sacrum

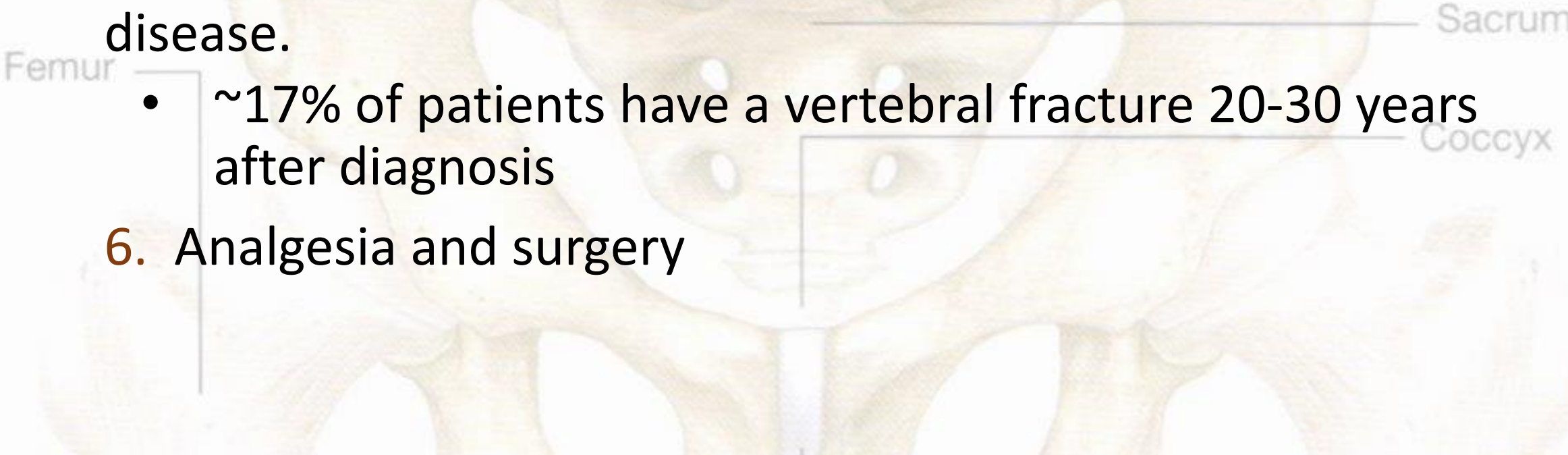
Coccyx

http://nass.co.uk/exercise/exercise-for-your-as/



Spondyloarthritis - Treatment

3. Medications – NSAIDs, IA steroid, anti-TNF
4. DMARDs for peripheral disease
5. Osteoporosis – odds ratio 7.7, increases with duration of disease.
   - ~17% of patients have a vertebral fracture 20-30 years after diagnosis
6. Analgesia and surgery

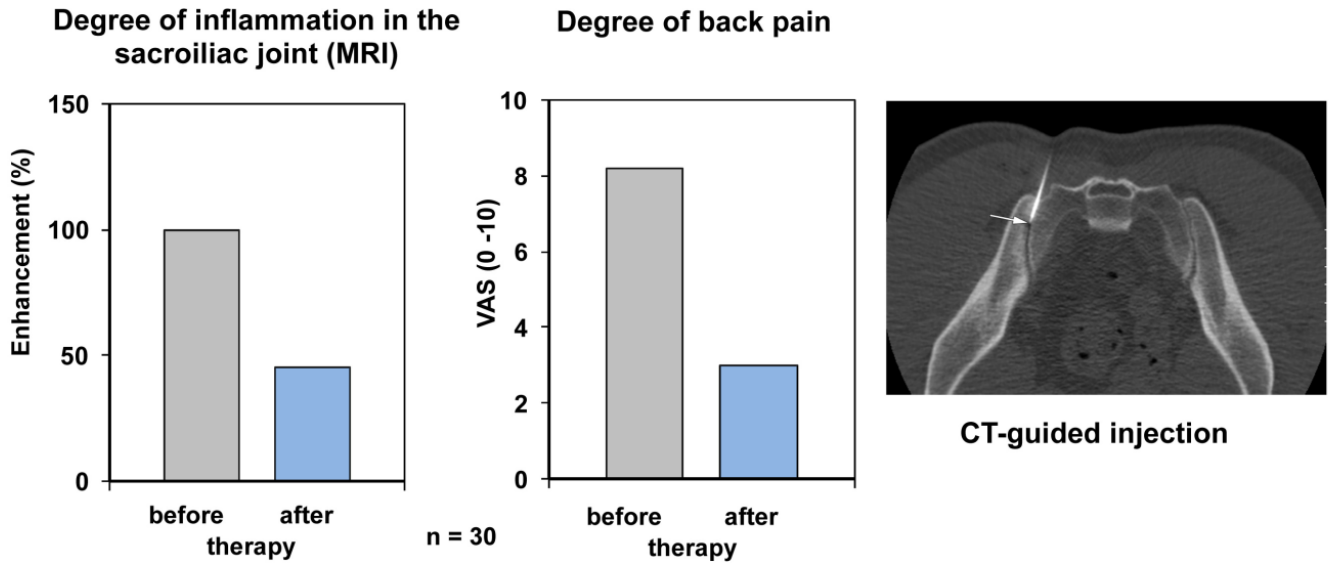


NSAIDs

- 70-80% of patients have a good clinical response to NSAIDs
- Some evidence suggests regular NSAIDs reduce radiographic progression compared with on-demand NSAIDS
- Full dose often needed
- Potential toxicity
  - Cardiovascular disease (~RR 1.5)
  - GI events (2-4% per year NSAIDs, 0.6-1.85 COX-2)
    - NSAIDs + PPI similar to COX2
  - Renal – hypertension, worsening CHF, oedema
  - Abnormal LFTs

SI joint injection

Injection of Corticosteroids into the Sacroiliac Joint of SpA Patients with Sacroiliitis



CT-guided injection

Braun J et al. J Rheumatol 1996;23:659-64

Femur

Sacrum

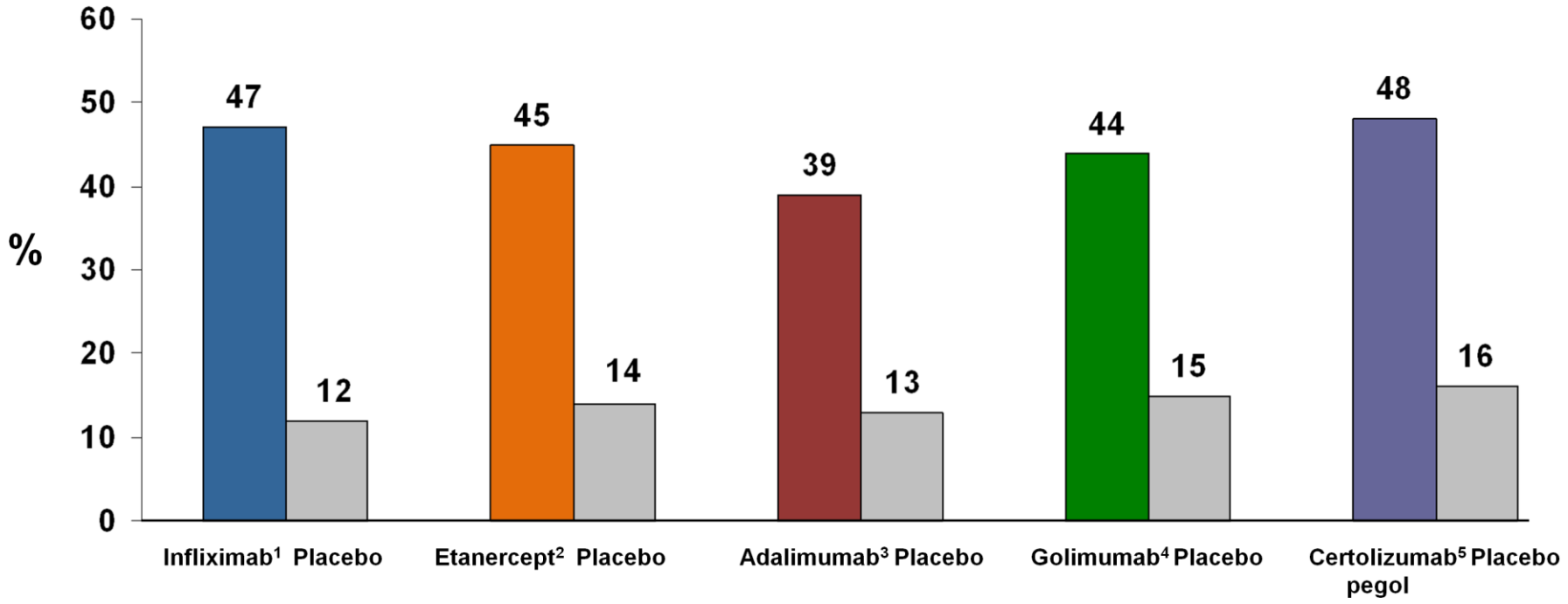
Coccyx

Anti-TNF therapy and Ankylosing Spondylitis

- Anti-TNF agents are very effective in patients who are refractory to NSAIDs
- In NZ, adalimumab, etanercept and infliximab available
- Approx 50% have a 50% reduction in pain, function, stiffness
- Reduce inflammatory lesions on MRI
- Response is rapid – within 6 weeks for most
- Response is persistent, at least 8 years
- Anecdotally, life-changing for many patients…

ASAS 40 Response after 24 Weeks of Treatment of AS Patients with TNFα Blocking Agents*

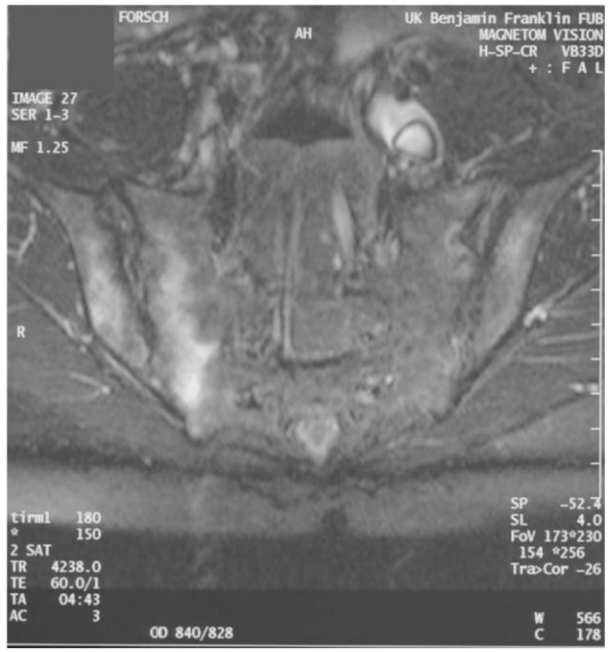
*Different studies, no head to head comparison



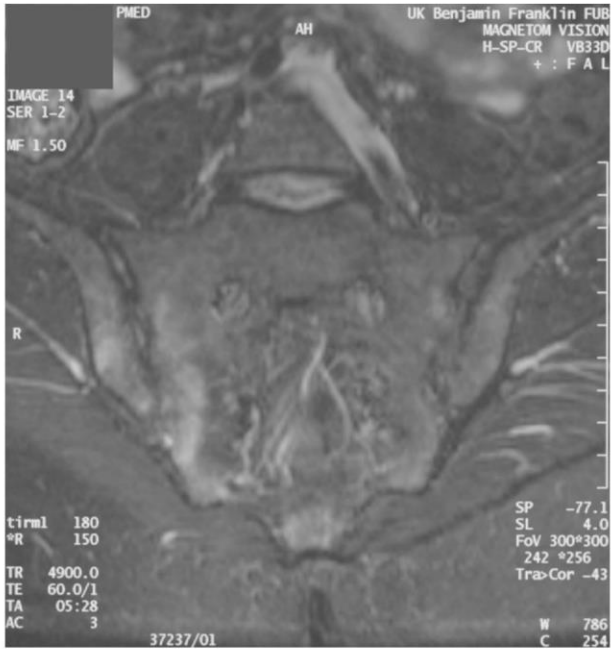
1. van der Heijde D et al. Arthritis Rheum 2005;52:582-91
2. Davis JC et al Ann Rheum Dis 2005;64:1557-62
3. van der Heijde D et al. Arthritis Rheum 2006;54:2136-46
4. Inman RD et al. Arthritis Rheum 2008;58:3402-12
5. Landewé et al. Ann Rheum Dis 2014;73:39-47

MRI of the Sacroiliac Joints
Before and After Etanercept Treatment (STIR)

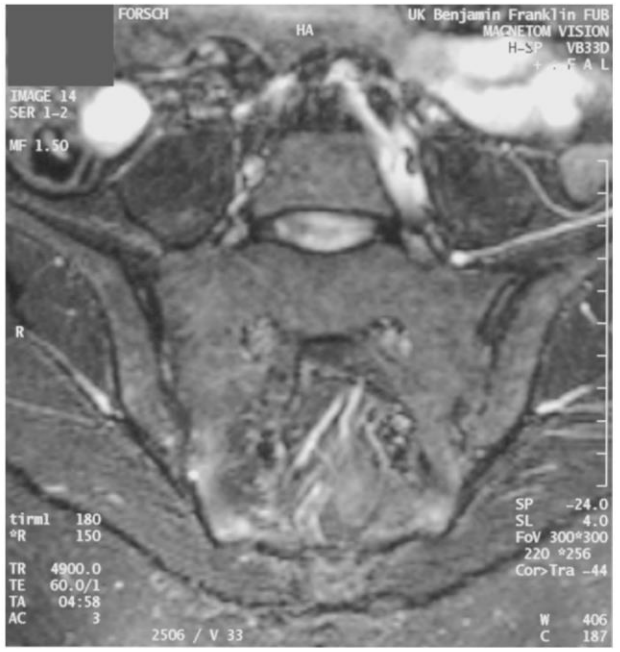
before



after 6 weeks



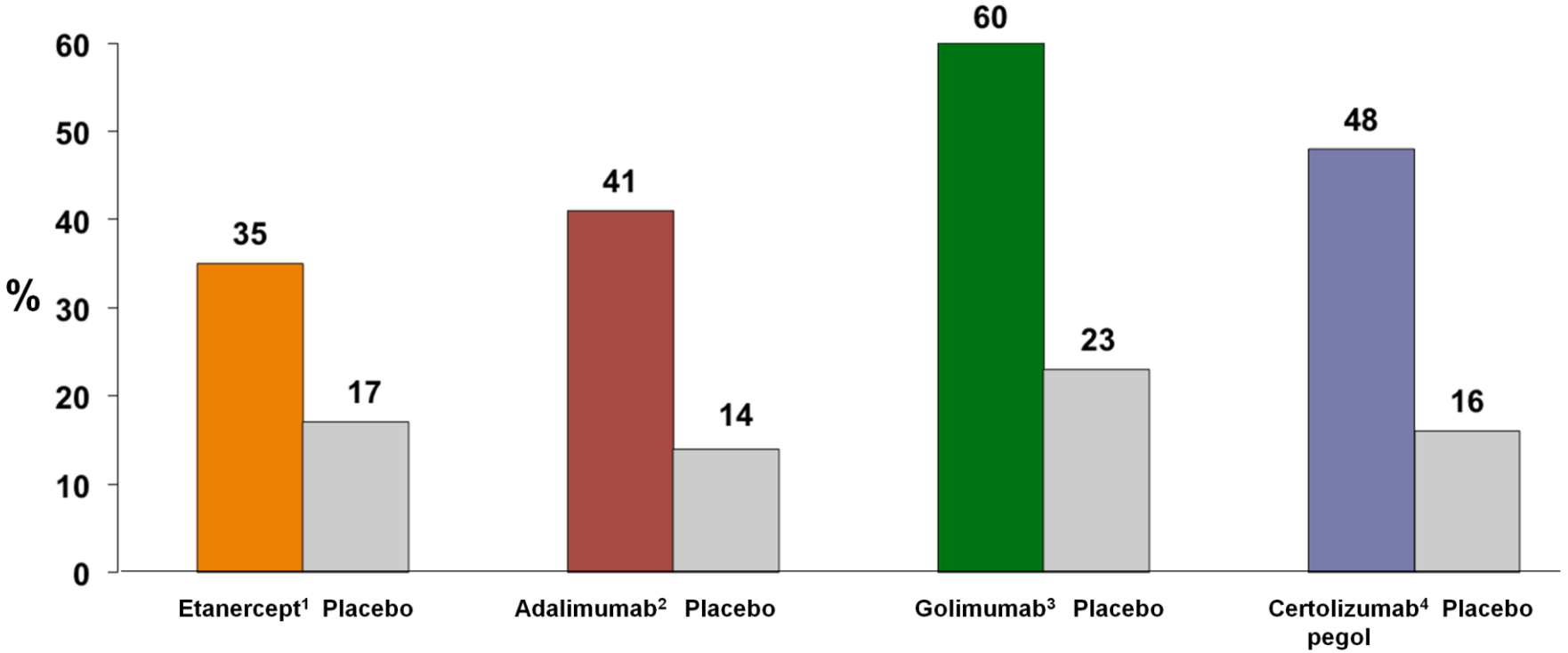
after 24 weeks



Rudwaleit M et al. Ann Rheum Dis 2005;64:1305-1310 (with permission)

ASAS 40 Response after 12 (16) Weeks of Treatment of Nr-axSpA Patients with TNFα Blocking Agents*

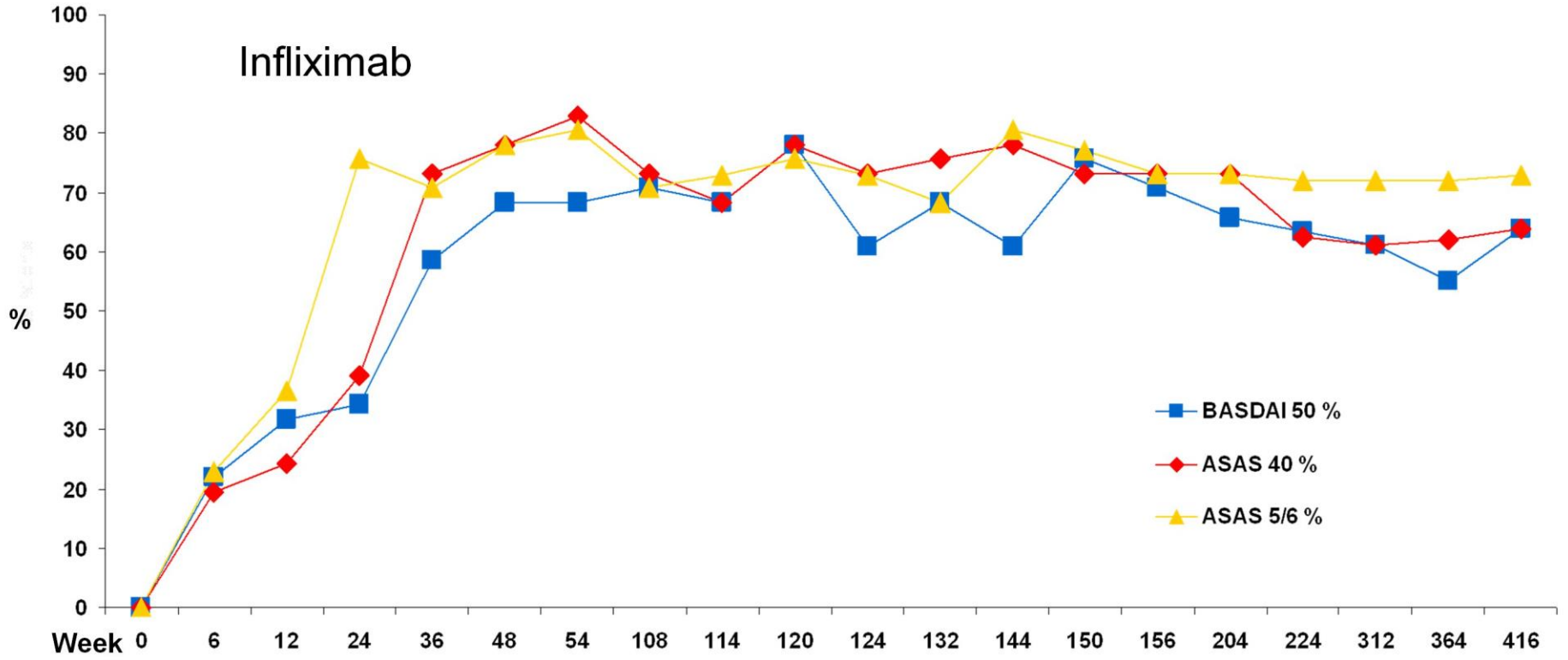
*Different studies, no head to head comparison
Response in patients with elevated CRP and/or active sacroiliitis on MRI at baseline is shown



Adalimumab, Certolizumab, Etanercept: evaluation at week 12
Golimumab: evaluation at week 16
Certolizumab results with 200 mg q2 weeks are shown

1. Dougados M et al. Arthritis Rheumatol 2014;66:2091-102; Pfizer, data on file
2. Sieper J et al. Ann Rheum Dis 2013;72:815-22
3. Sieper J et al. Arthritis Rheumatol 2015
4. Landewé et al. Ann Rheum Dis 2014;73:39-47

Longterm Clinical Efficacy of TNFα-Blocker in AS
Results over 8 years



N= 69 54 43 33

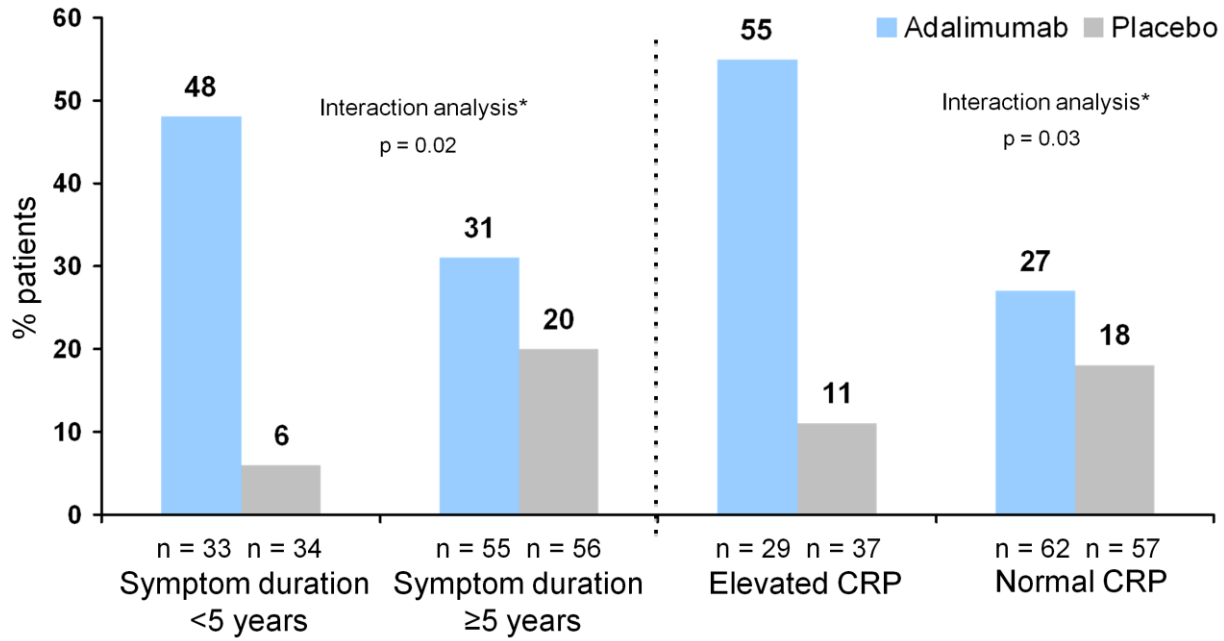
N = number of patients on therapy

Braun J et al. Lancet 2002;359:1187-93
Braun J et al. Ann Rheum Dis 2008;67:340-5
Baraliakos X et al. Rheumatology (Oxford) 2011;50:1690-9

Is early treatment better? Yes.

ASAS40 Response to Adalimumab by Symptom Duration and Baseline CRP at Week 12 in Patients with non-radiographic axial SpA

ABILITY-I Study: 40 mg Adalimumab s.c. EOW vs placebo over 12 weeks



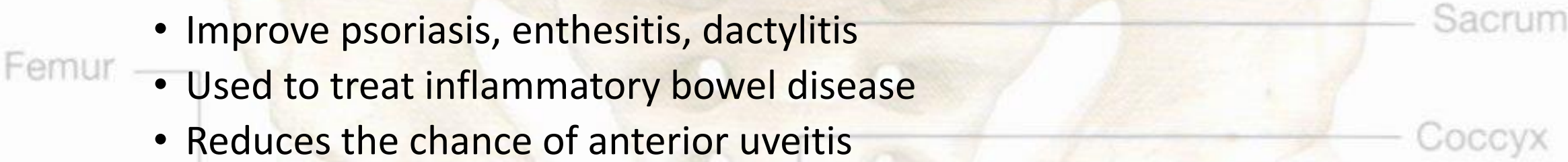
**logistic model used to assess treatment and subgroup interaction, with significant interaction defined as p≤0.10*

Sieper J et al. Ann Rheum Dis 2013;72:815-22 (with permission)

NRI

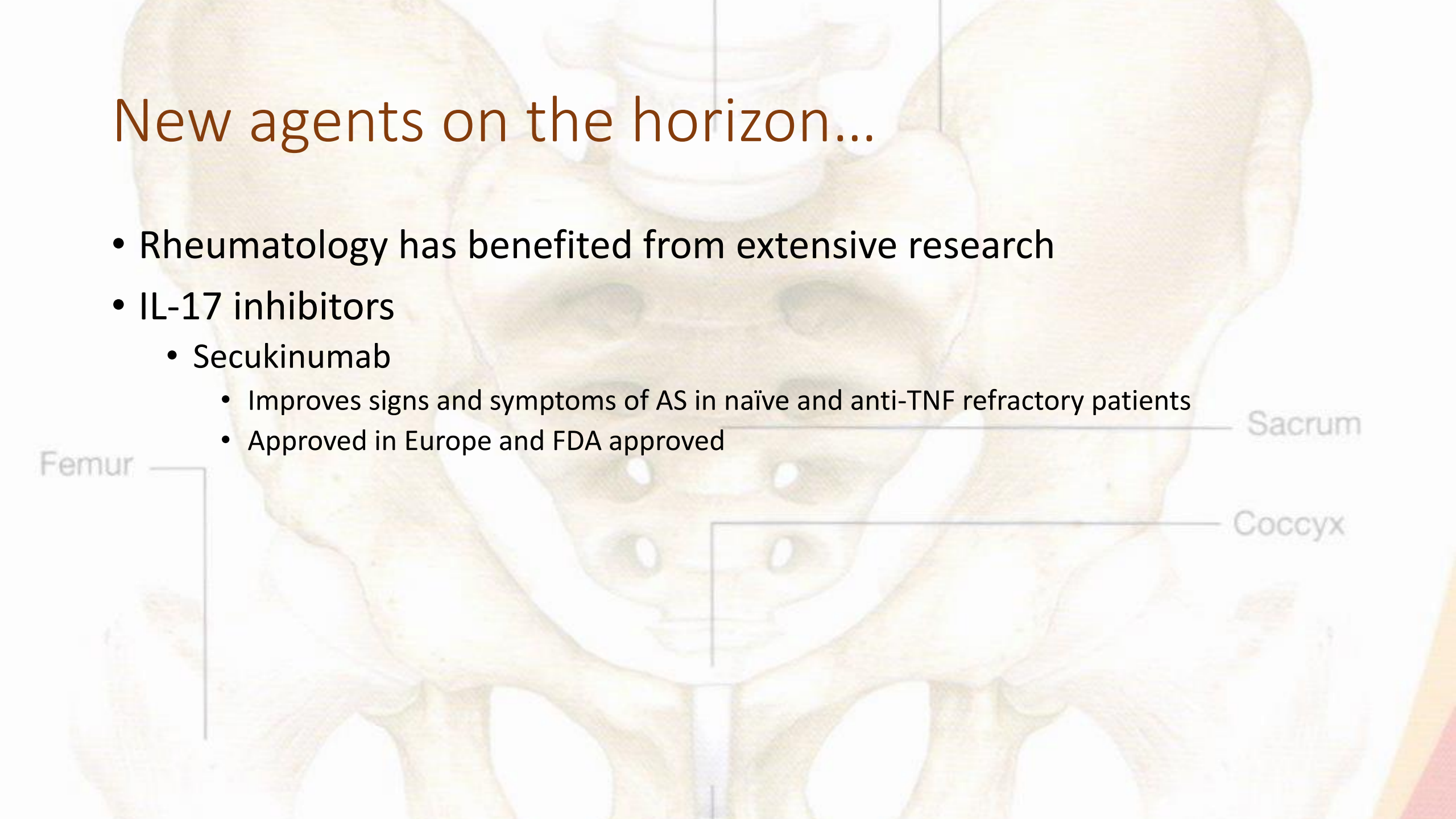
Anti-TNF therapy and Ankylosing Spondylitis

- Anti-TNF agents treat many components of disease with spondyloarthropathies, i.e. one drug to treat all/most manifestations
- Adalimumab and infliximab
  - Improve peripheral and axial arthritis
  - Improve psoriasis, enthesitis, dactylitis
  - Used to treat inflammatory bowel disease
  - Reduces the chance of anterior uveitis
- Etanercept
  - Improves peripheral and axial arthritis
  - Improves psoriasis, enthesitis and dactylitis
  - May increase the risk of anterior uveitis



New agents on the horizon…

- Rheumatology has benefited from extensive research
- IL-17 inhibitors
  - Secukinumab
    - Improves signs and symptoms of AS in naïve and anti-TNF refractory patients
    - Approved in Europe and FDA approved



Summary

- 5% of patients with chronic back pain onset before age 45 years have a spondyloarthritis
- Screen patients with chronic back pain for inflammatory back pain symptoms, consider testing HLA-B27, CRP and AP pelvis x-ray
- In patients with chronic back pain, look for a history of anterior uveitis, psoriasis, inflammatory bowel disease, family history of AS
- Effective treatments are available
- Treatment can be life changing…

Not to labour the topic…but

- **Inflammatory back pain symptoms:**
  - **Chronic back pain with onset before age 40 years**
  - **Pain at night or early morning**
  - **Pain improves with exercise but not with rest**
  - **Morning stiffness > 30 minutes**
  - Insidious onset

MINIMUM PRODUCT INFORMATION

HUMIRA

(adalimumab)

PHARMAC Pharmaceutical Schedule: HUMIRA is fully subsidised under Special Authority for the treatment of adults with rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, severe chronic plaque psoriasis, polyarticular juvenile idiopathic arthritis. Refer to Pharmaceutical Schedule for full Criteria. HUMIRA is not funded for ulcerative colitis, non-radiographic axial spondyloarthritis, enthesitis-related arthritis, uveitis, and hidradenitis suppurativa.

Please review full Data Sheet before prescribing. Full Data Sheet is available on request from AbbVie Limited, 6th Floor, 156-158 Victoria St, Wellington or by phoning 0800 900 030, or on the Medsafe website.

Humira is a Prescription Medicine containing adalimumab 10 mg/0.2 mL, 20 mg/0.4 mL or 40 mg/0.8 mL for injection.

INDICATIONS: Rheumatoid Arthritis (RA): Reducing signs & symptoms, and inhibiting the progression of structural damage, in adults with moderate to severely active RA; including patients with recently diagnosed moderate to severely active disease who have not received methotrexate. Humira can be used alone or in combination with methotrexate. **Polyarticular Juvenile Idiopathic Arthritis (pJIA):** in combination with methotrexate is indicated for reducing the signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients aged 2 years of age and older. Humira can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate. **Enthesitis-Related Arthritis (ERA):** Treatment of enthesitis-related arthritis in patients, 6 years of age and older, who have had an inadequate response to, or who are intolerant to, conventional therapy. **Psoriatic Arthritis (PsA):** Treatment of signs and symptoms, as well as inhibiting the progression of structural damage, of moderate to severely active PsA in adult patients where response to previous DMARDS has been inadequate. **Ankylosing Spondylitis (AS):** Reducing signs and symptoms in patients with active AS. **Non-radiographic Axial Spondyloarthritis (nr-axial SpA):** Treatment of adults with severe axial spondyloarthritis without radiographic evidence of AS but with objective signs of inflammation by elevated CRP and/or MRI, who have had an inadequate response to, or are intolerant to NSAIDs. **Crohn's Disease (CD) in Adults and Children (≥6 years):** Treatment of moderate to severe CD, to reduce the signs and symptoms of the disease and to induce and maintain clinical remission in patients; • who have had an inadequate response to conventional therapies or, • who have lost response to or are intolerant to infliximab. **Ulcerative Colitis (UC):** Treatment of moderately to severely active ulcerative colitis in adult patients who have had an inadequate response to conventional therapy including corticosteroids and 6-mercaptopurine (6-MP) or azathioprine (AZA), or who are intolerant to or have medical contraindications for such therapies. **Psoriasis in Adults and Children (≥ 4 years):** Treatment of moderate to severe chronic plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. Treatment of severe chronic plaque psoriasis in children and adolescent patients from 4 years of age who have had an inadequate response to or are inappropriate candidates for topical therapy and phototherapy. **Hidradenitis Suppurativa (HS):** Treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adult patients with an inadequate response to conventional systemic HS therapy. **Uveitis:** Treatment of non-infectious intermediate, posterior and panuveitis in adult patients who have had an inadequate response to corticosteroids, in patients in need of corticosteroid-sparing, or in whom corticosteroid treatment is inappropriate. **CONTRAINDICATIONS:** Severe infections including sepsis, active tuberculosis, opportunistic infections; concurrent anakinra administration; moderate to severe heart failure; known hypersensitivity to HUMIRA or its excipients. **PRECAUTIONS:** Infections (bacterial, mycobacterial, invasive fungal e.g, histoplasmosis, viral or other opportunistic); hepatitis B, TB (reactivation, new onset or latent); demyelinating disorders* (neurologic evaluation should be performed prior to initiation, regularly and during treatment for patients with non-infectious intermediate uveitis); haematologic events; live vaccines; immunosuppression; new or worsening CHF; renal, hepatic impairment; malignancy; hypersensitivity reactions; latex sensitivity; concurrent biologic DMARDs or other TNF antagonists; elderly; pregnancy, lactation, surgery. *Refer to Datasheet under Neurologic Events. **ADVERSE REACTIONS:** Respiratory tract infections, leucopaenia, anaemia, lipid increase, headache, abdominal pain, nausea and vomiting, elevated liver enzymes, rash, musculoskeletal pain, injection site reaction are very commonly seen adverse events. Benign neoplasm and skin cancer including basal cell and squamous cell carcinoma were commonly reported. Fatal infections such as TB and invasive opportunistic infections have rarely been reported. For others, see full Data Sheet. **DOSAGE & METHOD OF USE: RA, PsA and AS:** 40 mg sc fortnightly as a single dose. **JIA:** Paediatric Patients (2 years and older for pJIA, 6 years and older for ERA), 10 kg to < 15 kg 10 mg fortnightly, 15 kg to < 30 kg 20 mg fortnightly, ≥ 30 kg 40 mg fortnightly. **nr-axial SpA:** 40 mg sc fortnightly as a single dose, clinical response is usually achieved within 12 weeks of starting treatment. Continued therapy should be carefully reconsidered in a patient not responding within this time period. **CD and UC:** Induction: 160mg sc (Four injections on Day 0 or Two injections on Day 0 and two injections on Day 1), then second dose 80mg as two sc injections on Day 14, then Maintenance: 40mg sc starting on Day 28 and continuing fortnightly. **pCD:** Paediatric Patients ≥6 years: < 40kg – Induction: 80mg sc (Two 40mg injections on Day 0, then a second dose as one 40 mg injection on Day 14, then Maintenance: 10mg sc (moderate CD) or 20mg sc (severe CD) starting on Day 28 and continuing fortnightly. ≥ 40kg Induction: 160mg sc (Four 40mg injections on Day 0 or Two 40 mg injections on Day 0 and two 40mg injections on Day 1, then second dose 80 mg as two 40 mg injections on Day 14, then Maintenance: 20mg sc (moderate CD) or 40mg sc (severe CD) starting on Day 28 and continuing fortnightly. **Psoriasis & Uveitis:** Initial dose of 80 mg, followed by 40 mg fortnightly, starting one week after the initial dose. **Paediatric Plaque-Psoriasis (4 years of age and older):** recommended dose is based on body weight, sc weekly for the first two doses, continuing fortnightly. Continued therapy beyond 16 weeks should be considered carefully in a patient not responding within this time period. < 30kg 20mg fortnightly ≥ 30kg 40mg fortnightly. **HS:** Induction: 160mg sc (four 40mg injections in one day or two 40mg injections per day for two consecutive days) on Day 1, followed by 80mg (as two 40mg injections) on Day 15, then Maintenance: 40mg sc starting on Day 29 and continuing weekly. Version 32

•NZ-HUM-0129. May 2017.