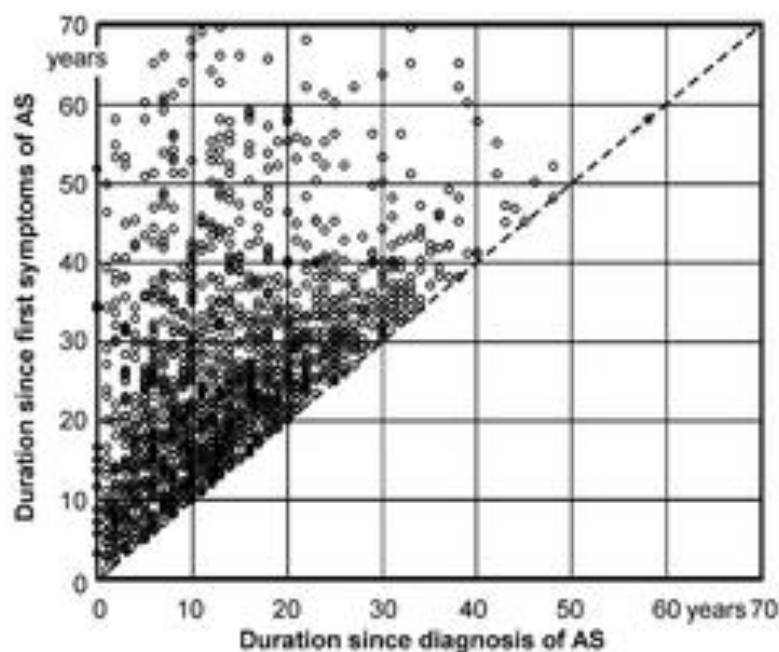


Ankylosing spondylitis

Diagnostic criteria

Soosan Soroosh
Associate professor

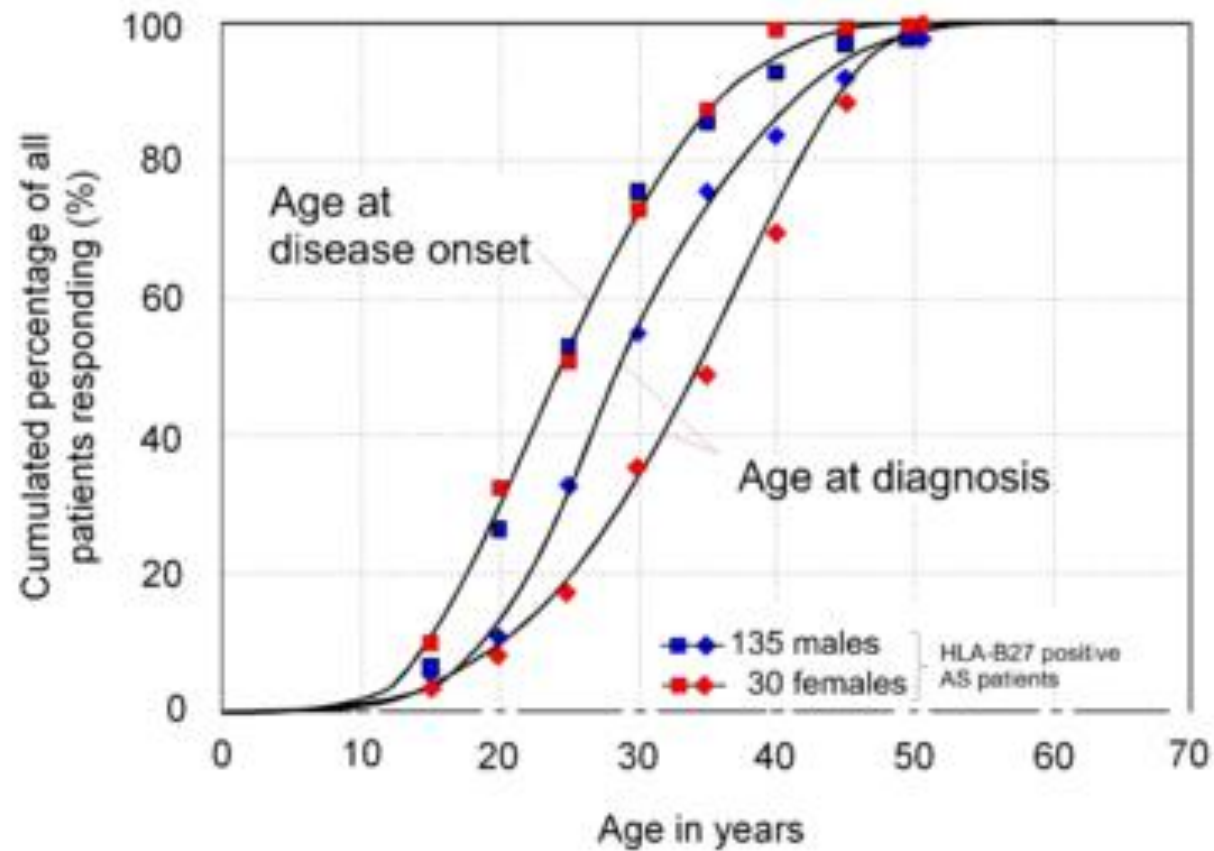
Disease Duration and Duration since Diagnosis in AS



The diagnosis of AS can be delayed up to 60 years after the disease onset (first symptoms of AS).

N = 5087 from surveys conducted between 1996 and 2005

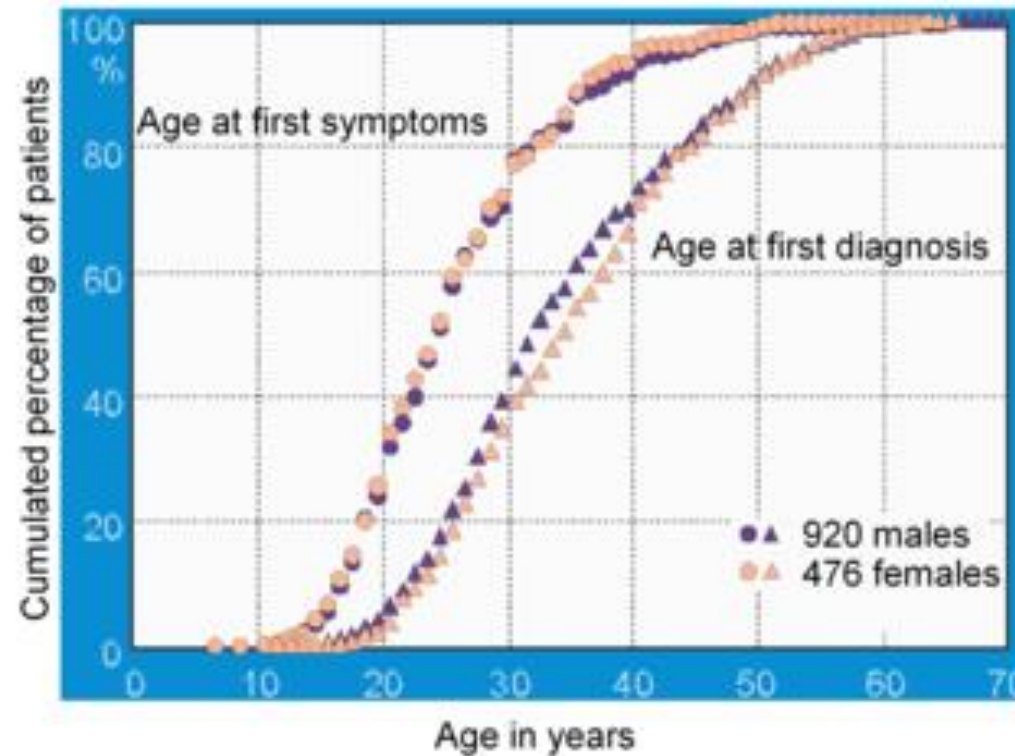
Age at Onset and Time of Ankylosing Spondylitis-Diagnosis



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



Age at First Symptoms and at First Diagnosis in Ankylosing Spondylitis Patients



Average delay in diagnosis: 9 years

Feldtkeller E et al. Curr Opin Rheumatol 2000;12:239-247 (with permission)



Concept of Spondyloarthritides (SpA)

Non-radiographic
axial SpA

Ankylosing Spondylitis

Predominantly Axial
SpA

Reactive arthritis

Psoriatic Arthritis

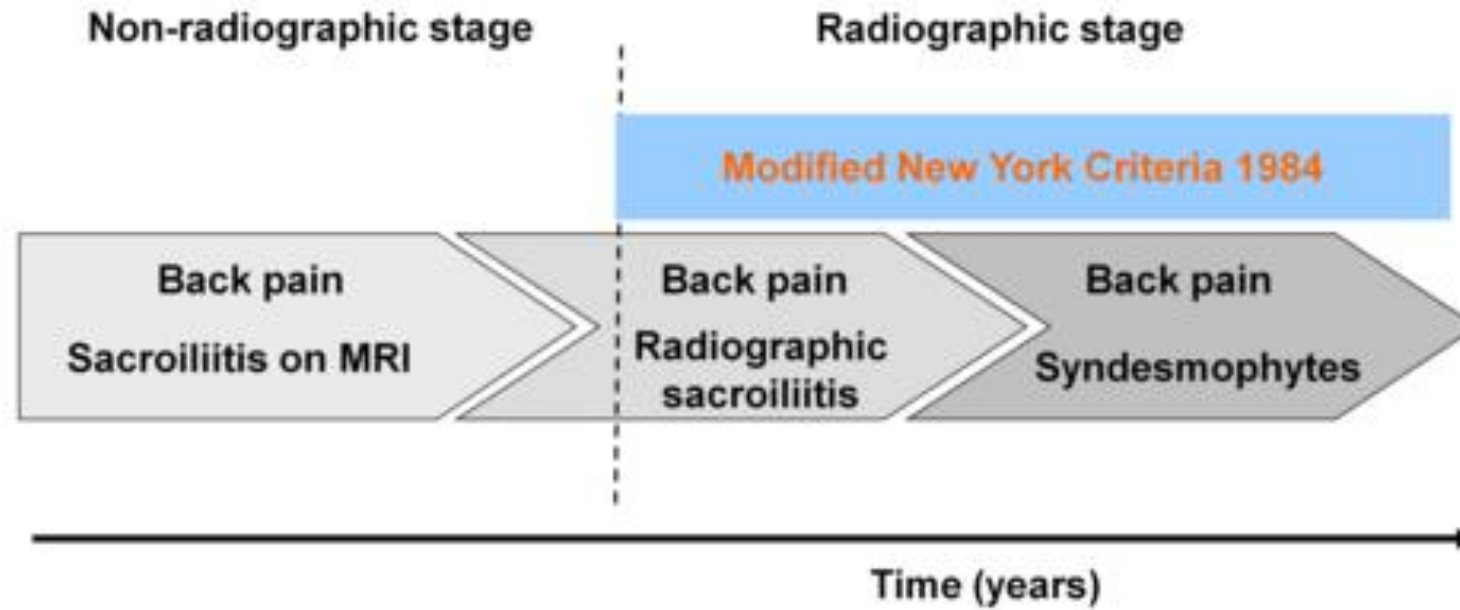
Arthritis with inflammatory
bowel disease

Undifferentiated SpA

Predominantly Peripheral
SpA



Axial Spondyloarthritis



Progression of Non-radiographic Axial SpA to AS: Data from GESPIC*

Non-radiographic axial SpA



no definite radiographic sacroiliitis (grade 0 at the right side, grade 1 – possible subchondral sclerosis – at the left side)

12%
in 2 years

Main predictor:
elevated CRP**

Ankylosing spondylitis

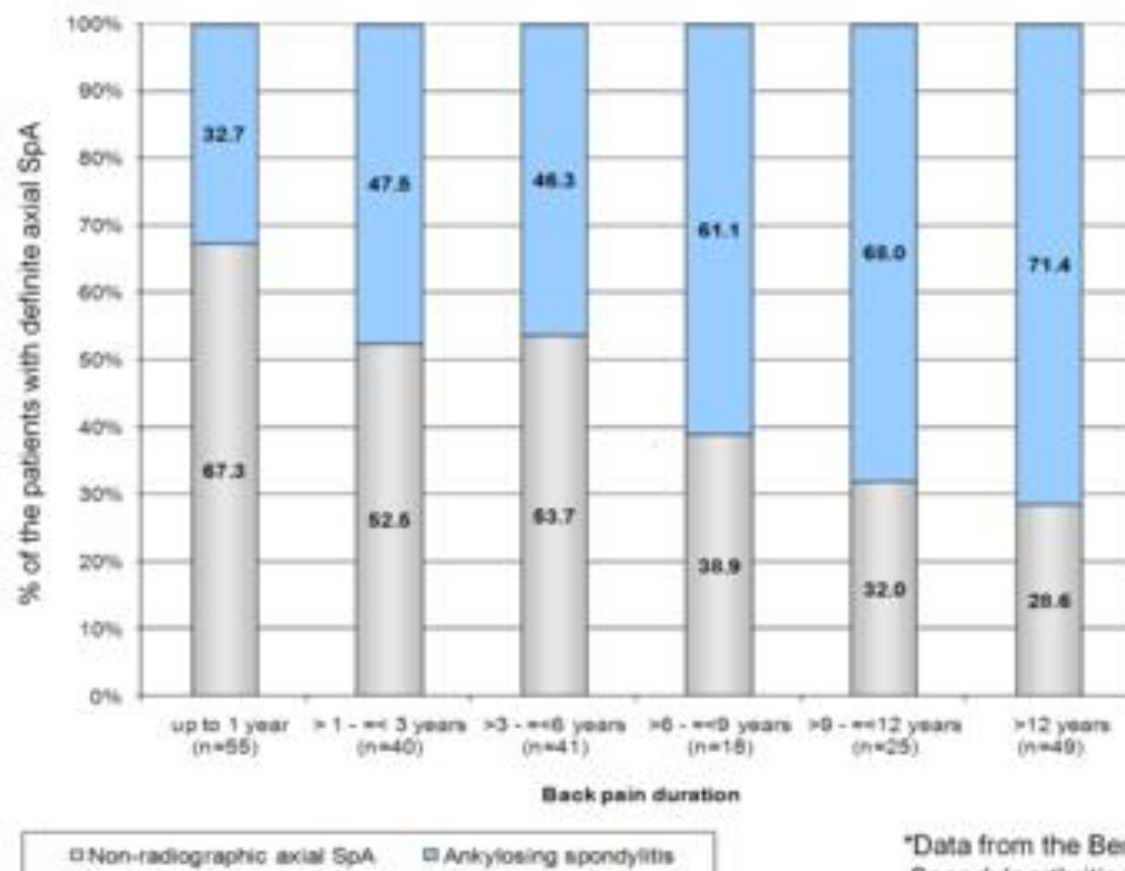


definite radiographic sacroiliitis (grade 2 bilaterally) fulfilling the radiographic criterion of the modified New York criteria

*GESPIC = GERman Spondyloarthritis Inception Cohort

**Odds ratio for progression in patients with elevated serum C-reactive protein level (>6 mg/l) was:
4.11 (95% CI 1.13-14.95).

Ratio of Non-radiographic Axial SpA to AS among Patients with Definite Axial SpA in Relation to Symptom Duration at the Time of Diagnosis*



*Data from the Berlin Early Spondyloarthritis Clinic

Poddubnyy D et al. Ann Rheum Dis 2012;71:1998-2001 (with permission)



Modified New York Criteria for Ankylosing Spondylitis (1984)

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 criterion:

Sacroiliitis grade ≥ 2 bilaterally or grade 3-4 unilaterally

Definite ankylosing spondylitis if the radiological criterion is associated with at least 1 clinical criterion.

Amor Classification Criteria for Spondyloarthritis

A. Clinical Symptoms/History	Score
1. Pain at night (spine) or morning stiffness	1
2. Asymmetrical oligoarthritis	2
3. Gluteal (buttock) pain (any) or alternating gluteal pain	1 2
4 Sausage like digit or toe (dactylitis)	2
5. Enthesitis (heel)	2
6. Uveitis	2
7. Urethritis/Cervicitis within 1 month before onset of arthritis	1
8. Diarrhea within 1 month before onset of arthritis	1
9. Psoriasis, balanitis or inflammatory bowel disease	2
B. X-rays	
10. Sacroiliitis (grade 2 bilaterally or grad 3 unilaterally)	3
C. Genetical background	
11. HLA-B27 positive or positive family history for AS, ReA, uveitis, psoriasis or inflammatory bowel disease	2
D. Good response to NSAIDs	
12. NSAIDs show a good response within 48 hours, or relapse within 48 hours after NSAID are stopped	2

At least 6 points are necessary

ESSG-Classification Criteria

(European Spondylarthropathy Study Group)

**Inflammatory
Back Pain**

or

Synovitis

- asymmetric or
- predominantly in the lower limbs

plus one of the following:

- enthesitis (heel)
- positive family history
- psoriasis
- Crohn's disease, Colitis ulcerosa
- urethritis / cervicitis or acute diarrhea within one month before arthritis
- buttock pain (alternating between right and left gluteal areas)
- sacroiliitis

Dougados M et al. Arthritis Rheum 1991;34:1218



Spondyloarthritis: Characteristic Parameters Used for Diagnosis I

Symptoms

Inflammatory
back pain



Imaging



Lab

ESR/CRP

Patient's history

Good response to NSAIDs



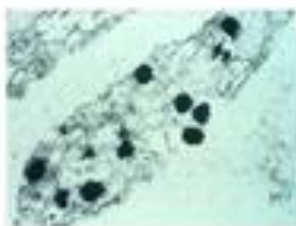
Spondyloarthritis: Characteristic Parameters Used for Diagnosis II

Genetics

HLA-B27
positive

family
history

Predisposing/
concomitant
diseases



Infection*



psoriasis



Crohn's

*positive staining for Chlamydia in synovial membrane¹

1. Schumacher HR et al. Arthritis Rheum 1988;31:937-946

Inflammatory Back Pain (IBP) According to Various Criteria

Calin et al.¹

- age at onset < 40 yrs
- duration of back pain > 3 months
- insidious onset
- morning stiffness
- improvement with exercise

IBP if 4 / 5 are present.

Rudwaleit et al.²

- morn. stiffness > 30 min
- improvement with exercise, not with rest
- awakening at 2. half of the night because of pain
- alternating buttock pain

IBP if 2 / 4 are present.

IBP experts (ASAS)³

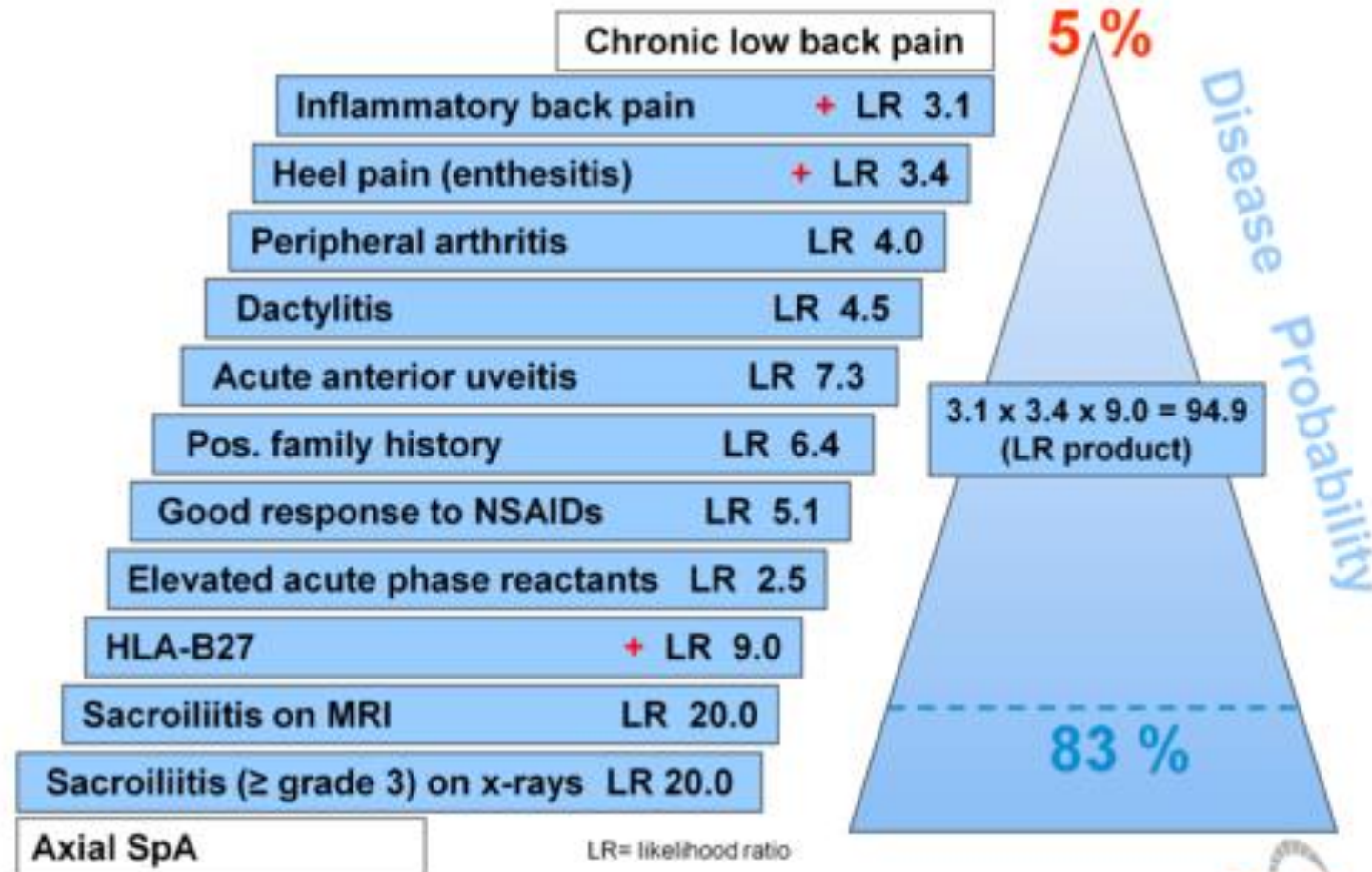
- age at onset < 40 yrs
- insidious onset
- improvement with exercise
- no improvement with rest
- pain at night
(with improvement upon getting up)

IBP if 4 / 5 are present.

1 Calin A et al. JAMA 1977;237:261; 2 Rudwaleit M et al. Arthritis Rheum 2006;54:569-78; 3 Sieper J et al. Ann Rheum Dis. 2009; 68: 784-788



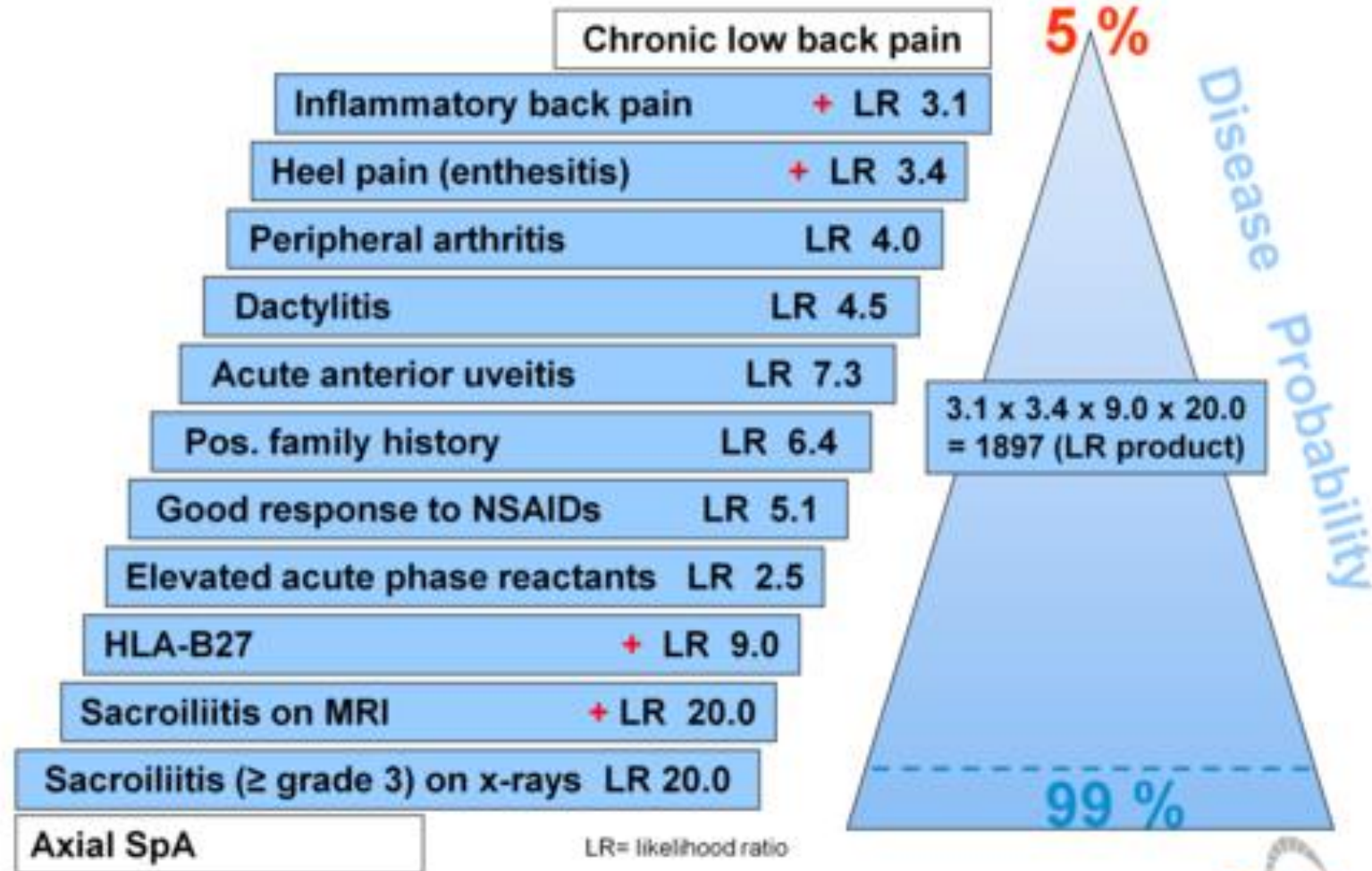
Diagnostic Pyramid for Axial Spondyloarthritis



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



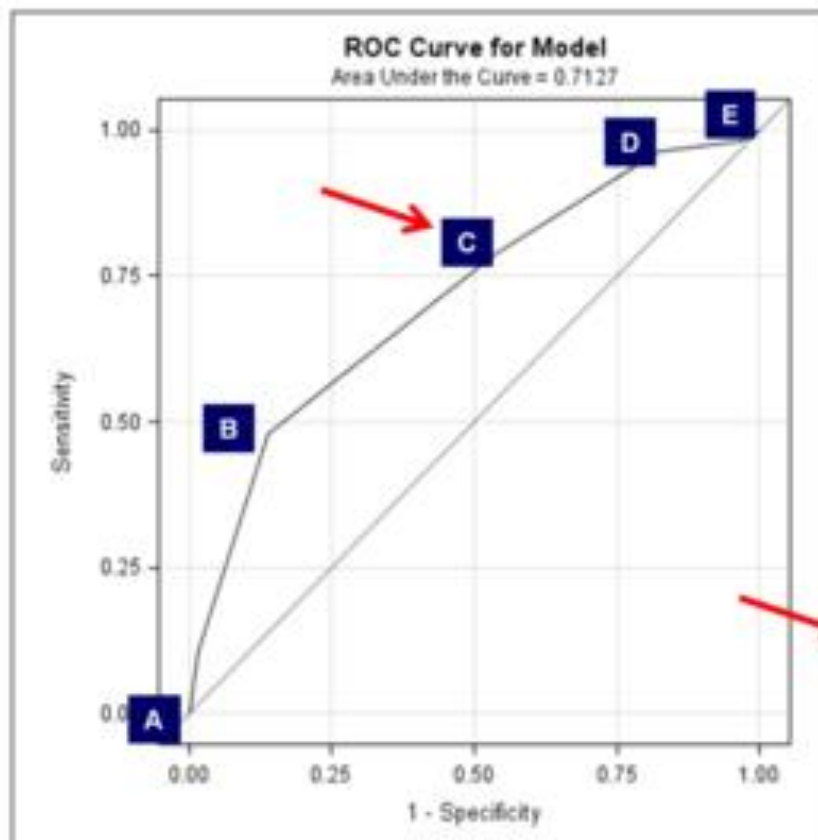
Diagnostic Pyramid for Axial Spondyloarthritis



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



Sensitivity and Specificity for Combinations of Clinical Criteria for Identifying Patients with Axial SpA in Primary Care



Patient numbers as diagnosed by the rheumatologists: axial SpA (n=113) vs. non-SpA back pain (n=209)

Criteria for the recognition of axial SpA

- age at onset ≤ 35 years
- wakening up in the 2nd half of the night
- alternating buttock pain
- improvement by movement, not rest
- improvement by NSAIDs within 48 hours

	Sensitivity	Specificity
A = 5 criteria	11%	96%
B ≥ 4 criteria	48%	86%
C ≥ 3 criteria	79%	46%
D ≥ 2 criteria	97%	18%
E ≥ 1 criterium	98%	3%

After exclusion of HLA B27

Braun A et al. Ann Rheum Dis 2011;70:1782-7 (with permission)



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

- *Sacroiliitis on imaging
- active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA
 - definite radiographic sacroiliitis according to the modified New York criteria

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

n=649 patients with back pain:

Overall

Sensitivity: 82.9%, Specificity: 84.4%

Imaging arm alone

Sensitivity: 66.2%, Specificity: 97.3%

Clinical arm alone

Sensitivity: 58.6%, Specificity: 83.3%

Specification of the Variables Used for the ASAS-Criteria for Classification of Axial Spondyloarthritis I

Clinical feature of axial SpA	Definition
Inflammatory back pain (IBP)	IBP according to experts: 4 out of 5 of the following parameters present: 1. age at onset < 40 years 2. insidious onset 3. improvement with exercise 4. no improvement with rest 5. pain at night (with improvement upon getting up)
Good response to NSAIDs	24-48 hours after a full dose of a non-steroidal anti-inflammatory drug (NSAID) the back pain is not present anymore or much better

Specification of the Variables Used for the ASAS-Criteria for Classification of Axial Spondyloarthritis II

Clinical feature of axial SpA	Definition
Arthritis	Past or present active synovitis diagnosed by a physician
Dactylitis	Past or present dactylitis diagnosed by a physician
Enthesitis	Heel enthesitis: past or present spontaneous pain or tenderness at examination of the site of the insertion of the Achilles tendon or plantar fascia at the calcaneus
Psoriasis	Past or present psoriasis diagnosed by a physician
Inflammatory bowel disease	Past or present Crohn's disease or ulcerative colitis diagnosed by a physician
Uveitis anterior	Past or present uveitis anterior, confirmed by an ophthalmologist

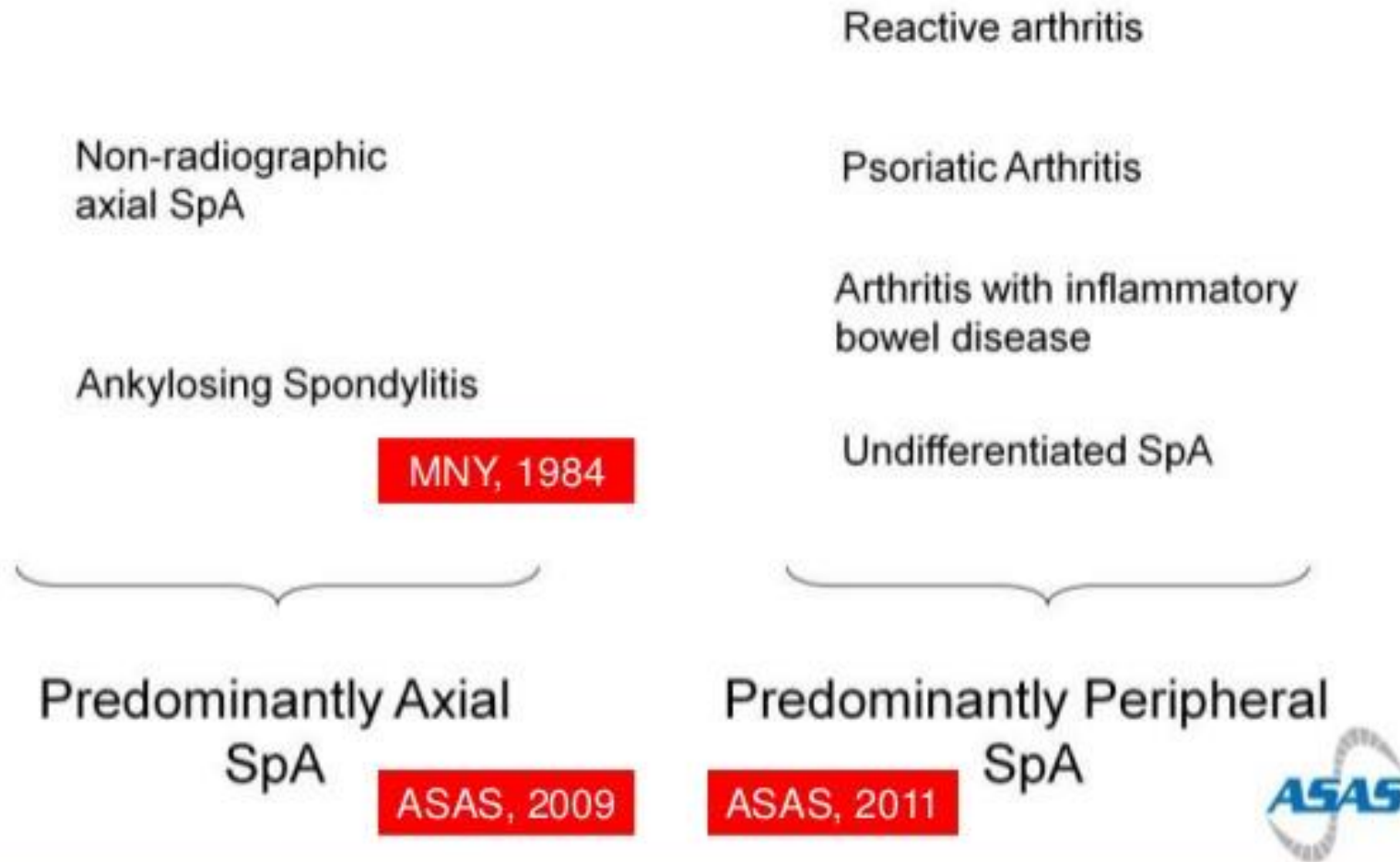
Specification of the Variables Used for the ASAS-Criteria for Classification of Axial Spondyloarthritis III

Clinical or lab feature of axial SpA	Definition
Family history	Presence in first-degree or second-degree relatives of any of the following: (a) ankylosing spondylitis (b) Psoriasis (c) Uveitis (d) reactive arthritis (e) inflammatory bowel disease
HLA-B27	Positive testing according to standard laboratory techniques
Elevated CRP	C-reactive protein above upper normal limit in the presence of back pain, after exclusion of other causes for elevated CRP concentration

Specification of the Variables Used for the ASAS-Criteria for Classification of Axial Spondyloarthritis IV

Imaging feature of axial SpA	Definition
Sacroiliitis by X-rays	Bilateral grade 2-4 or unilateral grade 3-4, according to the modified New York criteria
Sacroiliitis by MRI	Active inflammatory lesions of sacroiliac joints with definite bone marrow edema/osteitis suggestive of sacroiliitis associated with spondyloarthritis

Concept of Spondyloarthritides (SpA)



ASAS Classification Criteria for Peripheral Spondyloarthritis (SpA)

Arthritis or enthesitis or dactylitis
plus

≥ 1 SpA feature

- uveitis
- psoriasis
- Crohn's/colitis
- preceding infection
- HLA-B27
- sacroiliitis on imaging

OR

≥ 2 other SpA features

- arthritis
- enthesitis
- dactylitis
- IBP (ever)
- family history for SpA

Peripheral arthritis: usually predominantly lower limbs and/or asymmetric arthritis

Enthesitis: clinically assessed

Dactylitis: clinically assessed

IBP: Inflammatory back pain

Sensitivity: 77.8%, Specificity: 82.2%; n=266

ASAS Classification Criteria for 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 (IBP)
- arthritis
- enthesitis (heel)
- uveitis
- dactylitis
- psoriasis
- Crohn's/colitis
- good response to NSAIDs
- family history for SpA
- HLA-B27
- elevated CRP

In patients with peripheral symptoms ONLY

Arthritis or enthesitis or dactylitis plus

≥ 1 SpA feature

- uveitis
- psoriasis
- Crohn's/colitis
- preceding infection
- HLA-B27
- sacroiliitis on imaging

OR

≥ 2 other SpA features

- arthritis
- enthesitis
- dactylitis
- IBP ever
- family history for SpA

Sensitivity: 79.5%, Specificity: 83.3%; n=975

Rudwaleit M et al. Ann Rheum Dis 2011;70:25-31 (with permission)



Specification of the Variables Used for the ASAS-Criteria for Classification of Peripheral Spondyloarthritis I

Entry criteria	Definition
Arthritis	Current peripheral arthritis compatible with SpA (usually asymmetric and/ or predominant involvement of the lower limb), diagnosed clinically by a physician.
Enthesitis	Current enthesitis, diagnosed clinically by a physician.
Dactylitis	Current dactylitis, diagnosed clinically by a physician.

Specification of the Variables Used for the ASAS-Criteria for Classification of Peripheral Spondyloarthritis II

Features of peripheral SpA	Definition
Inflammatory back pain (IBP) in the past	IBP in the past according to the rheumatologist's judgement. Here, only IBP in the past is considered. In patients with current IBP (and concomitant peripheral manifestations), the ASAS classification criteria for axial SpA should be applied.
Arthritis	Past or present peripheral arthritis compatible with SpA (usually asymmetric and/ or predominant involvement of the lower limb), diagnosed clinically by a physician.
Enthesitis	Enthesitis: past or present spontaneous pain or tenderness at examination of an enthesis. Any site of enthesitis can be affected whereas in the ASAS classification criteria for axial SpA only enthesitis of the heel is considered.

Specification of the Variables Used for the ASAS-Criteria for Classification of Peripheral Spondyloarthritis III

Features of peripheral SpA	Definition
Uveitis	Past or present uveitis anterior, confirmed by an ophthalmologist.
Dactylitis	Past or present dactylitis, diagnosed by a physician.
Psoriasis	Past or present psoriasis, diagnosed by a physician.
Inflammatory bowel disease	Past or present Crohn's disease or ulcerative colitis diagnosed by a physician.
Preceding infection	Urethritis / cervicitis or diarrhoea within one month before the onset of arthritis / enthesitis / dactylitis.

Specification of the Variables Used for the ASAS-Criteria for Classification of Peripheral Spondyloarthritis IV

Features of peripheral SpA	Definition
Family history	Presence in first-degree (mother, father, sisters, brothers, children) or second-degree (maternal and paternal grandparents, aunts, uncles, nieces, and nephews) relatives of any of the following: (a) ankylosing spondylitis, (b) psoriasis, (c) acute uveitis, (d) reactive arthritis, (e) inflammatory bowel disease.
HLA-B27	Positive testing according to standard laboratory techniques.
Sacroiliitis by imaging	Bilateral grade 2-4 or unilateral grade 3-4 sacroiliitis on plain radiographs, according to the modified New York criteria, or active sacroiliitis on MRI according to the ASAS consensus definition.

ASAS Axial SpA Criteria are Highly Sensitive and Specific

Gold standard = expert physician's diagnosis

694 patients with onset of chronic low back pain (≥ 3 months) prior to age 45

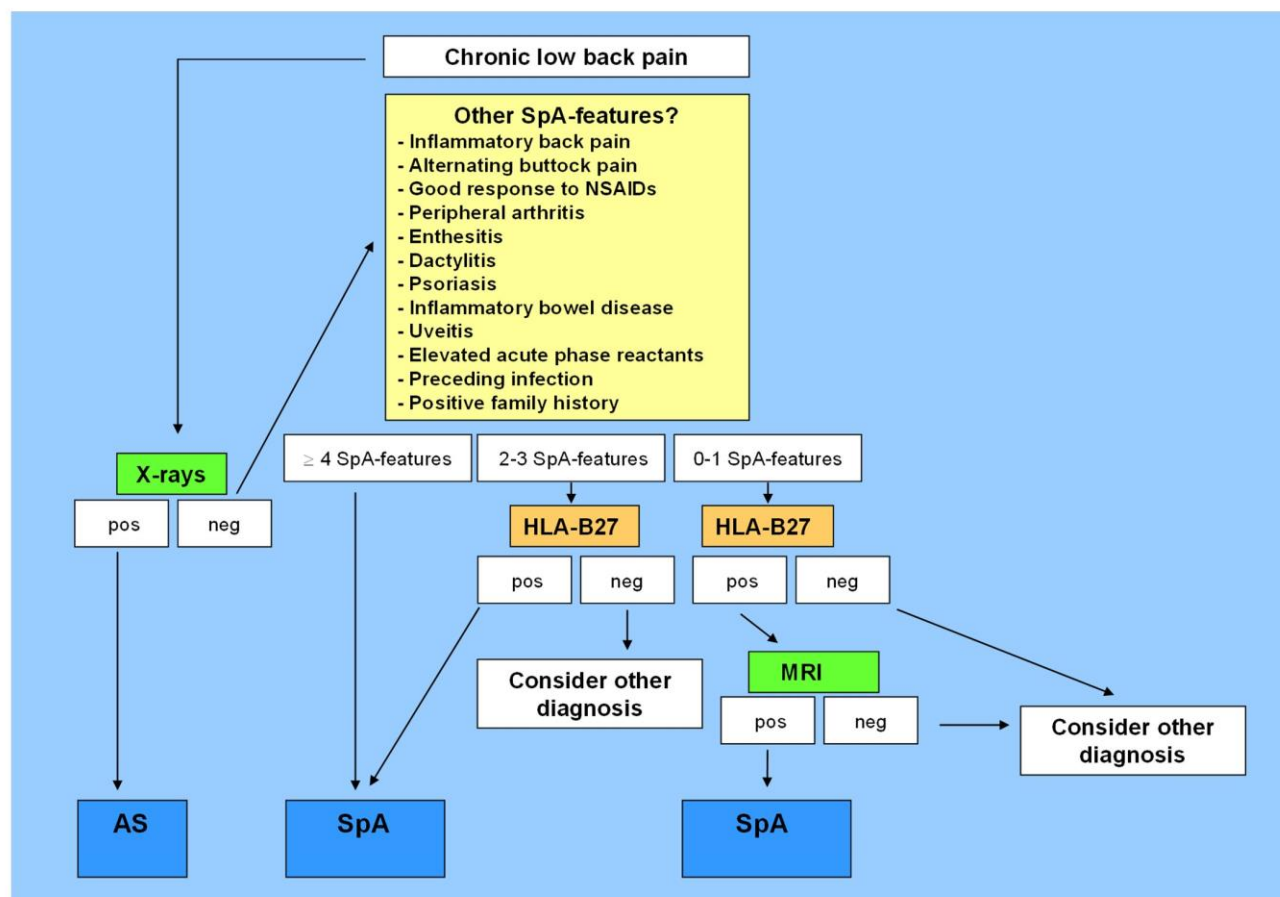
	Sensitivity, %	Specificity, %
ASAS Criteria for Axial SpA	82.9	84.4
Amor Criteria	69.3	77.9
Modified Amor Criteria*	82.9	77.5
ESSG Criteria	72.4	66.3
Modified ESSG Criteria*	85.1	65.1

* Modified with MRI

Rudwaleit M et al. Ann Rheum Dis 2009;68:777-783
Rudwaleit M et al. Ann Rheum Dis 2011;70:25-31



ASAS Modification of the Berlin Algorithm* for Diagnosing Axial Spondyloarthritis

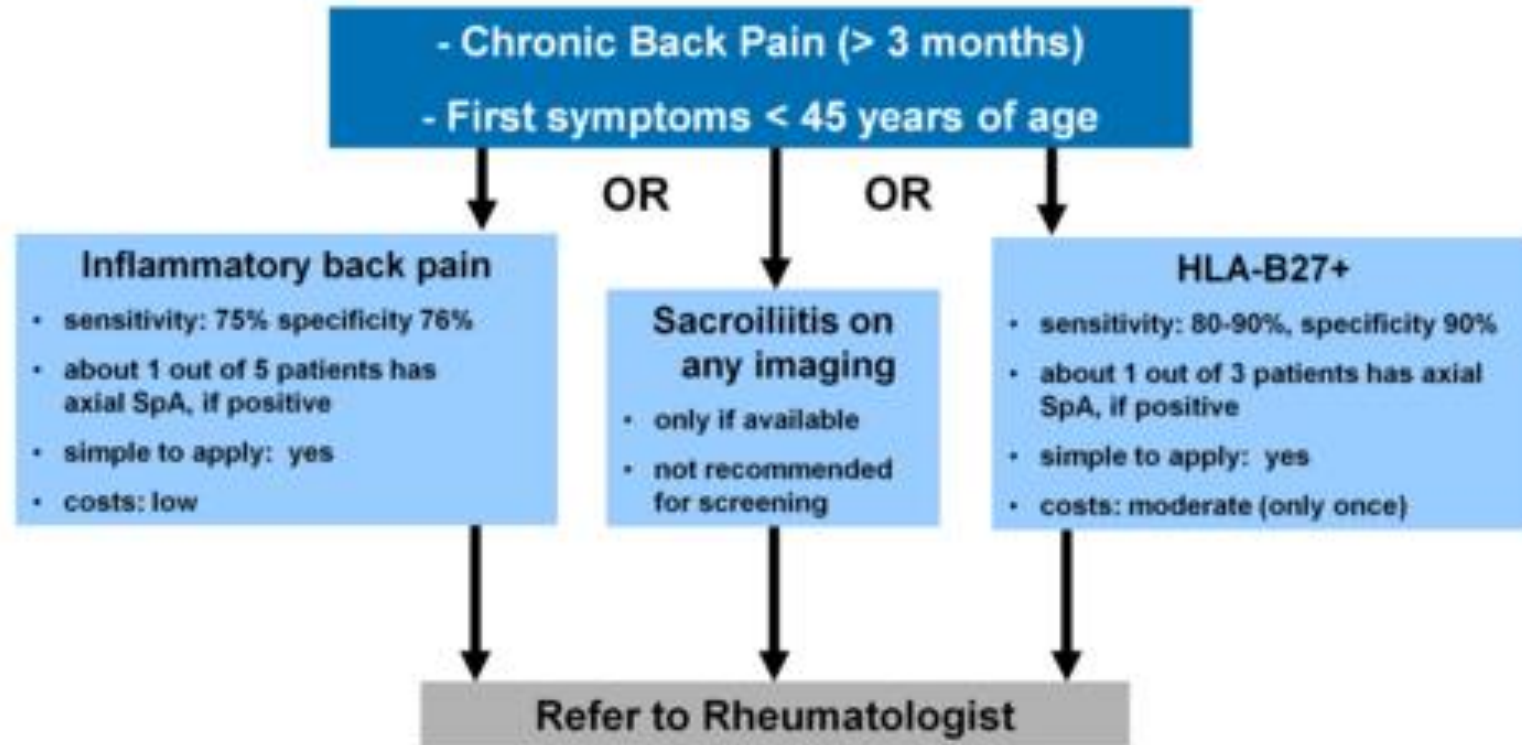


Adapted from: van den Berg R et al. Ann Rheum Dis 2013;72:1646-53 (with permission)

*Rudwaleit M et al. Ann Rheum Dis 2004;63:535-43



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

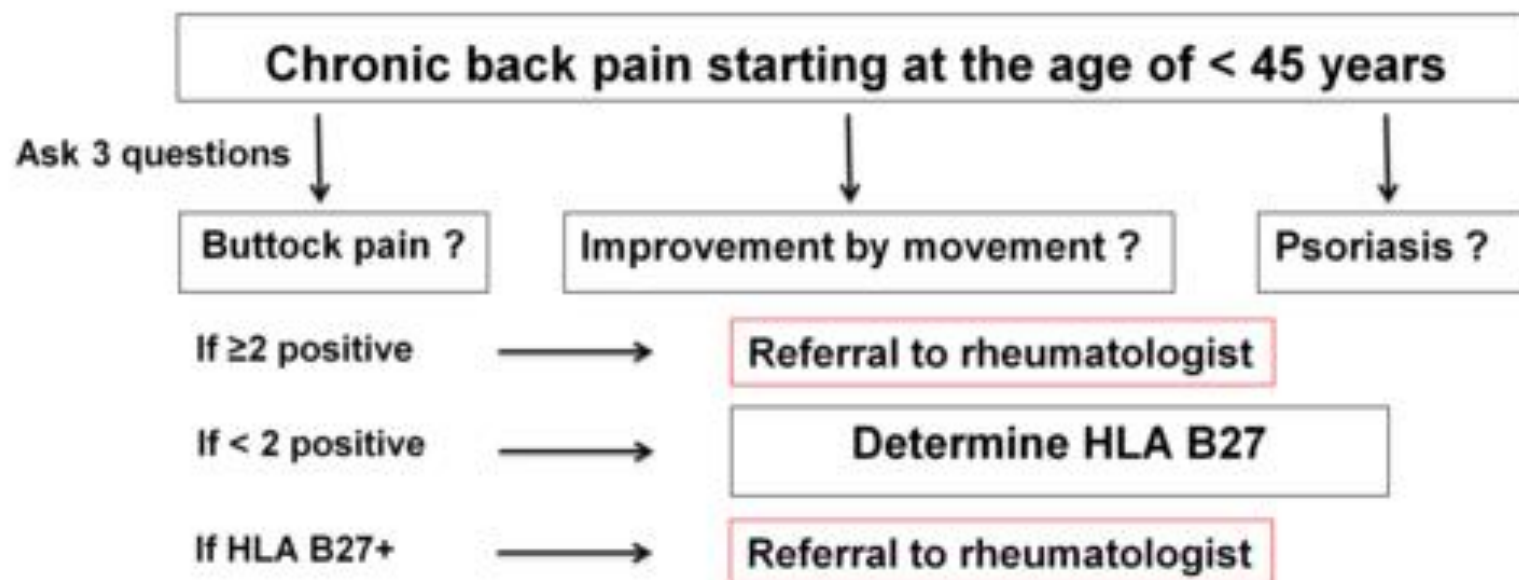


Adapted from Sieper J et al. Ann Rheum Dis 2005;64:659-63



A Possible 2-Step Referral Strategy

Primary care setting



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

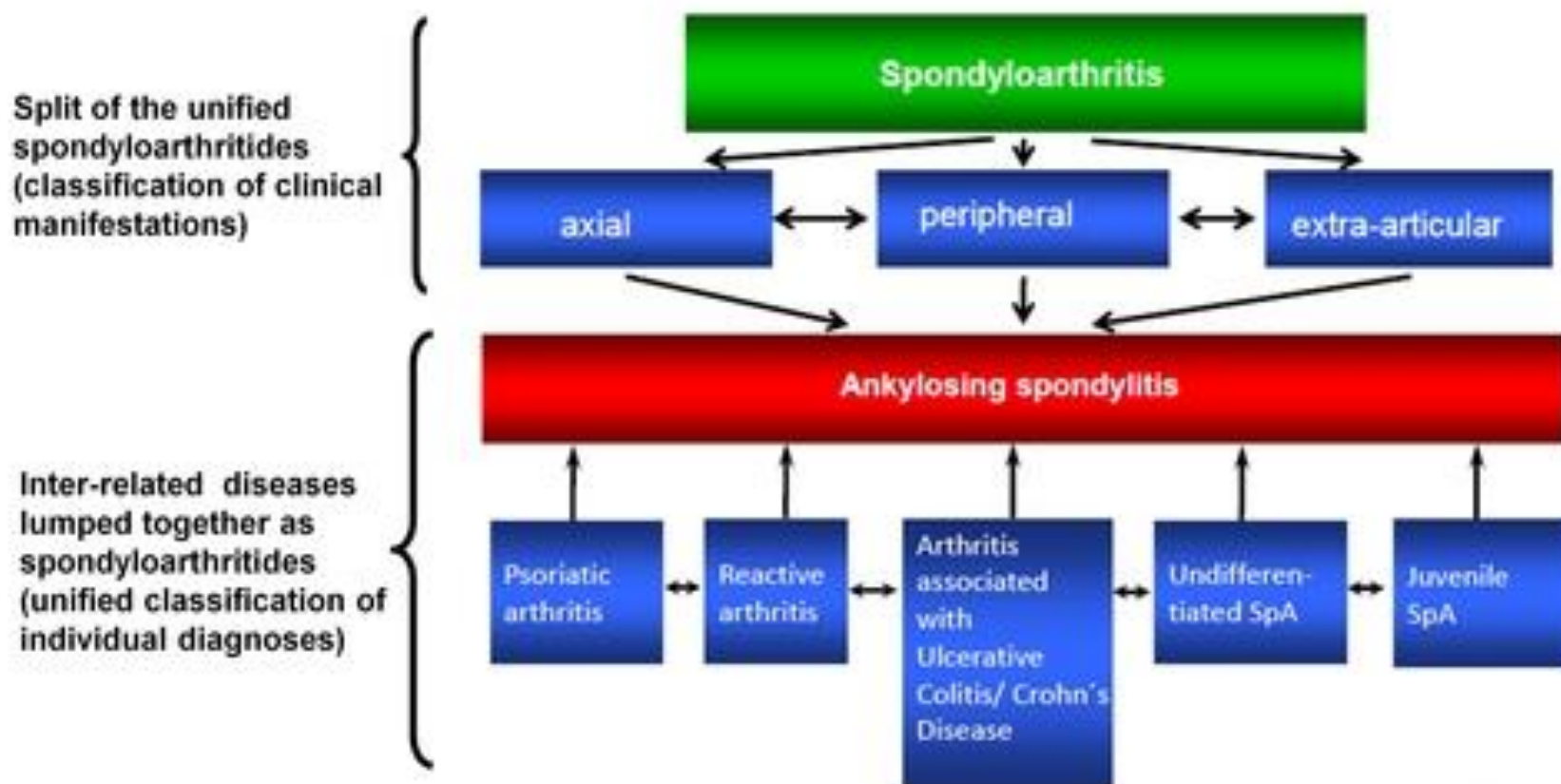
Sensitivity 80.4%
Specificity 75.4%

ASAS Endorsed Recommendations for Early Referral of Patients Suspected for Axial Spondyloarthritis

Patients with **chronic back pain (duration ≥ 3 months)** and **back pain onset before 45 years of age** should be referred to a rheumatologist if at least one of the following parameters is present:

- Inflammatory back pain;
- HLA-B27 positivity;
- Sacroiliitis on imaging if available (X-rays or magnetic resonance imaging);
- Peripheral manifestations (arthritis, enthesitis, dactylitis);
- Extra-articular manifestations (psoriasis, inflammatory bowel disease, uveitis);
- Positive family history for SpA;
- Good response to non-steroidal anti-inflammatory drugs;
- Elevated acute phase reactants.

Inter-Relationship between the ASAS Classification Criteria and the Disorders Lumped Together in the Unified Concept of SpA



Adapted from: Zeidler H and Amor B. Ann Rheum Dis 2011;70:1-3 (with permission)

**It is time to modify the ASAS
criteria?**