’ Radiological evolution in Axial SpA: what is of clinical importance and the effect of biologics'

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Agenda

- The radiographic progression of ankylosing spondylitis
  - SIJs
  - Spine
- Predicting radiographic progression
- Clinical importance of progression
- Can we prevent progression with biologics

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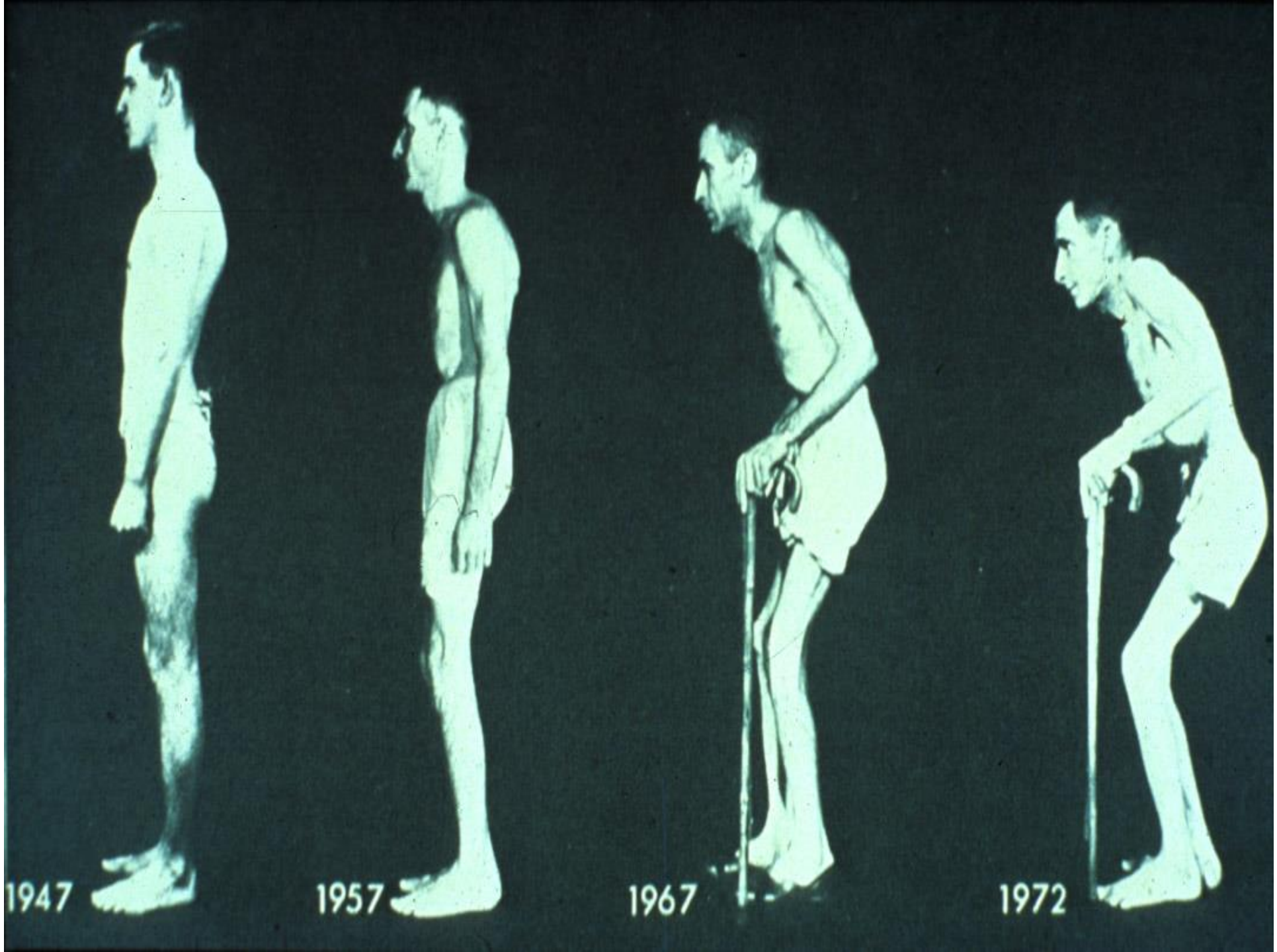
1947
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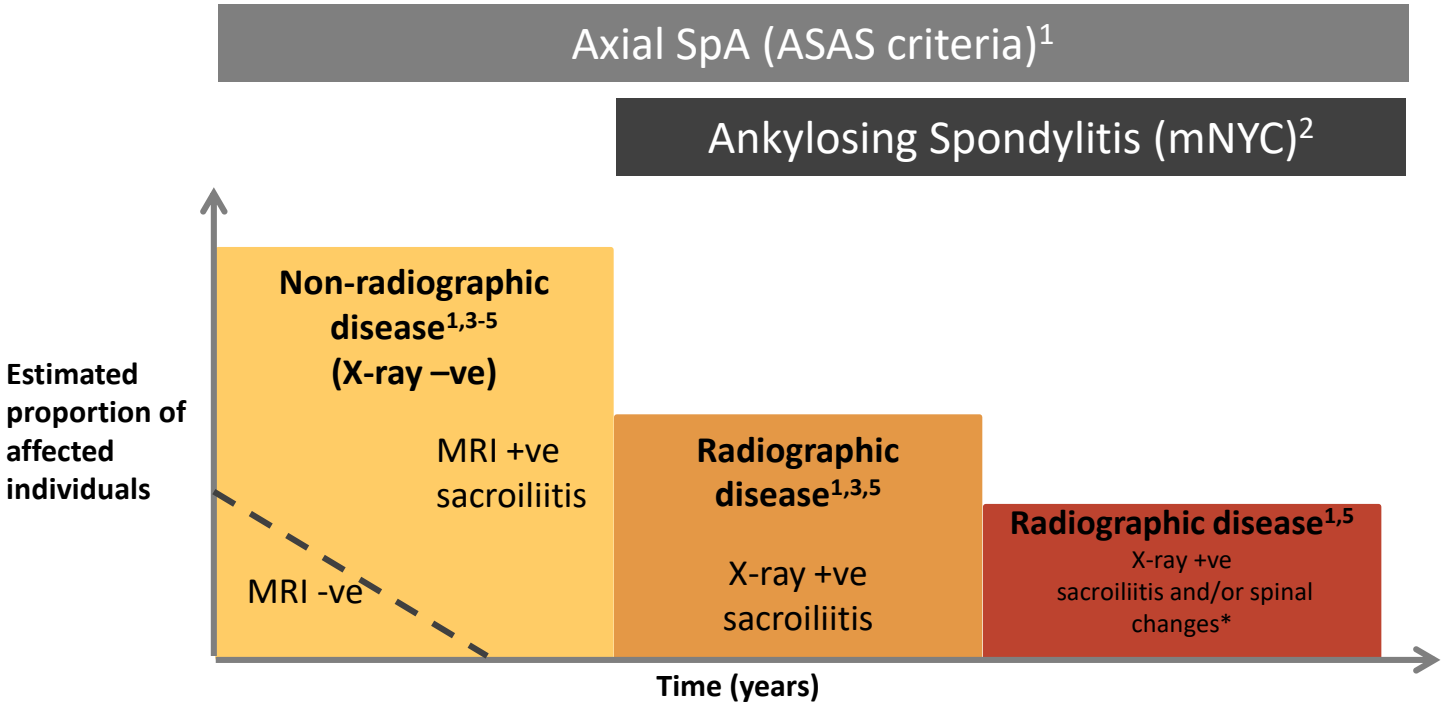
Axial SpA spectrum of disease

Patients with chronic back pain ≥3months and aged <45 years under



*Radiographic evidence of spinal changes including i.e., syndesmophytes, fusion or posterior element involvement.

1. Rudwaleit M, et al. *Arthritis Rheum* 2005;52:1000-8. 2. van der Linden S, et al. *Arthritis Rheum* 1984;27:361–8. 3. Rudwaleit M et al. *Ann Rheum Dis* 2009;68 777-83; 4. Marzo-Ortega H, et al. *Ann Rheum Dis* 2009;68:1721-2; 5. Heuft-Dorenbosch L, et al. *Ann Rheum Dis* 2007;66:92-8.

Radiographic methods to assess progression

- MRI
- Xray - hip/spine

Endpoints in radiological progression

- Fulfill criteria eg mNYC
- Develop syndesmophytes
- Scores eg mSASSS or sacroiliac joint grading

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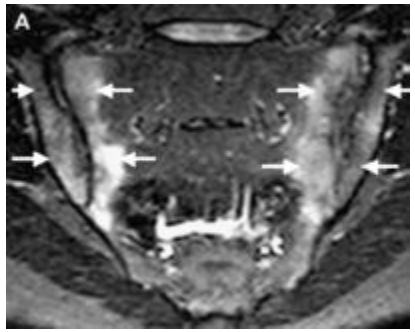
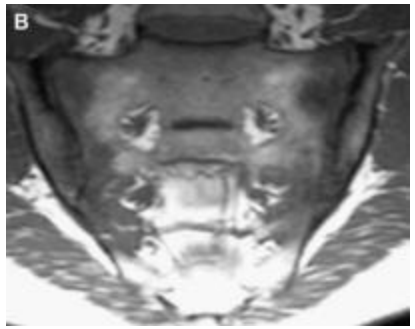
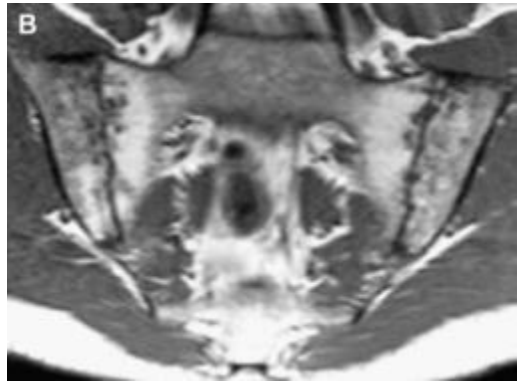
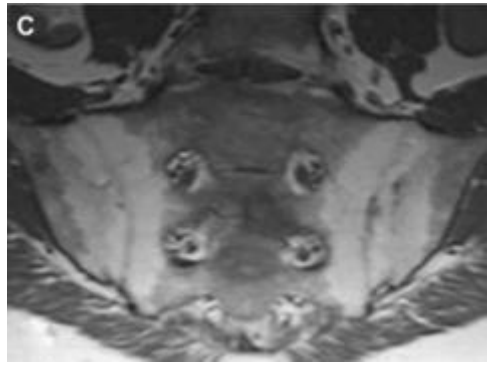
Progression in the SI joints (MRI)





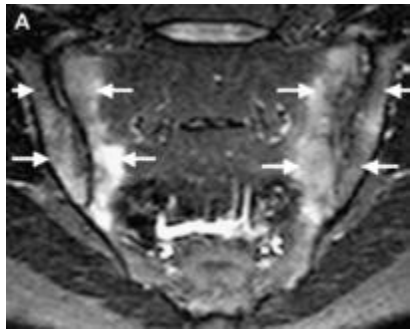


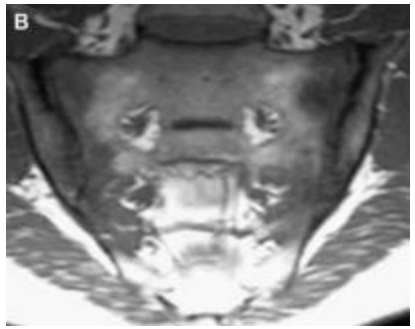


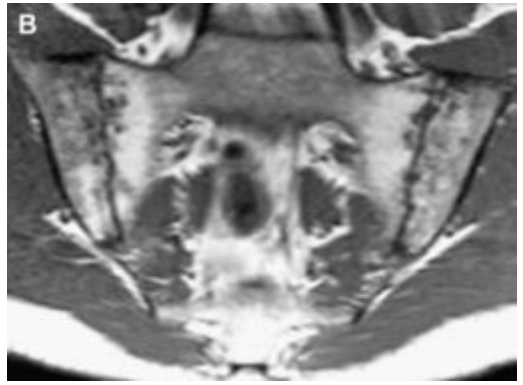
SIJs

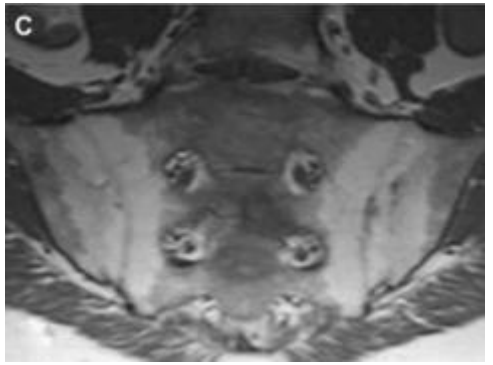
MRI → MRI → Xrays → Xrays

Progression in the SI joints (Xray)





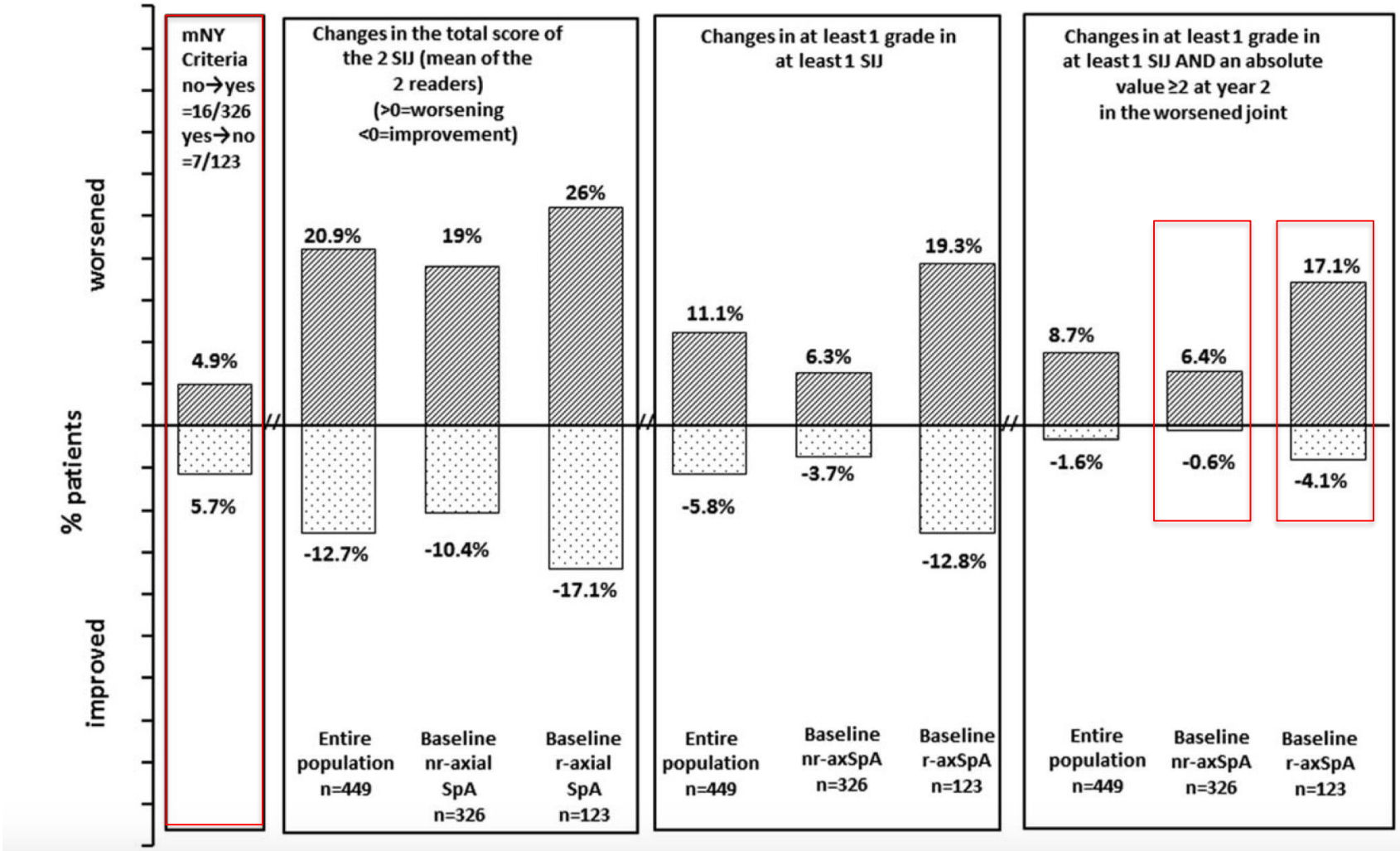




SIJs

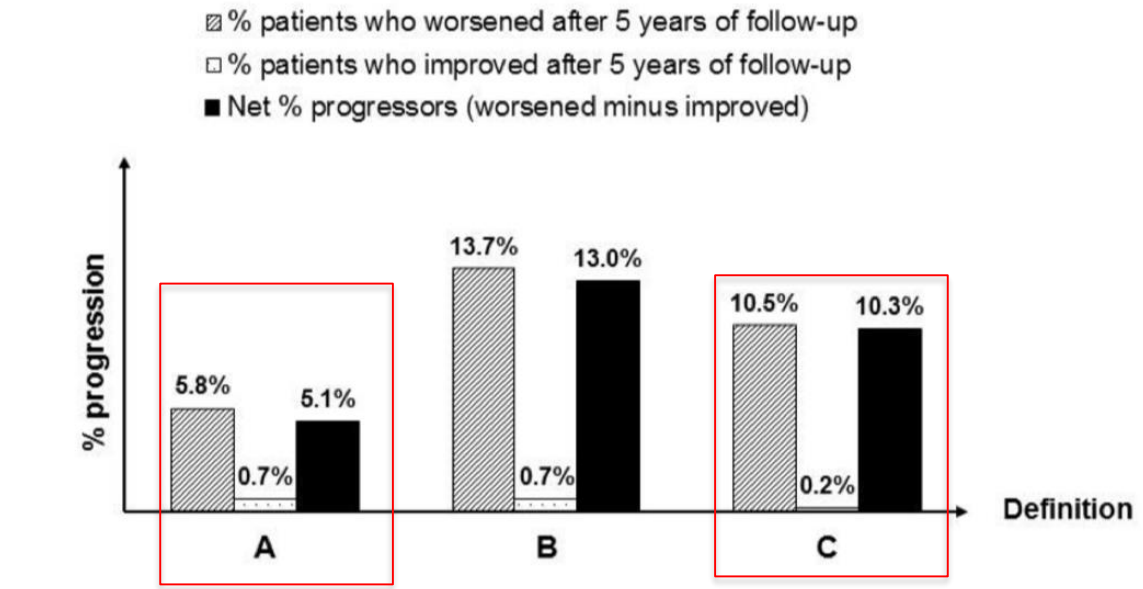
MRI → MRI → Xrays → Xrays

Radiographic progression at the SIJs over 2 years

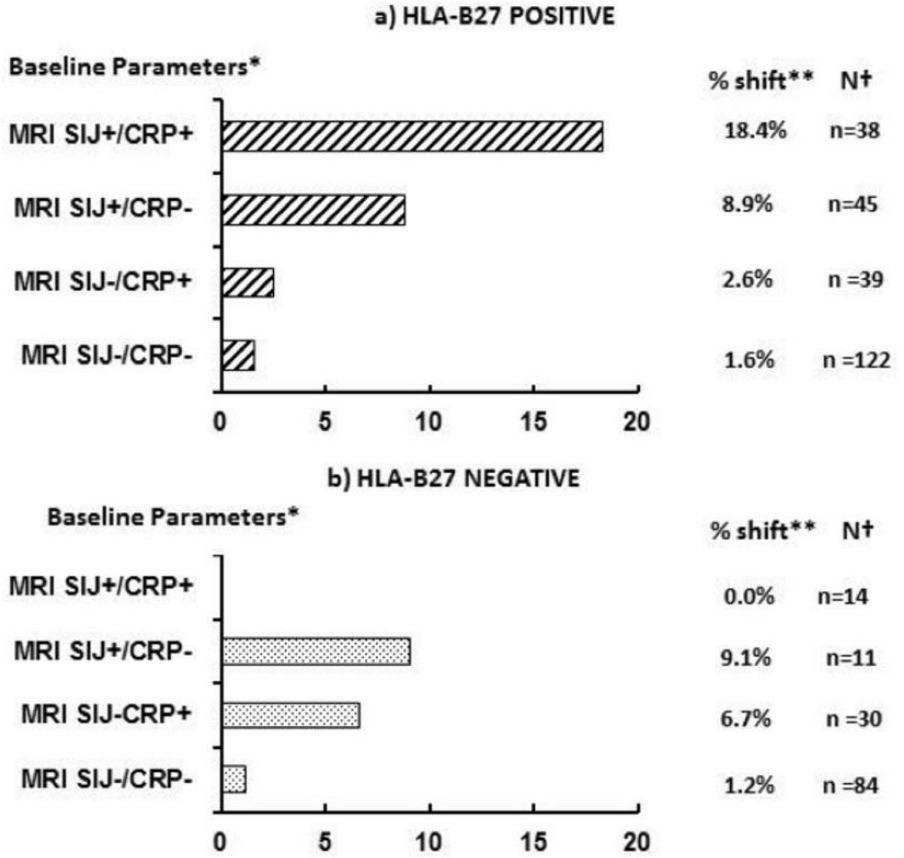


Dougados et al. Rate and Predisposing Factors for Sacroiliac Joint Radiographic Progression After a Two-Year Follow-up Period in Recent-Onset Spondyloarthritis. ARTHRITIS & RHEUMATOLOGY Vol. 68, No. 8, August 2016, pp 1904–1913

Radiographic progression at the SIJs over 5 years



A = Switch from nr to r-axSpA according to the mNY criteria (worsened) *minus* switch from r to nr-axSpA (N=416)
B = Change in at least one grade in at least one SIJ (N=408)
C = Change in at least one grade in at least one SIJ and a final (at year 5) absolute value of at least 2 in the worsened joint (worsened) *minus* change in at least one grade in at least 1 SIJ and a baseline (year 0) absolute value of at least 2 in the improved joint (N=408)



Dougados et al. Sacroiliac radiographic progression in recent onset axial spondyloarthritis: the 5-year data of the DESIR cohort. Ann Rheum Dis 2017;76:1823–1828. doi:10.1136/annrheumdis-2017-211596

Rates and predictors of radiographic sacroiliitis progression after central reading in patients with axial spondyloarthritis from the ASAS cohort: a 5-year follow-up study

Mikhail Protopopov[1], Fabian Proft[1], Alexandre Sepriano[2,3], Robert Landewé[4,5], Désirée van der Heijde[2], Joachim Sieper[1], Martin Rudwaleit[6], Denis Poddubnyy[1,7]

[1]Charité - Universitätsmedizin Berlin, Germany [2]Leiden University Medical Center, the Netherlands, [3]NOVA Medical School, Universidade Nova de Lisboa, Portugal, [4]Amsterdam Rheumatology & Clinical Immunology Center, the Netherlands, [5]Zuyderland Medical Center, Heerlen, the Netherlands, [6]Klinikum Bielefeld Rosenhöhe, Bielefeld, Germany, [7]German Rheumatism Research Centre, Berlin, Germany.

Table 1. Baseline characteristics of included patients with axSpA.

	All patients with axSpA from the ASAS Cohort (n=444)	Patients with axSpA and X-Rays at baseline (n=205)	Patients with axSpA and X-rays at baseline and follow-up (n=106)
Male sex	235 (52.9%)	105 (51,2%)	60 (56.6%)
Age, years	34.6 ± 11.3	32.0 ± 10.6	32.1 ± 11.1
Symptom duration, years	6.2 ± 7.8	6.6 ± 8.0	6.8 ± 8.0
HLA-B27 positive	288 (64.9%)	137 (66.8%)	72 (67.9%)
Radiographic sacroiliitis fulfilling the mNY Criteria*	126 (28.4%)	45 (22.0%)	22 (20.8%)
Syndesmophytes*	66 (14.9%)	31 (15.1%)	16 (15.1%)

** According to local assessment*

Figure 1. Results of central reading of pelvic radiographs

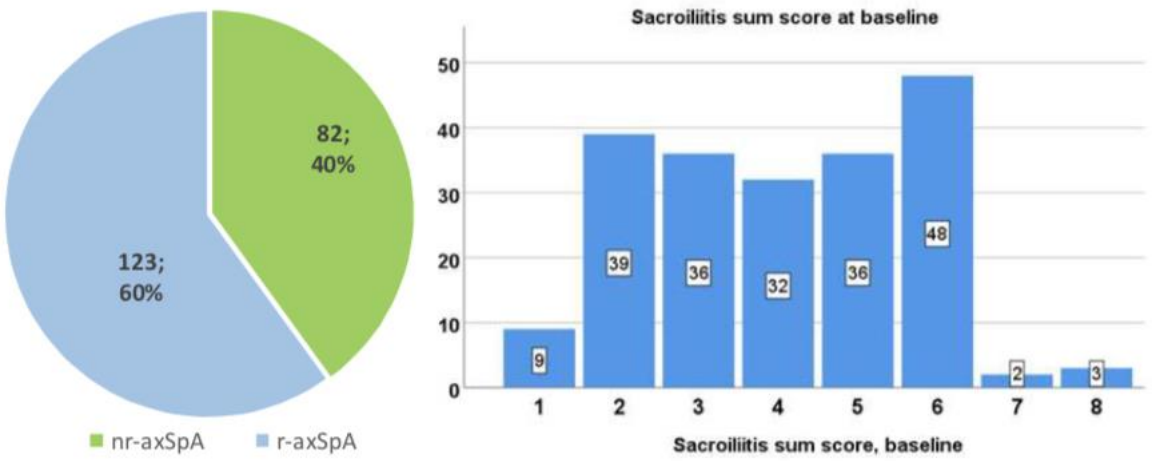


Figure 2. Progression of radiographic sacroiliitis

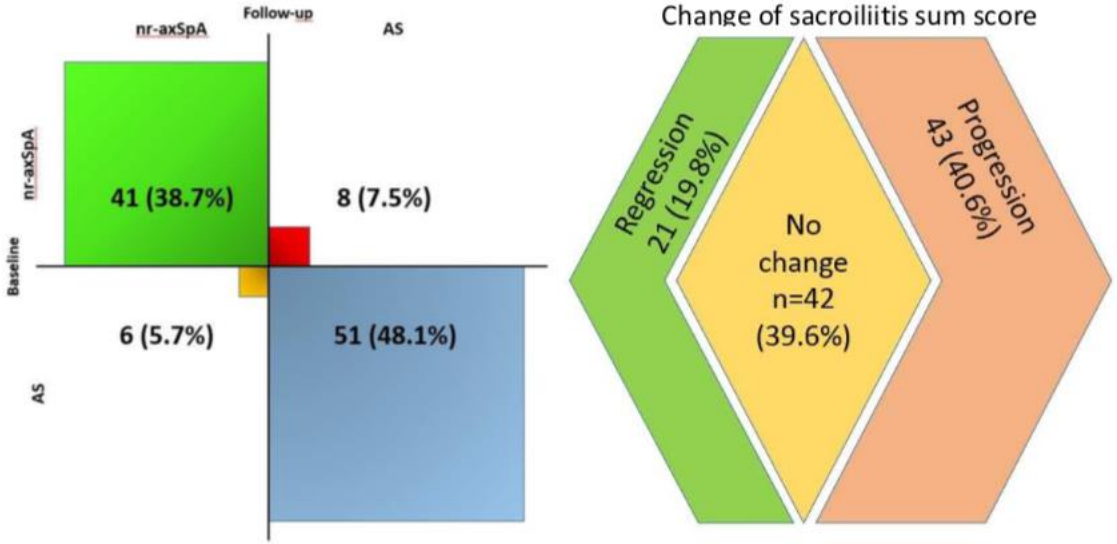


Table 2. Association of baseline demographic and SpA-related parameters with classification as r-axSpA at the follow-up visit.

Parameter at baseline	Univariable analysis OR (95% CI)	Multivariable model 1 OR (95% CI)	Multivariable model 2 OR (95% CI)
Male sex	**2.84 (1.28 to 6.30)**	1.55 (0.46 to 5.19)	1.22 (0.35 to 4.24)
Age at baseline, years	**0.95 (0.91 to 0.98)**	**0.93 (0.86 to 0.99)**	**0.92 (0.85 to 0.94)**
Symptom duration, years	1.00 (0.95 to 1.05)	-	-
HLA-B27 positivity	**10.03 (3.77 to 26.67)**	**6.22 (1.57 to 24.64)**	**5.71 (1.34 to 24.23)**
Active inflammation on MRI of SIJ	**14.63 (4.71 to 45.40)**	**7.68 (2.16 to 27.34)**	-
Structural changes on MRI of SIJ	**10.77 (3.41 to 34.02)**	-	**7.58 (2.04 to 28.20)**
Elevated CRP (local lab)	0.99 (0.46 to 2.16)	-	-

Summary - SIJ progression

- SIJ progression is slow and occurs in the minority
- Net progression is variable at 5 years
- Predictors for SIJ progression include active inflammation/ structural changes on MRI SIJs, HLA B27 positivity, older age at baseline and smoking

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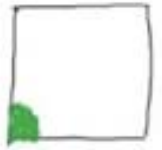
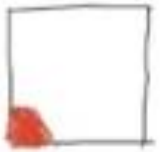
Progression in the spine (MRI)



Corner inflammatory lesions



Fatty Romanus Lesions

Syndesmophytes

Baraliakos X, Heldmann F, Callhoff J et al. Which spinal lesions are associated with new bone formation in patients with ankylosing spondylitis treated with anti-TNF agents? A long-term observational study using MRI and conventional radiography. Ann Rheum Dis 2014;73:1819 25.

Maksymowych WP, Morency N, Conner-Spady B, Lambert RG. Suppression of inflammation and effects on new bone formation in ankylosing spondylitis: evidence for a window of opportunity in disease modification. Ann Rheum Dis 2013;72:23 8.

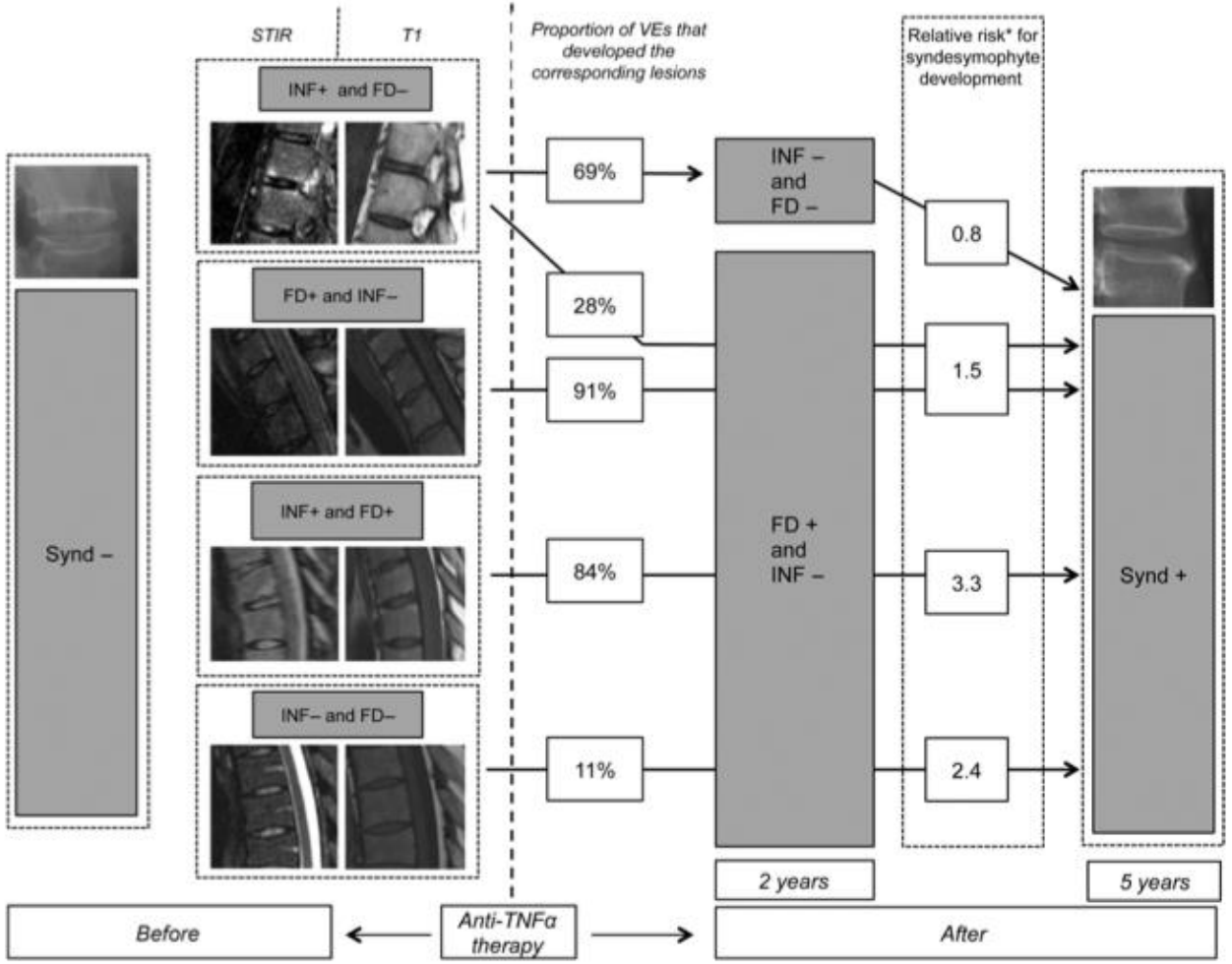
Machado PM, Baraliakos X, van der Heijde D, Braun J, Landewe´ R. MRI vertebral corner inflammation followed by fat deposition is the strongest contributor to the development of new bone at the same vertebral corner: a multilevel longitudinal analysis in patients with ankylosing spondylitis. Ann Rheum Dis 2016;75:1486 93.

Which spinal lesions are associated with new bone formation in patients with ankylosing spondylitis treated with anti-TNF agents?

Table 1 Baseline characteristics of the 73 patients who were included in this MRI substudy

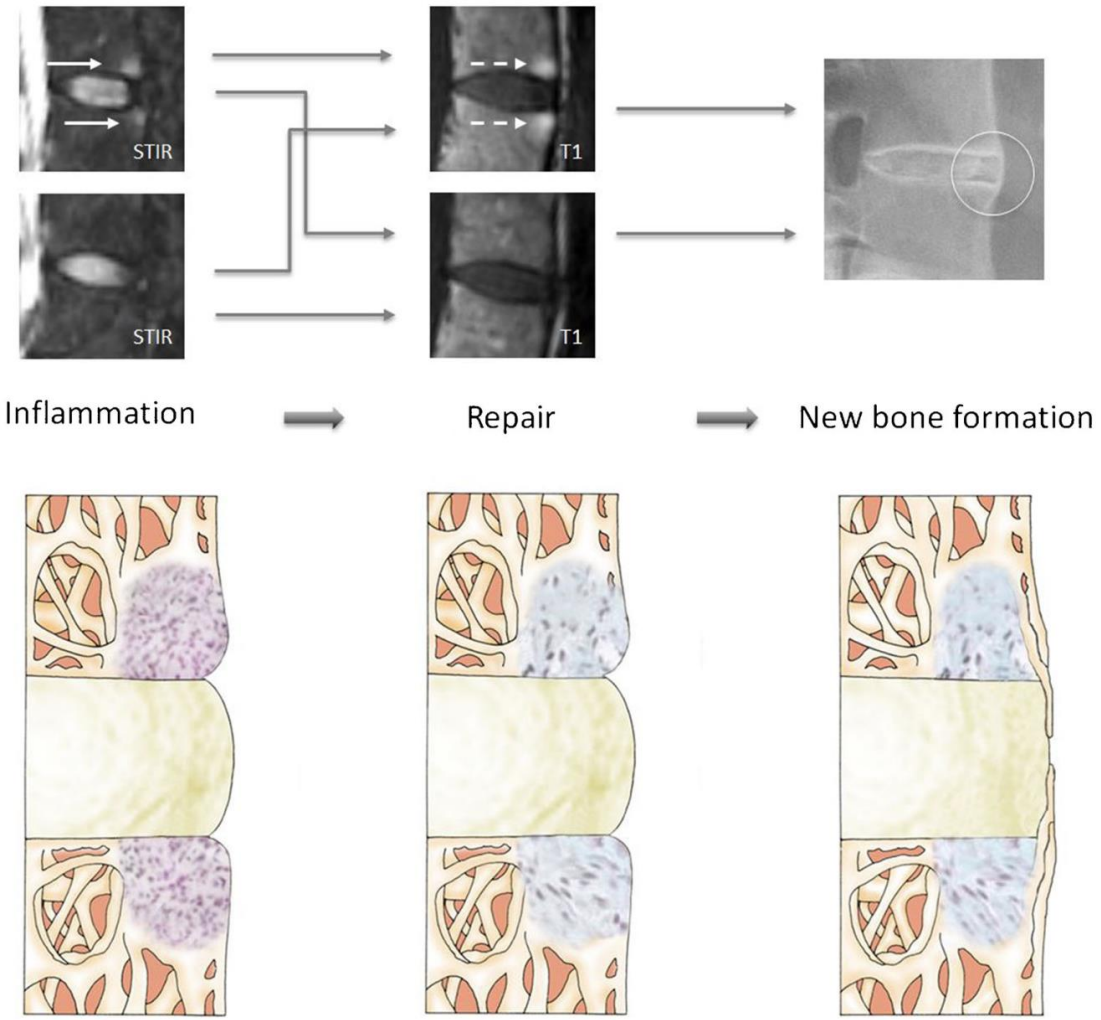
Baseline parameter	Value
Age (years), mean±SD	40.5±10.5
BASDAI (0–10 units), mean±SD	6.5±1.4
BASFI (0–10 units), mean±SD	5.9±1.6
BASMI (0–10 units), mean±SD	4.1±1.7
CRP (mg/dL), mean±SD	2.9±2.3
Disease duration (years), mean±SD	10±8.4
HLA B27+ (%)	61 (83.6%)
Male (%)	63 (86.3%)

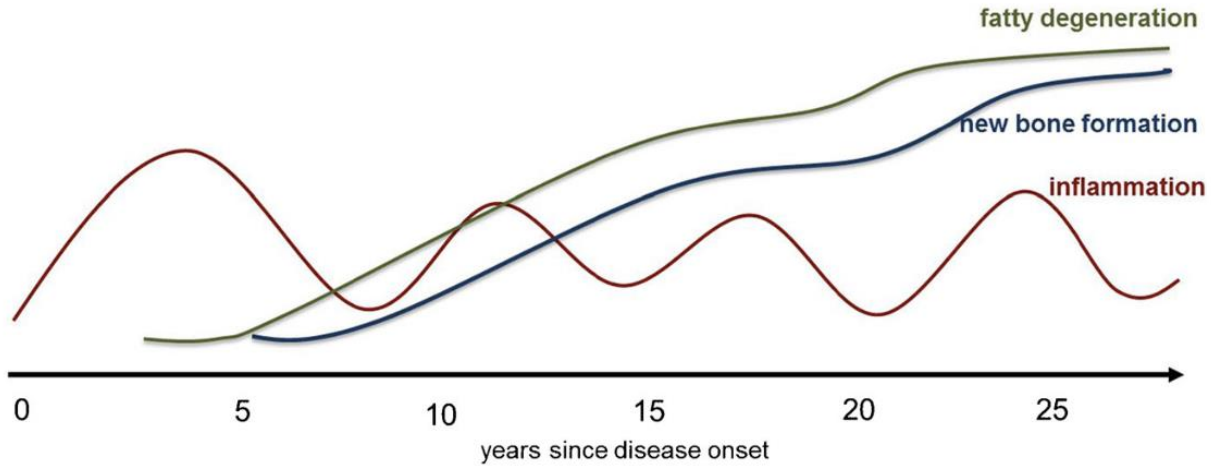
There was no difference in comparison with patients who were initially included in AS Study for the Evaluation of Recombinant Infliximab Therapy (ASSERT)[24] and with all patients who participated in European AS Infliximab Cohort.[25] The normal range of CRP was <0.5 mg/dL.
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Function Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; CRP, C-reactive protein; HLA, human leukocyte antigen.



Baraliakos et al. Which spinal lesions are associated with new bone formation in patients with ankylosing spondylitis treated with anti-TNF agents? A long-term observational study using MRI and conventional radiography.. Ann Rheum Dis 2014;73:1819–1825

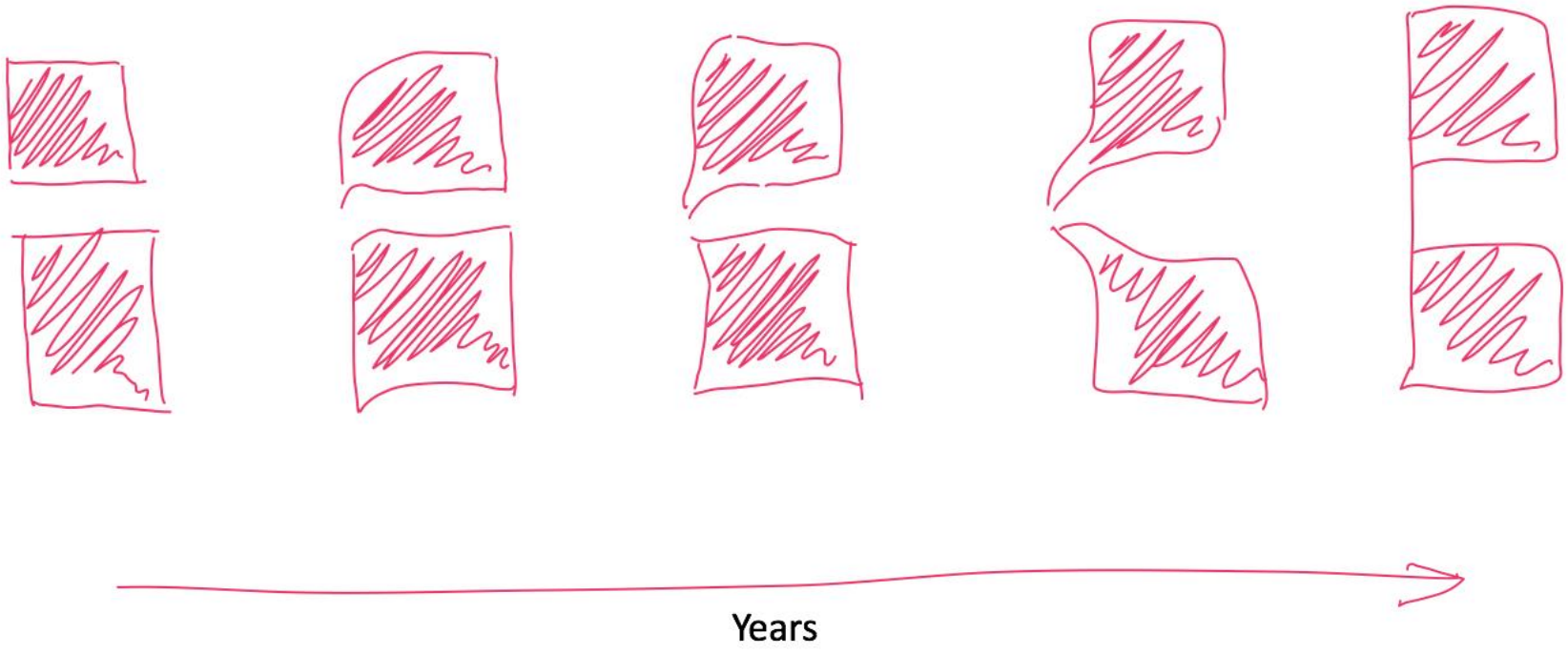
Proposed mechanism of bone formation





Poddubnyy et al. Mechanism of New Bone Formation in Axial Spondyloarthritis. Curr Rheumatol Rep (2017) 19:55 DOI 10.1007/s11926-017-0681-5

Radiographic Progression

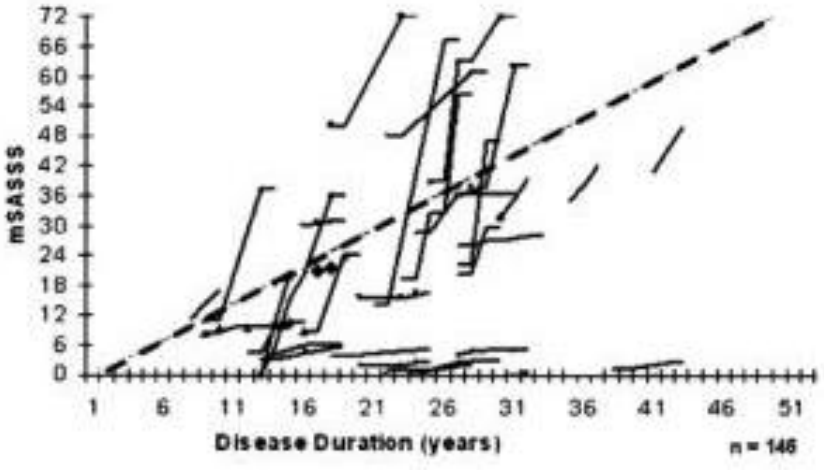


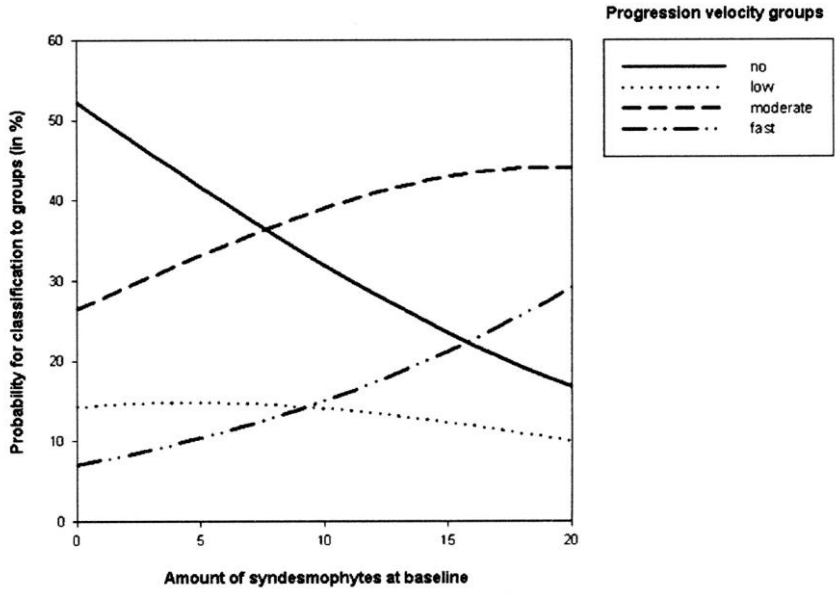
Spine

MRI → MRI → Xrays → Xrays

GESPIC – Radiographic spinal progression

N=146	
Mean age	54.2+/-12.3
Time since diagnosis	22.6+/-12.1yrs
Male	81%
HLA B27 positive	78%
Mean BASDAI	4.4+/-1.9
Mean BASFI	3.8+/-2.6
Currently taking NSAID	80.2%





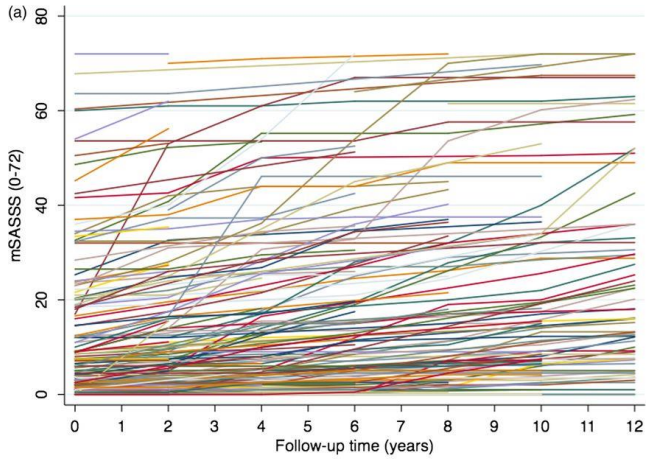
Definition of Progression	mSASSS Change	Development of New Syndesmophytes
Slow	< 2 mSASSS units within 2 yrs	Not more than 1 syndesmophyte within 2 yrs
Moderate	2.0–5.0 mSASSS units within 2 yrs	Not more than 2 syndesmophytes within 2 yrs
Fast	> 5 mSASSS units within 2 yrs	More than 2 syndesmophytes within 2 yrs

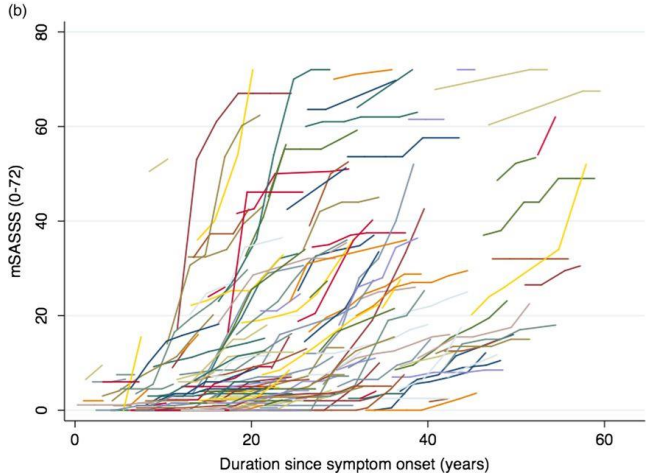
mSASSS 1.3+/-2.5 units/yr

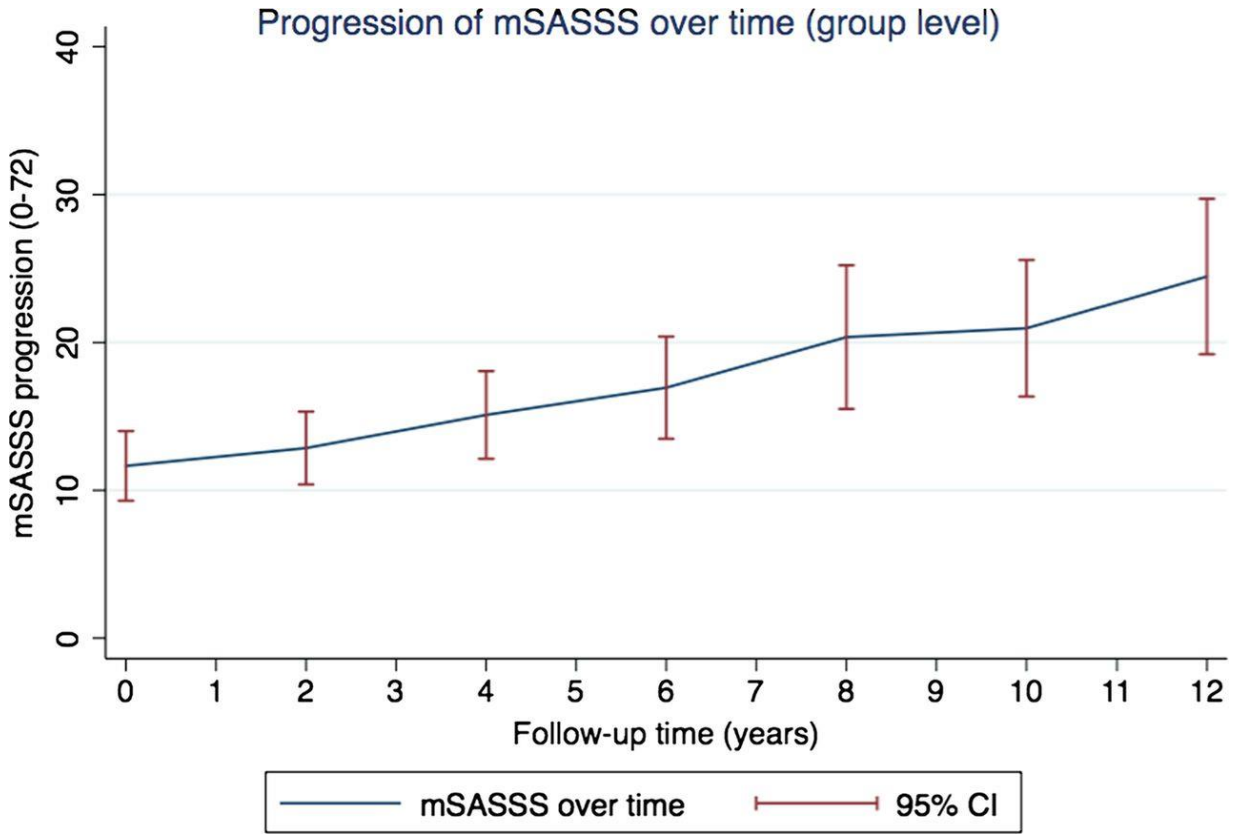
Spine

MRI → MRI → Xrays → Xrays

Baraliakos, et al: Radiographic progression in AS The Journal of Rheumatology 2009; 36:5







Spinal radiographic progression rates from the OASIS cohort

Ramiro et al. Evolution of radiographic damage in ankylosing spondylitis: a 12 year prospective follow-up of the OASIS study. Ann Rheum Dis 2015;74:52–59. doi:10.1136/annrheumdis-2013-204055

Table 2 Progression of radiographic damage over time

Progression*	No of intervals out of all 2 year intervals (n (%)) (n=520)	No of patients during all 2 year intervals (maximum progression)† (n (%)) (n=186)	No of patients from the '12 year completers' during all 2 year intervals (maximum progression)† (n (%)) (n=68)	No of patients during the first 2 year interval (Y0–Y2) (n (%)) (n=164)
0 mSASSS units	204 (39)	45 (24)	12 (18)	75 (46)
>0 and <1 mSASSS units‡	0 (0)	8 (4)	1 (1)	11 (7)
≥1 mSASSS unit	282 (54)	133 (72)	54 (79)	78 (48)
≥2 mSASSS units (mean progression)§	152 (29)	86 (46)	39 (57)	36 (22)
≥1 and <3 mSASSS units	161 (31)	60 (32)	21 (31)	20 (12)
≥3 mSASSS units	121 (23)	73 (39)	33 (49)	42 (26)
≥3 and <5 mSASSS units	58 (11)	32 (17)	12 (18)	16 (10)
≥5 mSASSS units	63 (12)	41 (22)	21 (31)	41 (25)

*Categories of progression are not mutually exclusive.
†Number and proportion of patients whose maximum 2 year progression score, during follow-up (up to 12 years), met the criterion of each of the rows.
‡This category of progression existed because of imputations, which made some status scores, and hence progression scores, have decimal values.
§Mean progression taking all 2 year intervals into account.
mSASSS, modified Stoke Ankylosing Spondylitis Spine Score.

Spinal radiographic progression rates from the OASIS cohort

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Spinal radiographic progression - summary

	mSASSS prog	Time	New syndesmophytes
OASIS[1]	2.5+/-4.2	2 years	33%
	4.2+/-6.4	4 years	48%
GESPIC[2]	0.95+/-2.78	Over 1 year	11%
GESPIC[3]	1.3+/-2.5	Over 1 year	

Further points
Radiographic progression is highly variable at the patient level
Baseline radiographic progression is a marker of progression

[1]van Tubergen A, Ramiro S, van der Heijde D, et al. Development of new syndesmophytes and bridges in ankylosing spondylitis and their predictors:a longitudinal study Ann Rheum Dis (2012);71:518

[2] Poddubnyy et al. Baseline radiographic damage, elevated acute phase reactants and cigarette smoking status predict radiographic progression in the spine in early axial SpA. A&R 2011; Epub

[3]Baraliakos, et al: Radiographic progression in AS The Journal of Rheumatology 2009; 36:5

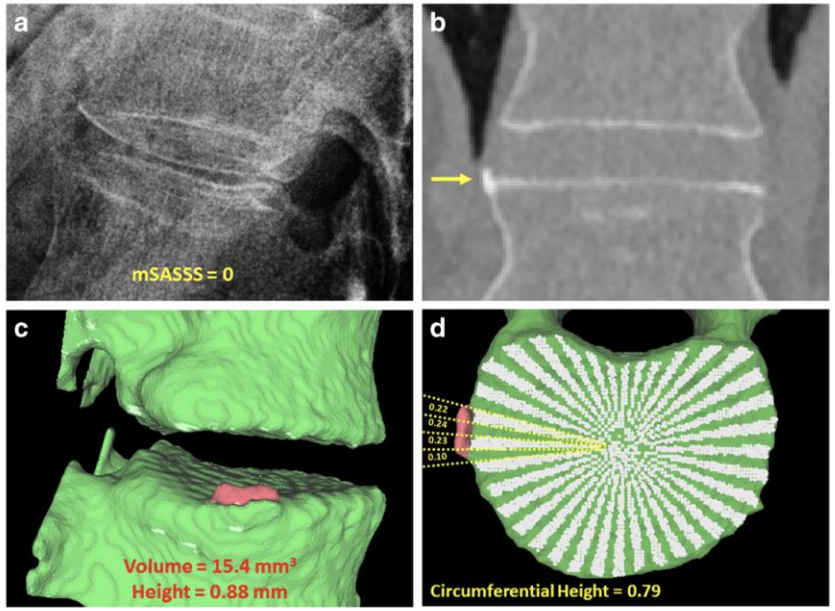


Fig. 1 A T12–L1 vertebral level with a syndesmophyte (arrow) quantitated by CT measures. **a** Lateral view of plain radiograph. **b** CT coronal view. **c** CT quantitation of volume and maximal height. **d** CT quantitation of circumferential height, where the alternating white and green bands mark 5° angular sectors

Table 1 Changes in syndesmophyte volume, maximum height, and circumferential height over 1 and 2 years in patients with ankylosing spondylitis

	Per intervertebral disc space		Per patient	
	Baseline to year 1	Baseline to year 2	Baseline to year 1	Baseline to year 2
Mean increase in volume, mm^3	21.7	50.3	87.0	201.0
% with any volume increase	48	60	73	79
Mean increase in maximum height*	1.4%	2.8%	5.8%	11%
% with any increase in maximum height	22	25	55	61
Mean increase in circumferential height, units (0–72)	0.63	1.14	2.52	4.57
% with any increase in circumferential height	46	55	70	82

*Height of the syndesmophyte normalized to disc height

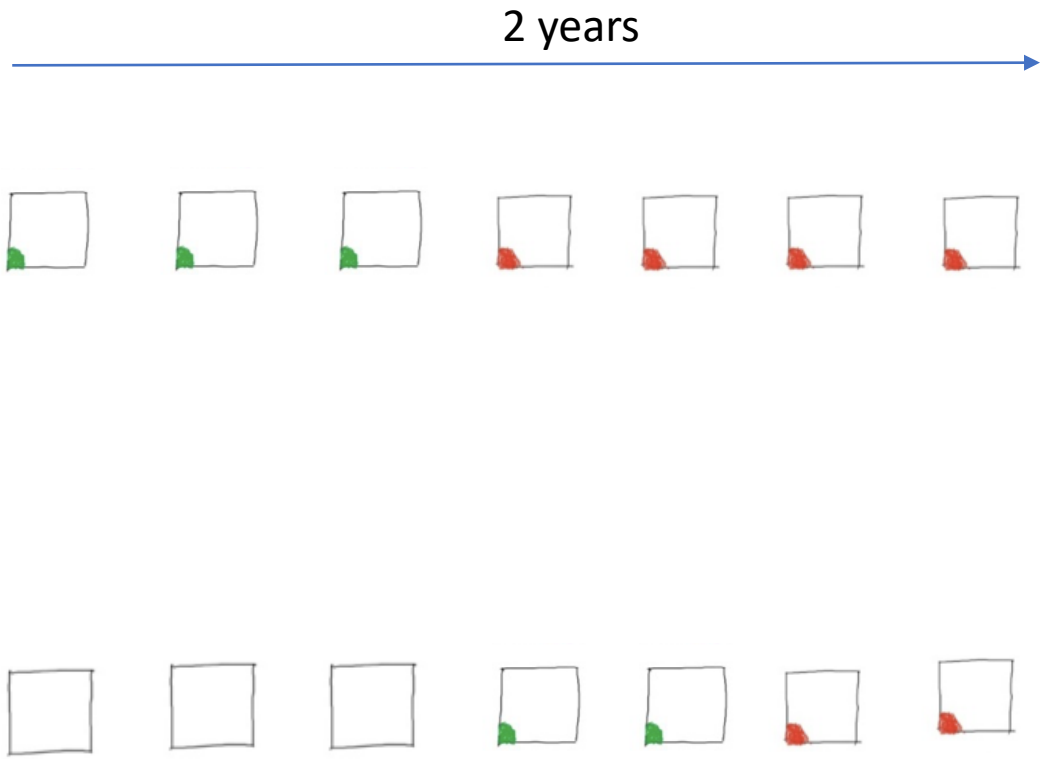
About 70% of patients had detectable growth in syndesmophyte volume or height in 1 year.

Posterolateral regions of the rim were more commonly affected

The use of CT to define volume based progression in AS over 1 year

Ward et al. Better Quantification of Syndesmophyte Growth in Axial Spondyloarthritis . Current Rheumatology Reports (2018) 20:46 https://doi.org/10.1007/s11926-018-0759-8

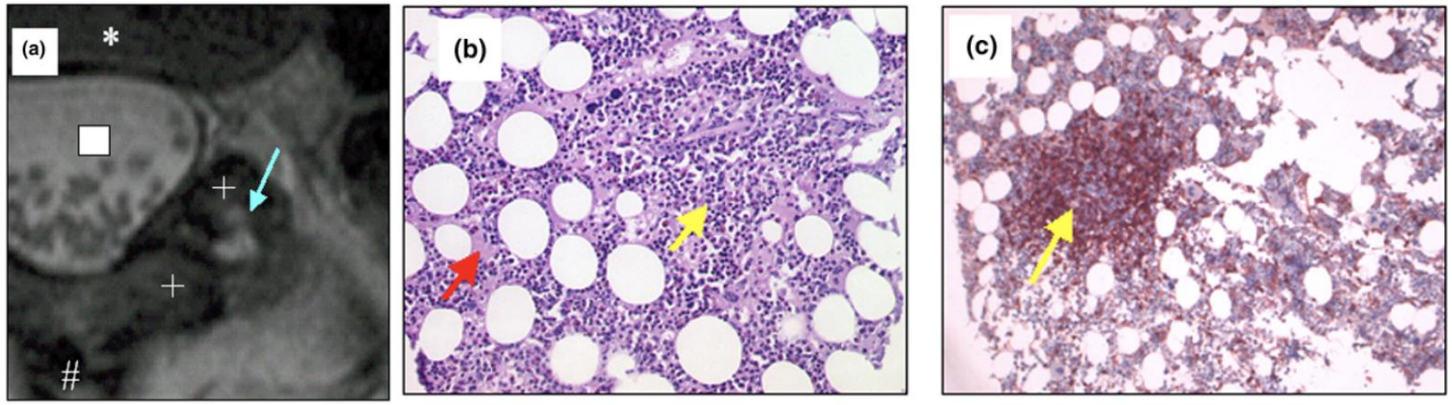
The problem with long imaging intervals….



Could patients with negative MRI scans have inflammation?

MRI positive | Biopsy positive

3



Correlation of histopathological findings and magnetic resonance imaging in the spine of patients with ankylosing spondylitis

Heiner Appel[1†], Christoph Loddenkemper[2†], Zarko Grozdanovic[3], Harald Ebhardt[2], Marc Dreimann[4], Axel Hempfing[4], Harald Stein[2], Peter Metz-Stavenhagen[4], Martin Rudwaleit[1] and Joachim Sieper[1]

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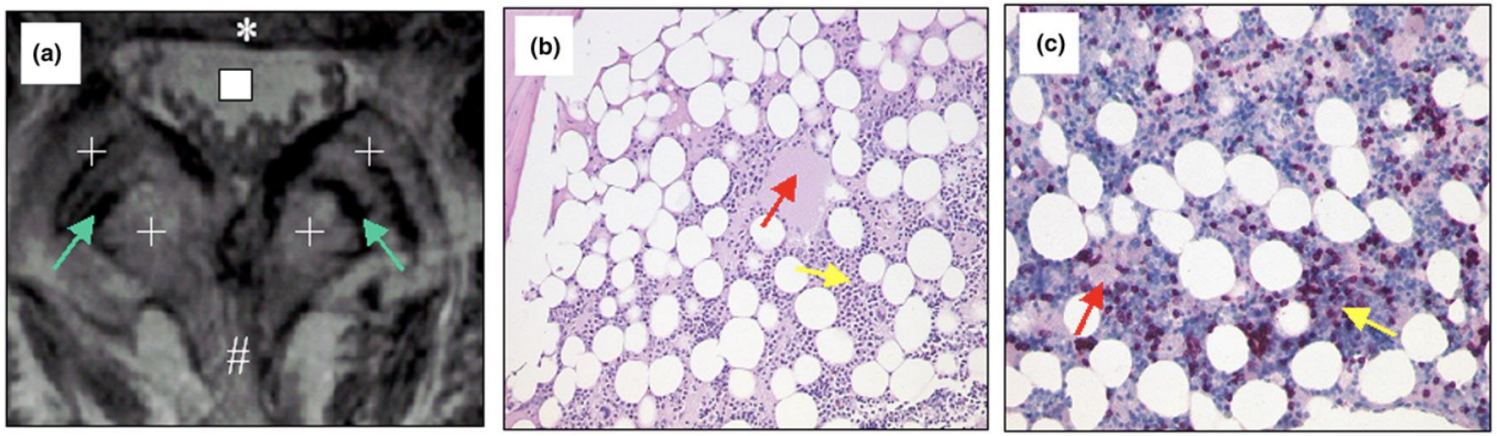


MRI negative | Biopsy positive

Arthritis Research & Therapy 2006, **8**:R143 (doi:10.1186/ar2035)

Challenges with defining radiographic progression in axSpA

- The process of new bone formation in the spine is slow
- mSASSS progression of 1 unit/ year and 10% new syndesmophytes/ year at the cohort level
- Interval between MRI images too long to accurately define what happens in the interim period
- CT looks a promising modality to better understand radiographic progression in axSpA

Agenda

- The radiographic progression of ankylosing spondylitis
  - SIJs
  - Spine
- Predicting radiographic progression
- Clinical importance of progression
- Can we prevent progression with biologics

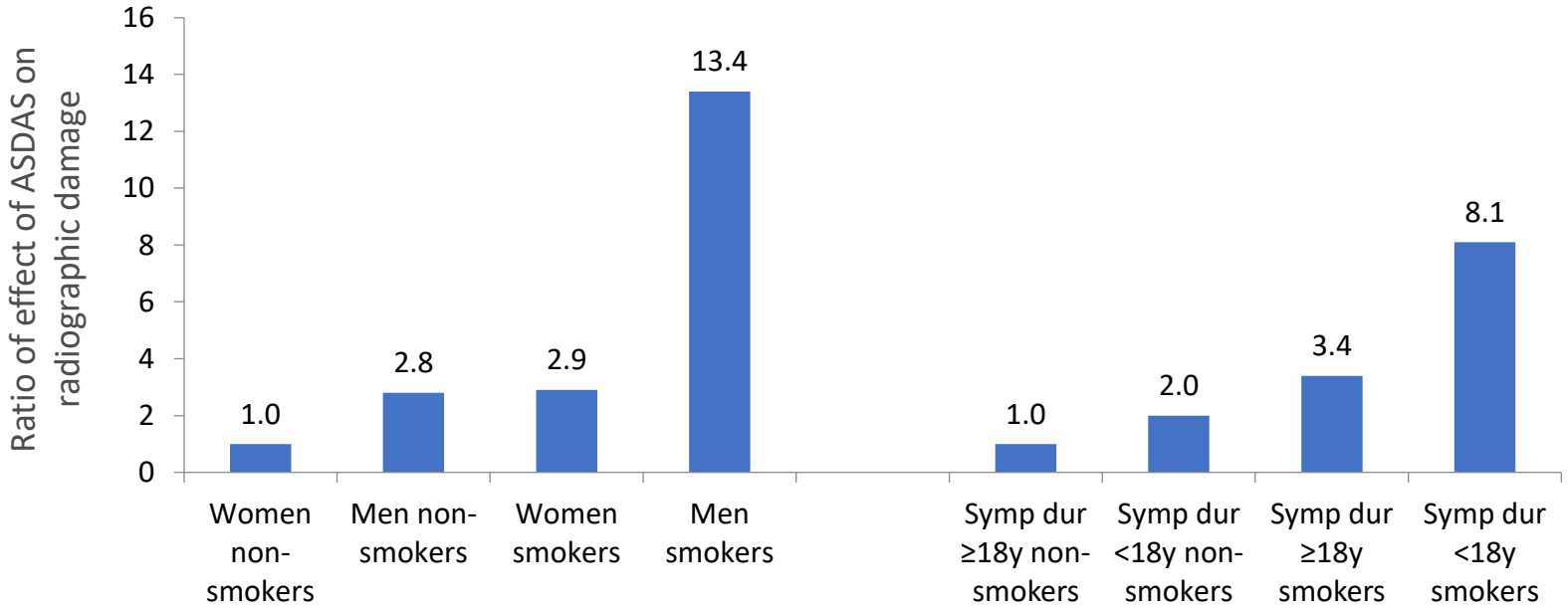
Disease activity in male smokers has a >10-fold amplified effect on radiographic damage in comparison with female non-smokers in ankylosing spondylitis

Method:

- 127 patients from the OASIS study were followed-up for 12 years, with biannual clinical and radiographic assessments
- X-rays were scored according to the mSASSS; disease activity was assessed by the ASDAS-CRP

Results:

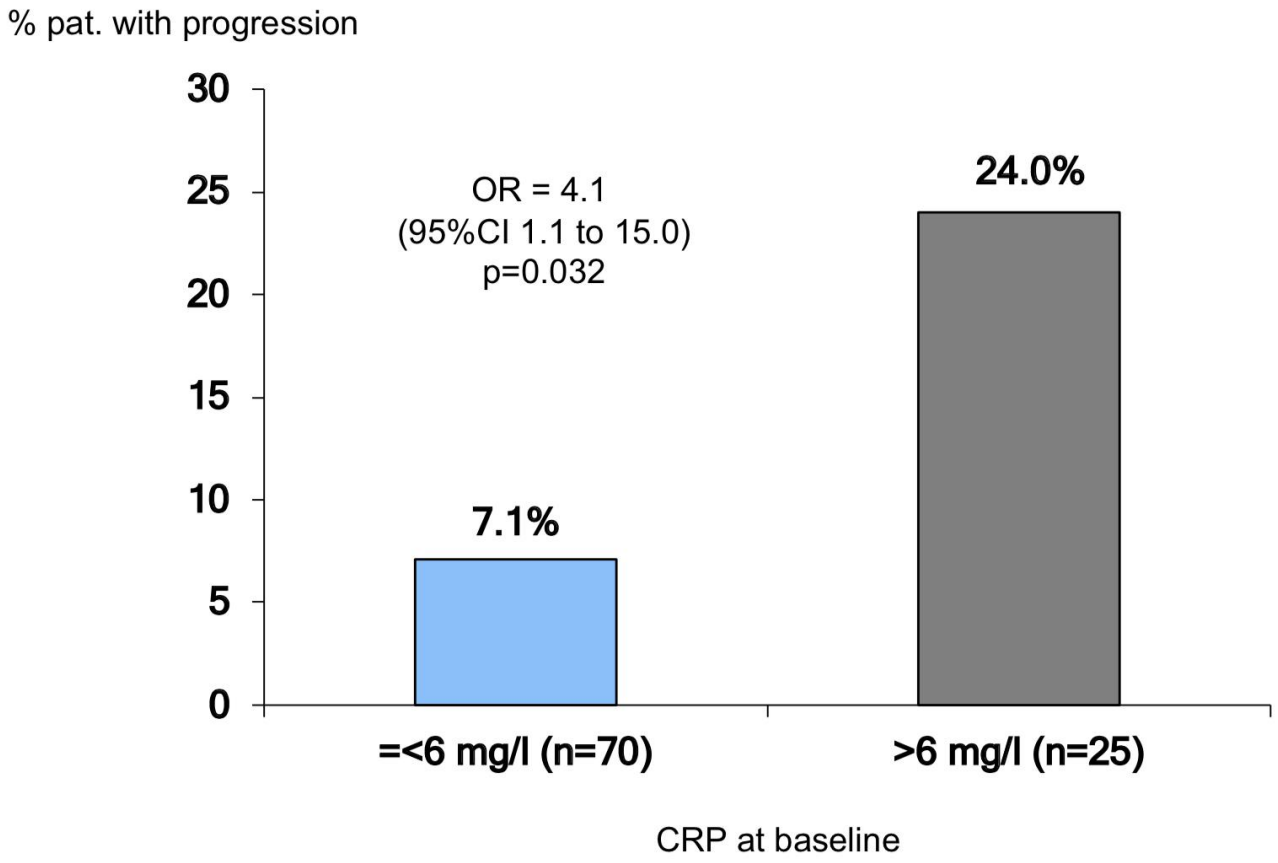
Ratio of the effect of ASDAS on radiographic damage across different comparisons



OASIS, Outcome in AS International Study

Ramiro *et al*. EULAR 2014. Poster THU0103

Radiographic progression is dependent on elevated CRP



Poddubnyy D, et al. Ann Rheum Dis 2011

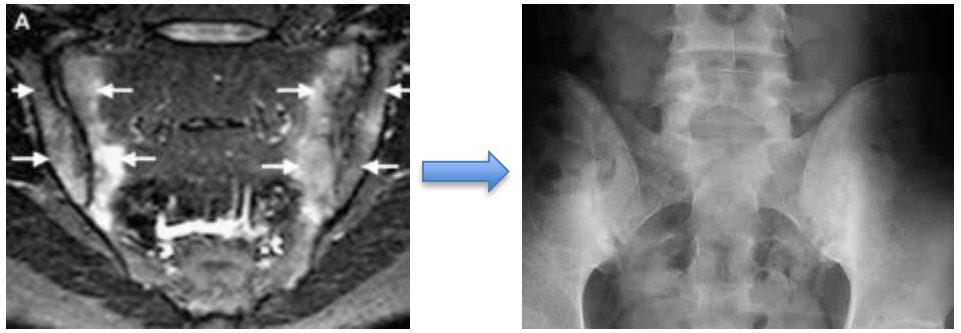
MRI osteitis and progression to radiographic sacroiliitis

50 patients with IBP

42 had MRI sacroiliitis

Mean disease duration
at presentation – 37 weeks

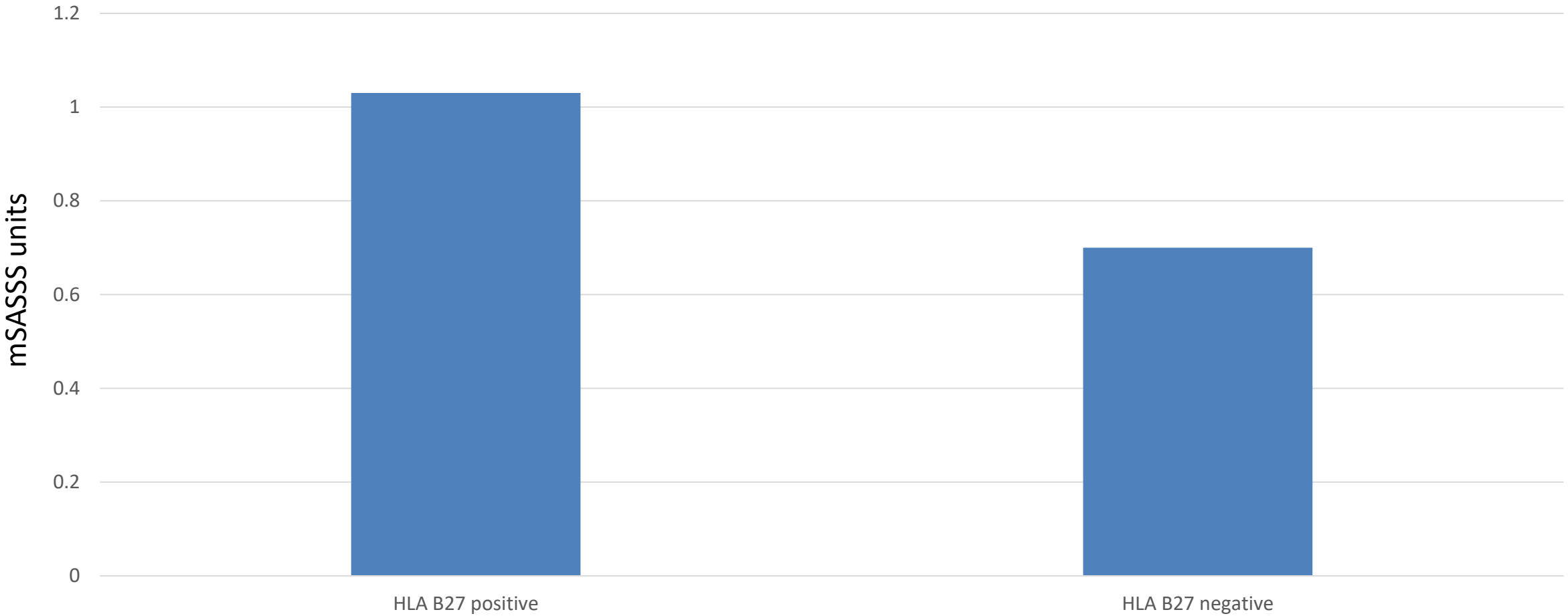
All patients followed up at 8 years



Pedictors of future AS	Specificity	Sensitivity	PPV	NPV	Likelihood Ratio
	Baseline predictors of developing AS				
Osteitis=grade 3 & B27 +ve	92	62	80	83	8.0
Osteitis>=grade 2 & B27 +ve	77	77	63	87	3.3
B27 +ve only	54	85	48	88	1.8
Osteitis<=grade 1 only	38	23	16	50	0.4

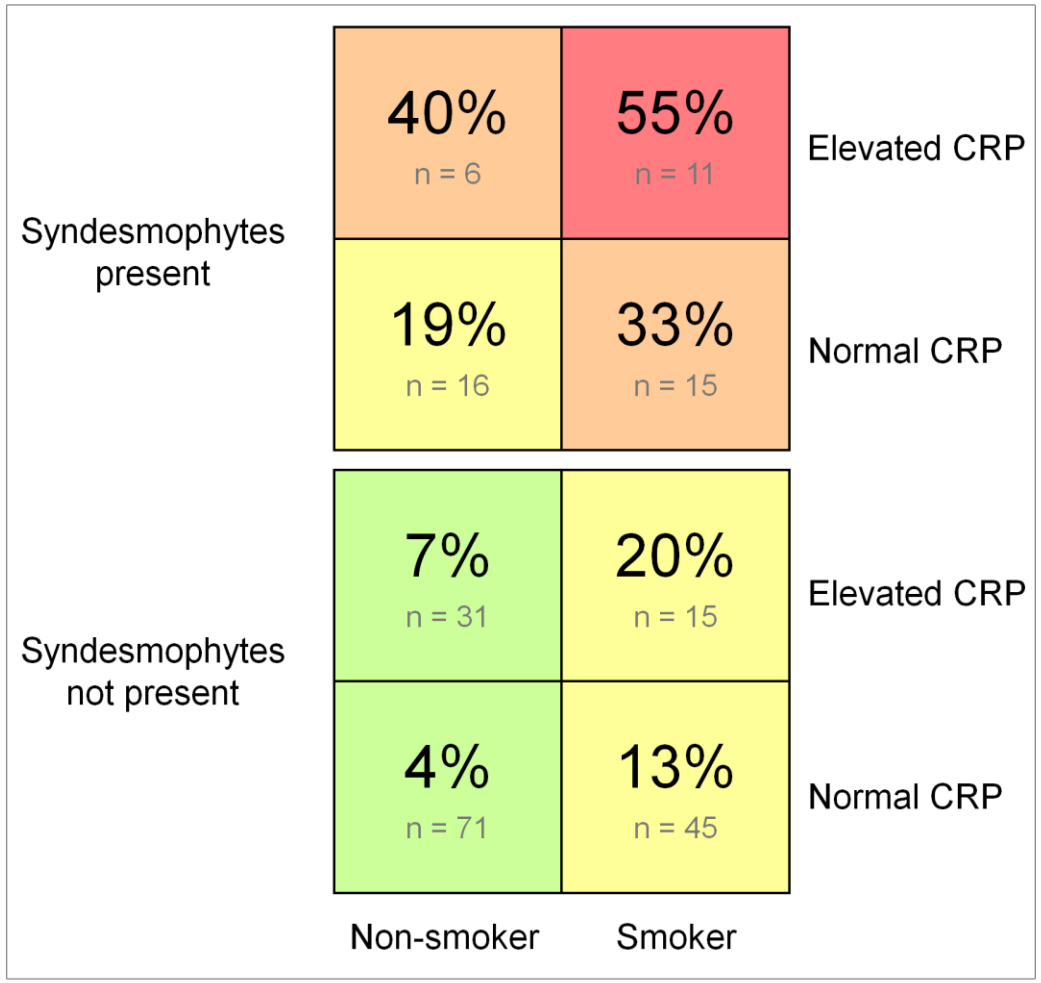
89. Bennett AN, McGonagle D, O'Connor P, Hensor EM, Sivera F, Coates LC: Severity of baseline magnetic resonance imaging-evident sacroiliitis and HLA-B27 status in early inflammatory back pain predict radiographically evident ankylosing spondylitis at eight years. *Arthritis Rheum* 2008, 58:3413-3418.

The influence of HLA B27 on radiographic progression



Ramiro S *et al. Ann Rheum Dis* 2015;74:52–9

A Matrix Model for Prediction of Radiographic Spinal Progression in Axial Spondyloarthritis



The percentages represent proportions of patients with spinal radiographic progression (2 mSASSS units over 2 years) with a respective combination of risk factors.

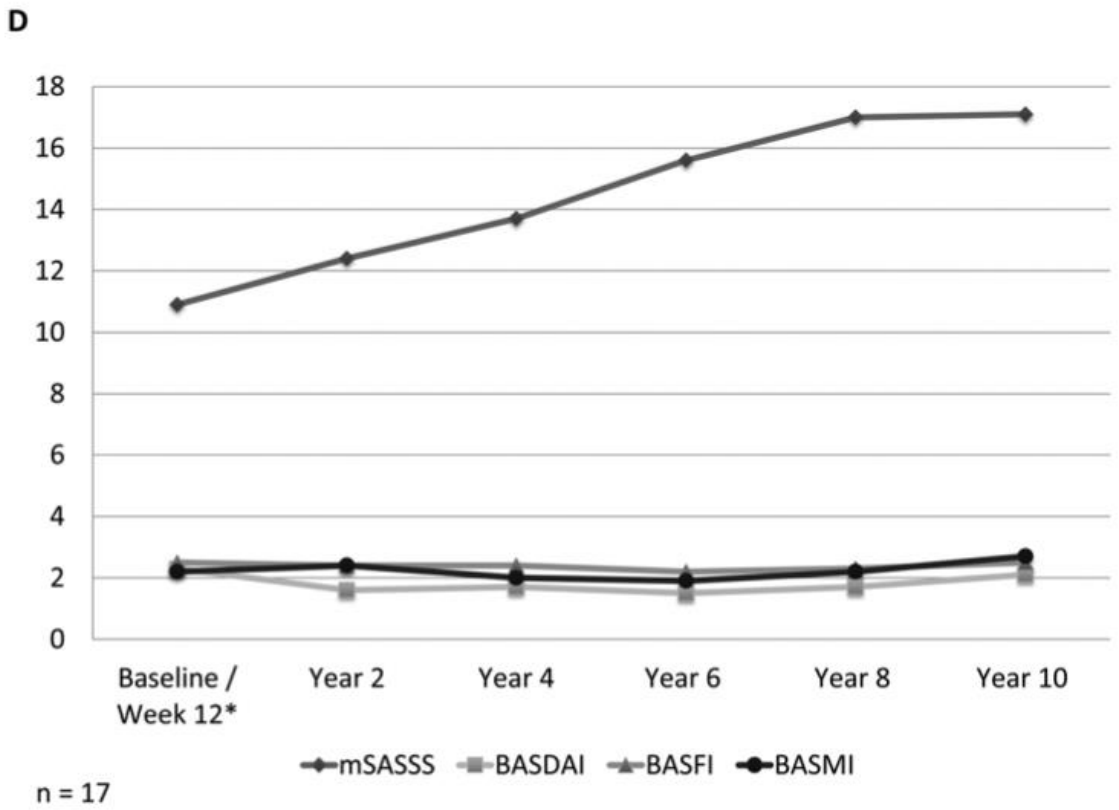
German Spondyloarthritis Inception Cohort (GESPIC), patients with axial spondyloarthritis, n = 210

Poddubnyy D et al. Arthritis Rheum 2012;64:1388-98 (with permission)

Agenda

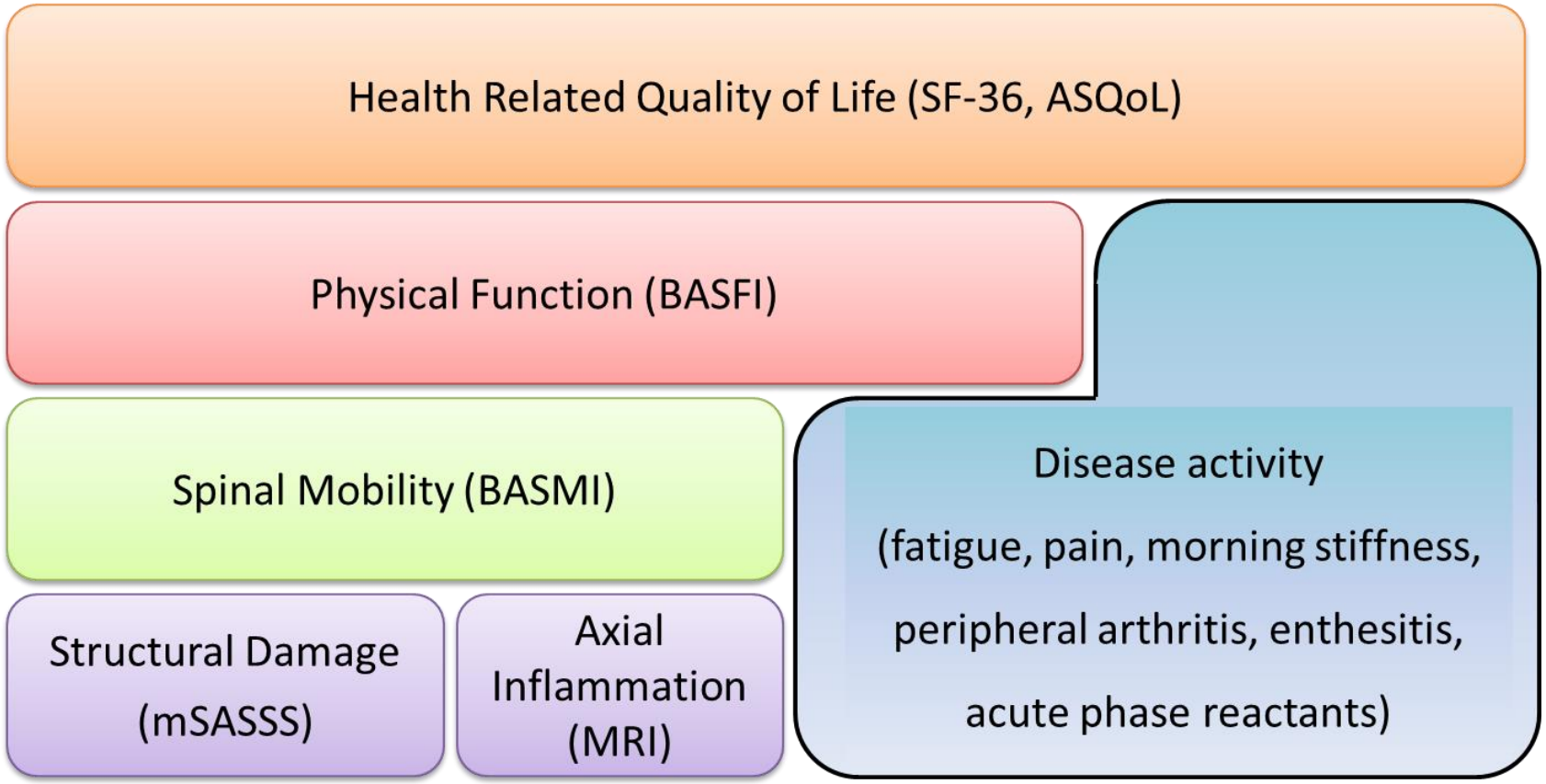
- The radiographic progression of ankylosing spondylitis
  - SIJs
  - Spine
- Predicting radiographic progression
- Clinical importance of progression
- Can we prevent progression with biologics

The impact of disease activity suppression on functional outcomes in axSpA



Poddubnyy et al. Physical Function and Spinal Mobility Remain Stable Despite Radiographic Spinal Progression in Patients with Ankylosing Spondylitis Treated with TNF-α Inhibitors for Up to 10 Years. *Journal of Rheumatology 2016; 43:12; doi:10.3899/jrheum.160594*

Hierarchical model of health outcomes in axial Spondyloarthritis



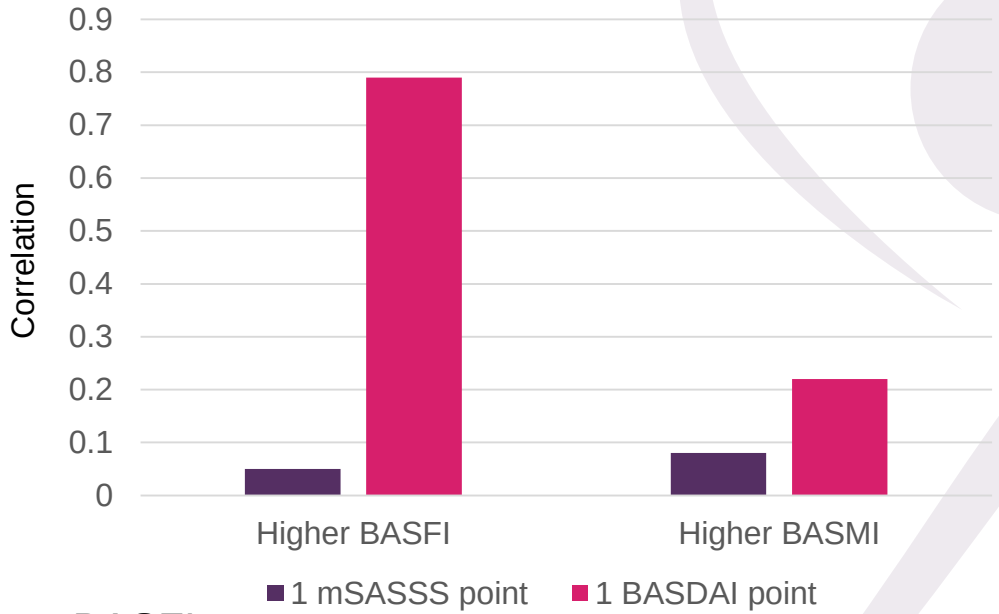
Machado et al. Ann Rheum Dis. 2011 Oct;70(10):1758-64.

Factors influencing physical function and spinal mobility in early axSpA

TABLE 3 Association between the change in modified Stoke AS Spine Score and change in BASFI or BASMI after 2 years in the linear regression analysis

	Model 1		Model 2[a]		Model 3[b]	
	β (95% CI)	β_{stand} (95% CI)	β (95% CI)	β_{stand} (95% CI)	β (95% CI)	β_{stand} (95% CI)
Outcome: change in BASFI						
Change in mSASSS	0.11 (0.01, 0.21)	0.16 (0.01, 0.29)	0.08 (0.01, 0.16)	0.12 (0.01, 0.22)	0.09 (0.01, 0.17)	0.12 (0.01, 0.23)
Change in BASDAI	–	–	0.59 (0.48, 0.70)	0.62 (0.51, 0.74)	0.58 (0.47, 0.69)	0.62 (0.50, 0.73)
Outcome: change in BASMI						
Change in mSASSS	0.01 (−0.07, 0.09)	0.02 (−0.12, 0.16)	0.05 (−0.03, 0.13)	0.09 (−0.05, 0.24)	0.05 (−0.04, 0.13)	0.08 (−0.06, 0.23)
Change in BASDAI	–	–	0.14 (0.04, 0.25)	0.20 (0.05, 0.34)	0.15 (0.04, 0.25)	0.20 (0.06, 0.35)

[a]Adjusted for BASFI/BASMI at baseline. [b]Adjusted for BASFI/BASMI at baseline, presence of the definite radiographic sacroiliitis according to the modified New York criteria for AS at baseline (⩾grade 2 bilaterally or ⩾grade 3 unilaterally), CRP (time averaged over 2 years), sex and HLA-B27 status. mSASSS: modified Stoke AS Spine Score.



- An increase of 20 mSASSS points would be responsible for an increase of one BASFI point.
- An increase of 12 mSASSS points would be responsible for an increase of one BASMI point.

Poddubnyy et al. Functional relevance of radiographic spinal progression in axial spondyloarthritis: results from the GErman SPondyloarthritis Inception Cohort. Rheumatology. doi:10.1093/rheumatology/kex475

Factors influencing spinal mobility in axSpA

Time since symptom onset

Disease activity

Radiographic damage

Table 3 Best-fit model for spinal mobility (BASMI).

	Entire ankylosing spondylitis population (n=214)	Disease duration ≤3 years (n=53)	Disease duration >3 years (n=161)
mSASSS			
B	0.865	0.380	0.924
95% CI	0.677–1.054	−0.099 to 0.858	0.715–1.134
p Value	<0.001	0.117	<0.001
ASspiMRI-a			
B	0.236	0.595	0.156
95% CI	0.041–0.432	0.173–1.016	−0.070 to 0.383
p Value	0.018	0.007	0.174
Gender (male)			
B	−0.305	−0.454	−0.299
95% CI	−0.738 to 0.127	−1.338 to 0.429	−0.796 to 0.198
p Value	0.165	0.307	0.237

Results are shown for the entire AS population and according to disease duration. ASspiMRI-a, Ankylosing Spondylitis spinal MRI activity; B, regression coefficient; BASMI, linear definition of the Bath Ankylosing Spondylitis Metrology Index; mSASSS, modified Stoke Ankylosing Spondylitis Spine Score.

Disease duration ≤3 years, B was greater for ASspiMRI-a than for mSASSS (0.595 vs 0.380),

Disease duration >3 years B was greater for mSASSS than for ASspiMRI-a (0.924 vs 0.156).

Machado P, Landewe´ R, Braun Jet al. Both structural damage and inflammation of the spine contribute to impairment of spinal mobility in patients with ankylosing spondylitis. Ann Rheum Dis 2010;69:146570.

Agenda

- The radiographic progression of ankylosing spondylitis
  - SIJs
  - Spine
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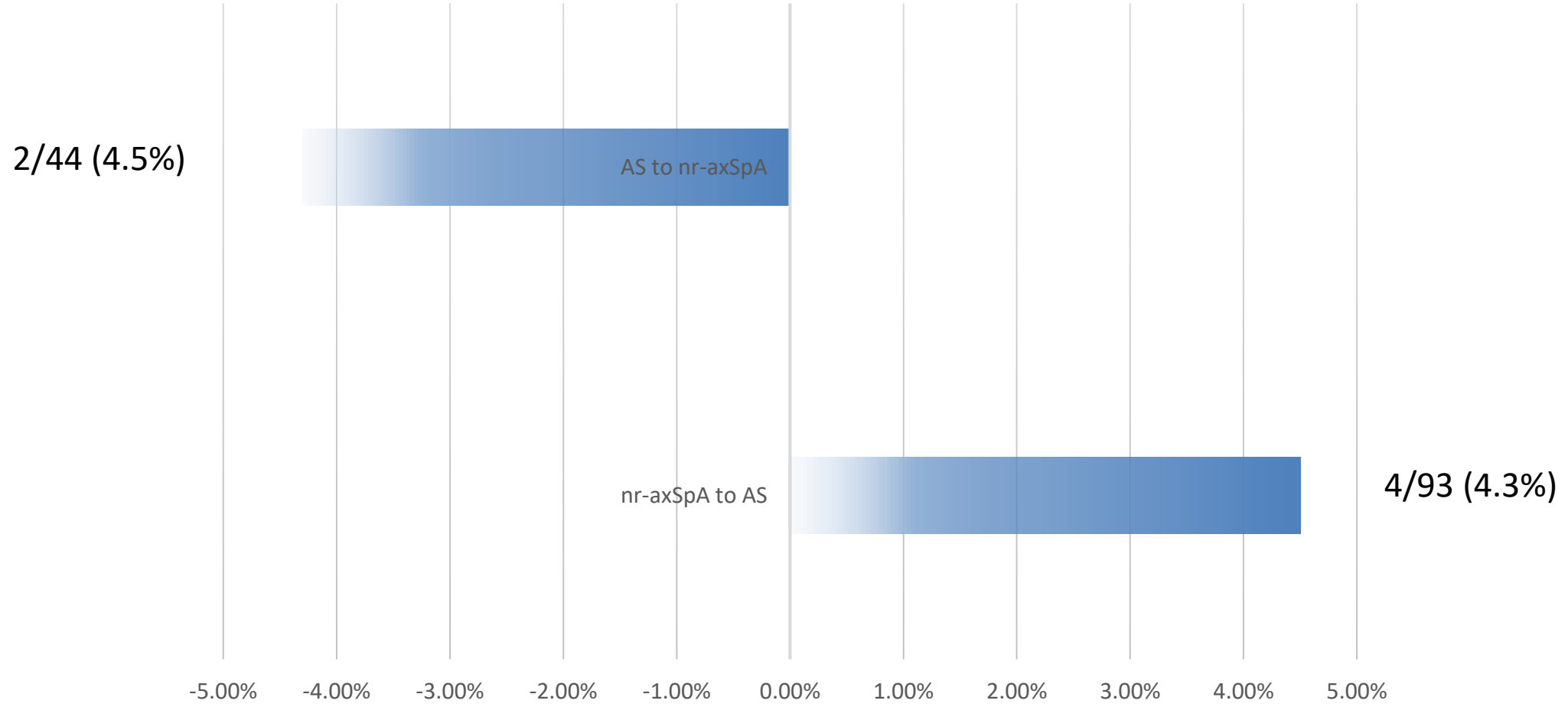
The effect of anti TNF on SIJ progression at week 204 - RAPID -axSpA study

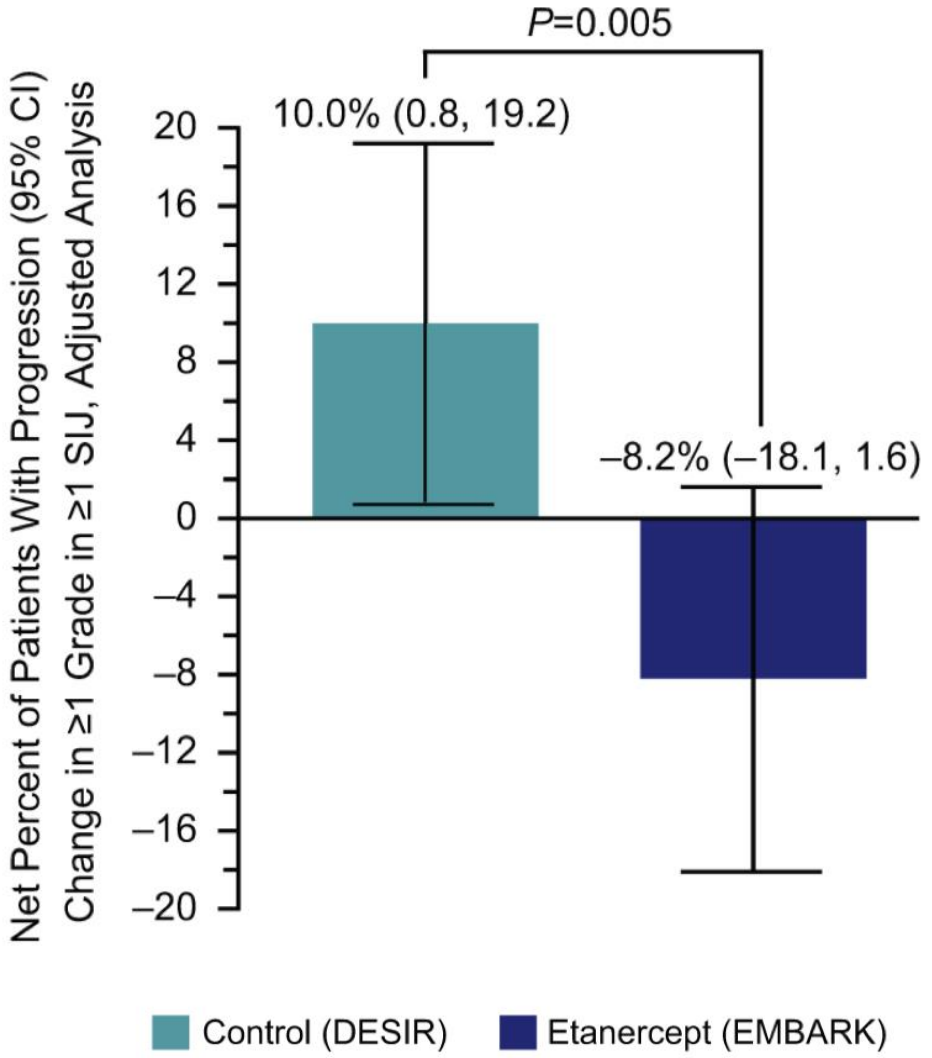


van der Heijde D, et al. Limited radiographic progression and sustained reductions in MRI inflammation in patients with axial spondyloarthritis: 4-year imaging outcomes from the RAPID-axSpA phase III randomised trial. Ann Rheum Dis 2018;0:1–7. doi:10.1136/annrheumdis-2017-212377

Radiographic progression at the SIJs over 2 years - EMBARK study

Table 1 Demographics and baseline disease characteristics

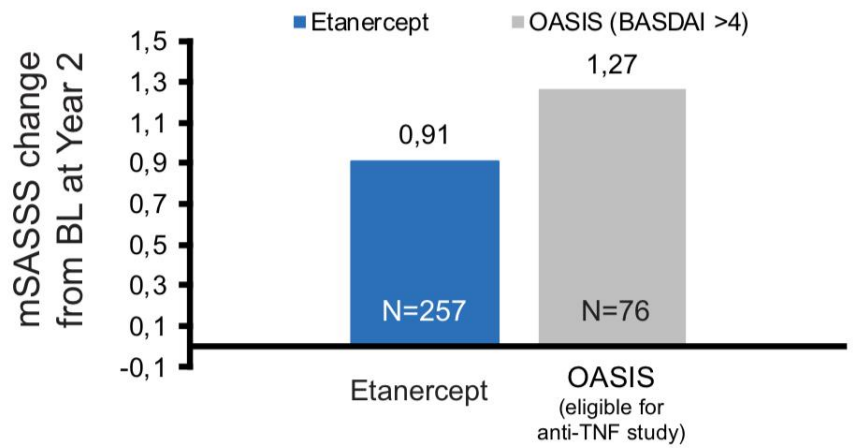
	Control (DESIR) n=193	Etanercept (EMBARK) n=162	p Value
Age, years	32.2 (7.0)	31.8 (7.7)	0.47*
Male, n/N (%)	100/193 (51.8)	106/162 (65.4)	0.01†
Symptom duration, years	1.7 (1.0)	2.4 (1.8)	<0.001*
Current smoker, n/N (%)	70/192 (36.5)	37/162 (22.8)	0.006†
HLA-B27(+), n/N (%)	162/193 (83.9)	113/156 (72.4)	0.009†
BASDAI (0–10)	3.6 (1.9)	5.9 (1.8)	<0.001*
ASDAS	2.2 (0.9)	3.0 (1.0)	<0.001*
BASFI (0–10 cm VAS)	2.2 (2.0)	4.0 (2.4)	<0.001*
CRP, mg/L	5.4 (7.5)	6.9 (11.2)	0.06*
SPARCC MRI SIJ score (0–72)	5.8 (9.5)	8.4 (11.0)	<0.001*
SPARCC MRI SIJ score ≥2, n/N (%)	78/191 (40.8)	95/159 (59.7)	<0.001†
Total SIJ score (mNY grade 0–8)	1.9 (1.6)	1.5 (1.2)	0.03*
SIJ score met mNY criteria, n/N (%)	39/193 (20.2)	19/162 (11.7)	0.03†

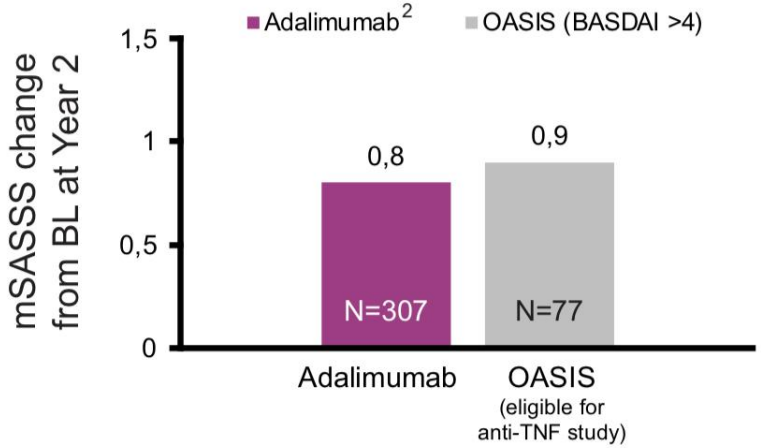


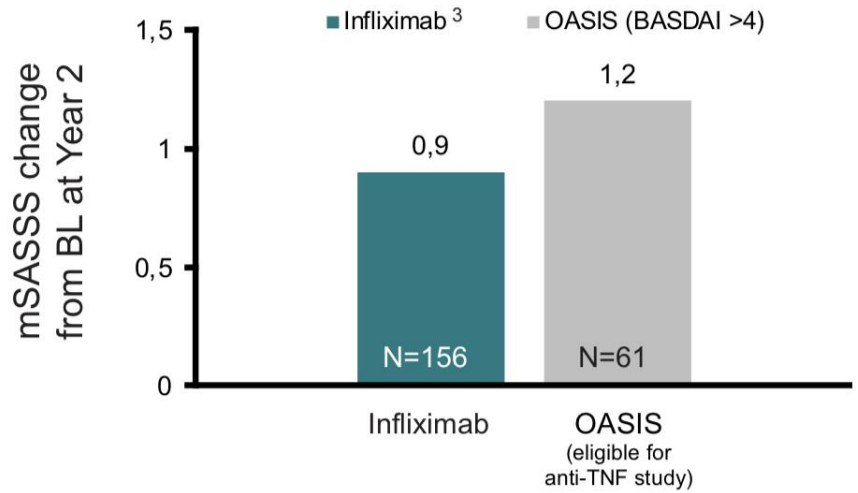
Dougados et al. Evaluation of the change in structural radiographic sacroiliac joint damage after 2 years of etanercept therapy (EMBARK trial) in comparison to a contemporary control cohort (DESIR cohort) in recent onset axial spondyloarthritis. Ann Rheum Dis 2018;77:221–227. doi:10.1136/annrheumdis-2017-212008

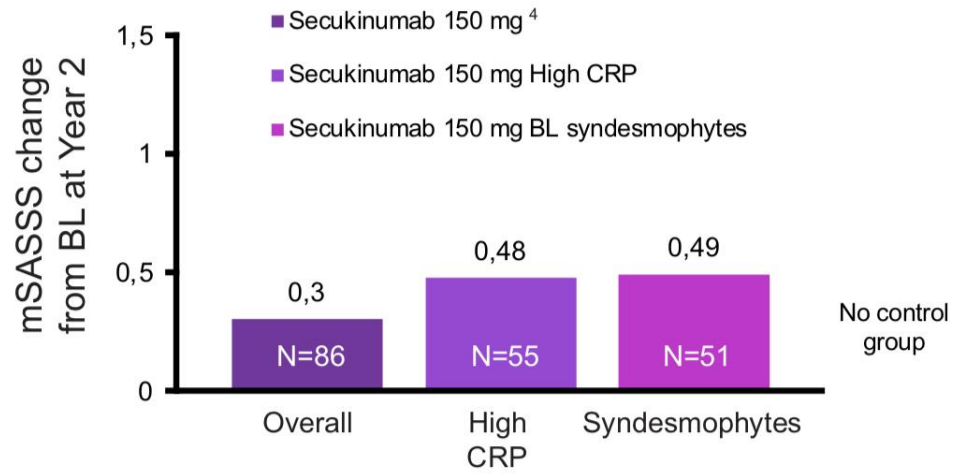
Effect of biologic therapies on radiographic progression in ankylosing spondylitis

No head-to-head comparison!



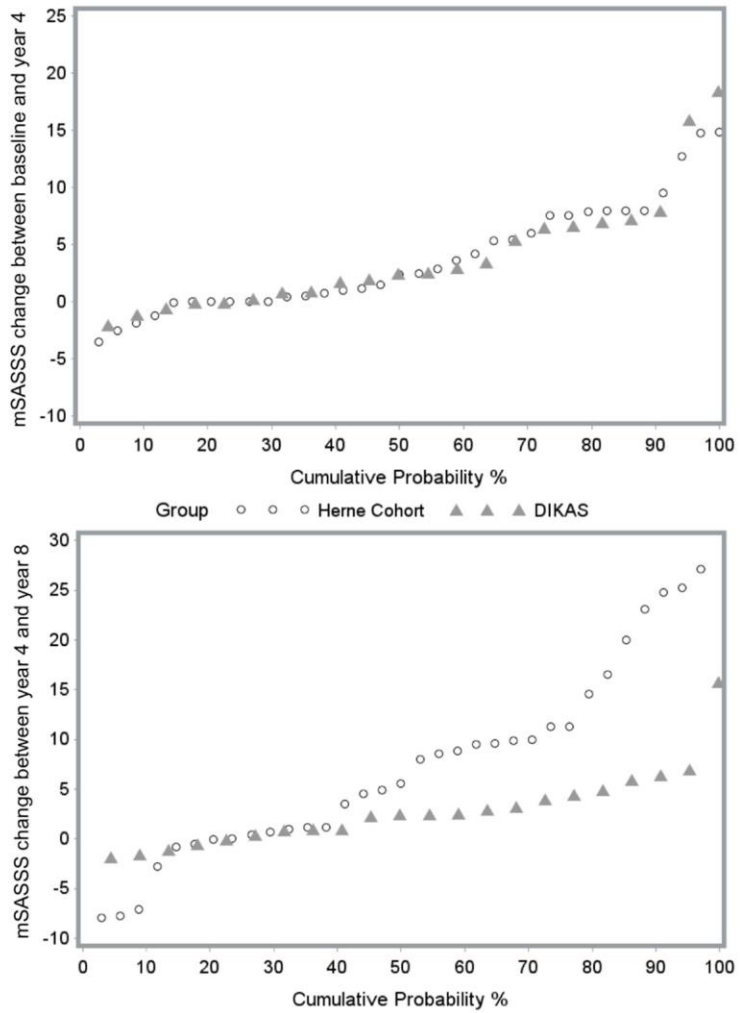


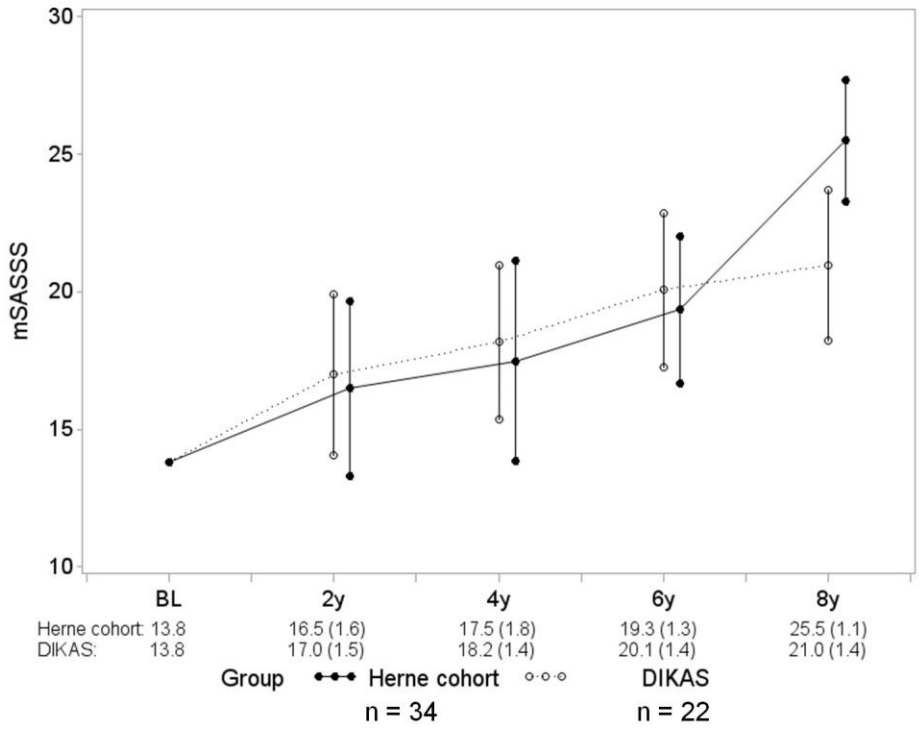




van der Heijde D, et al. Arthritis Rheum 2008, Arthr Res Ther 2009, Arthritis Rheum 2008; Braun J, et al. Ann Rheum Dis 2017;

Continuous Long-Term Anti-TNF Therapy Might not Lead to an Increase of New Bone Formation over 8 Years in AS

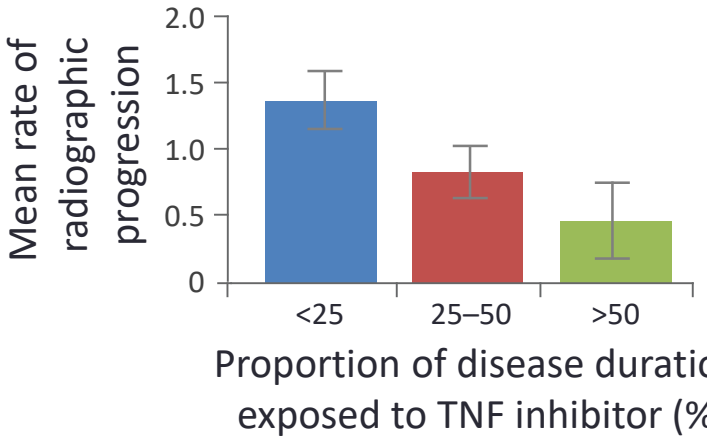


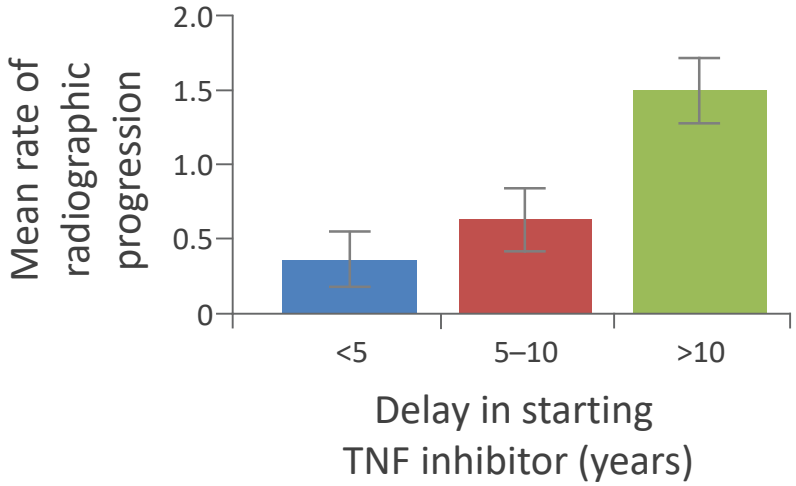


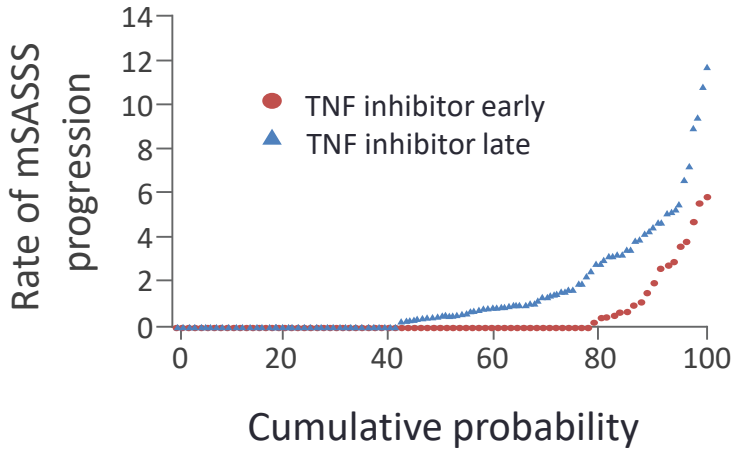
DIKAS: German Infliximab AS Cohort
Herne cohort: patients on NSAIDs only

Baraliakos X et al. Ann Rheum Dis 2014;73:710-5 (with permission)

TNF blockers and radiographic progression







Haroon *et al*. *Arthritis Rheum* 2013;65:2645–54

Reduction in Spinal Radiographic Progression in Ankylosing Spondylitis Patients Receiving Prolonged Treatment With Tumor Necrosis Factor Inhibitors

Table 1. Baseline characteristics of all included ankylosing spondylitis patients and of patients with complete data over 4, 6, or 8 years*

Characteristics	All patients (n = 210)	4-year data (n = 110)	6-year data (n = 53)	8-year data (n = 19)
Male, no. (%)	145 (69)	79 (72)	38 (72)	16 (84)
Age, mean ± SD years	41.6 ± 11.5	41.2 ± 11.7	39.7 ± 11.1	39.3 ± 10.7
Symptom duration, years	14 (8–24)	15 (7–23)	15 (7–21)	17 (9–23)
Time since diagnosis, years	6 (1–15)	5 (1–14)	5 (1–14)	9 (3–17)
HLA–B27+, no. (%)	160 (78)	88 (80)	43 (81)	17 (90)
BMI, mean ± SD kg/m^2	25.8 ± 4.3	26.2 ± 3.9	25.3 ± 3.8	24.9 ± 2.0
Smoking duration, years	12 (0–23)	13 (0–24)	13 (0–26)	13 (0–27)
NSAID use, no. (%)	164 (80)	89 (81)	45 (85)	18 (95)
ASAS-NSAID index	60 (25–100)	69 (17–100)	67 (38–100)	50 (25–100)
DMARD use, no. (%)	38 (18)	21 (19)	16 (30)	5 (26)
First TNF inhibitor, no. (%)				
Infliximab	28 (13)	17 (15)	12 (23)	5 (26)
Etanercept	132 (63)	71 (65)	35 (66)	14 (74)
Adalimumab	50 (24)	22 (20)	6 (11)	0 (0)
BASDAI (range 0–10), mean ± SD	6.0 ± 1.7	6.0 ± 1.6	5.8 ± 1.7	6.0 ± 1.4
ASDAS-CRP, mean ± SD	3.7 ± 0.8	3.7 ± 0.7	3.8 ± 0.8	4.0 ± 0.6
CRP, mg/liter	13 (4–22)	12 (4–22)	14 (7–25)	17 (12–40)
ESR, mm/hour	21 (10–34)	20 (9–34)	21 (11–34)	21 (11–37)
Patient's GDA (range 0–10)	7 (5–8)	7 (6–8)	7 (5–8)	7 (5–8)
mSASSS (range 0–72)				
Mean ± SD	10.0 ± 15.5	10.7 ± 16.0	8.2 ± 12.9	10.0 ± 12.9
Median (IQR)	2.8 (0.0–12.0)	3.6 (0.0–15.8)	3.7 (0.0–11.4)	5.4 (1.0–17.1)
≥1 syndesmophyte, no. (%)	108 (54)	60 (55)	28 (53)	12 (63)

* Values are the median (interquartile range [IQR]) unless indicated otherwise. BMI = body mass index; NSAID = nonsteroidal antiinflammatory drug; ASAS = Assessment of SpondyloArthritis international Society; DMARD = disease-modifying antirheumatic drug; TNF = tumor necrosis factor; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; ASDAS = Ankylosing Spondylitis Disease Activity Score; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; GDA = global disease activity; mSASSS = modified Stoke Ankylosing Spondylitis Spine Score.

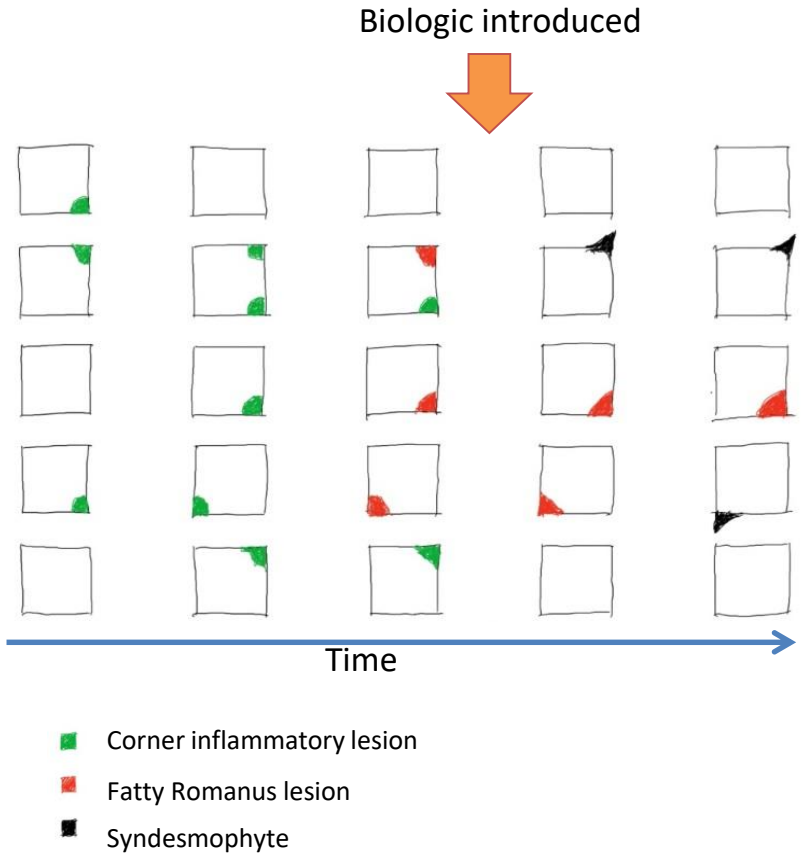
Table 3. Baseline damage and spinal radiographic progression in ankylosing spondylitis patients with complete data over 4, 6, or 8 years of followup (observed data)*

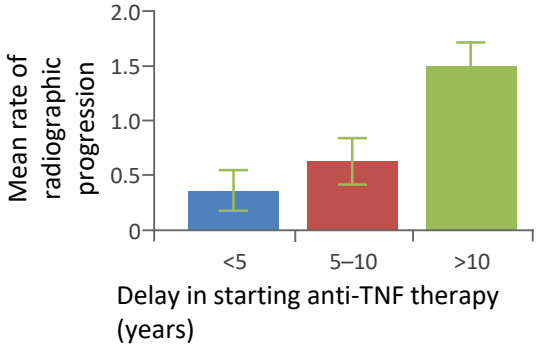
mSASSS data	No.	Mean ± SD	Median (IQR)
Complete 4-year			
Baseline	110	10.7 ± 16.0	3.6 (0.0–15.8)
Progression 0–2 years	110	1.8 ± 3.0	0.5 (0.0–2.3)
Progression 2–4 years	110	1.5 ± 2.5	0.0 (0.0–2.3)
Complete 6-year			
Baseline	53	8.2 ± 12.9	3.7 (0.0–11.4)
Progression 0–2 years	53	1.6 ± 2.7	0.5 (0.0–2.6)
Progression 2–4 years	53	1.8 ± 2.3	0.5 (0.0–3.8)
Progression 4–6 years	53	1.0 ± 1.5	0.0 (0.0–1.4)
Complete 8-year			
Baseline	19	10.0 ± 12.9	5.4 (1.0–17.1)
Progression 0–2 years	19	2.2 ± 2.7	1.0 (0.0–4.5)
Progression 2–4 years	19	1.6 ± 2.1	0.5 (0.0–3.5)
Progression 4–6 years	19	0.9 ± 1.3	0.0 (0.0–1.5)
Progression 6–8 years	19	0.9 ± 1.4	0.0 (0.0–1.5)

* IQR = interquartile range; mSASSS = modified Stoke Ankylosing Spondylitis Spine Score.

Maas et al. Reduction in Spinal Radiographic Progression in Ankylosing Spondylitis Patients Receiving Prolonged Treatment With Tumor Necrosis Factor Inhibitors. Arthritis Care & Research. Vol. 69, No. 7, July 2017, pp 1011–1019. DOI 10.1002/acr.23097

Optimising the timing of biologic initiation to prevent radiographic damage





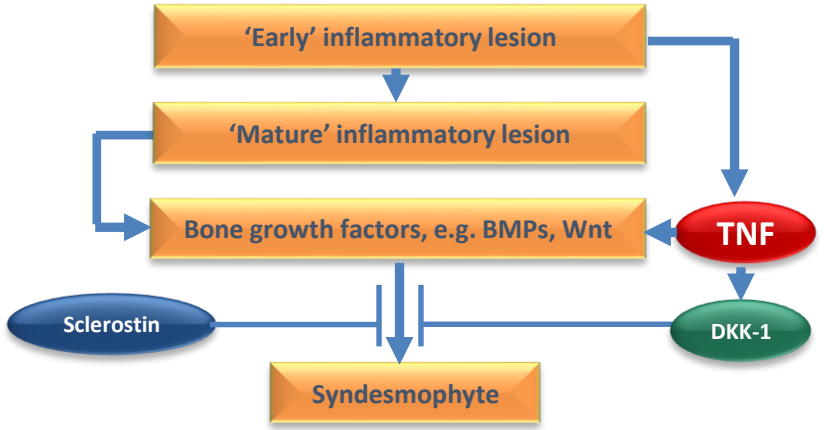
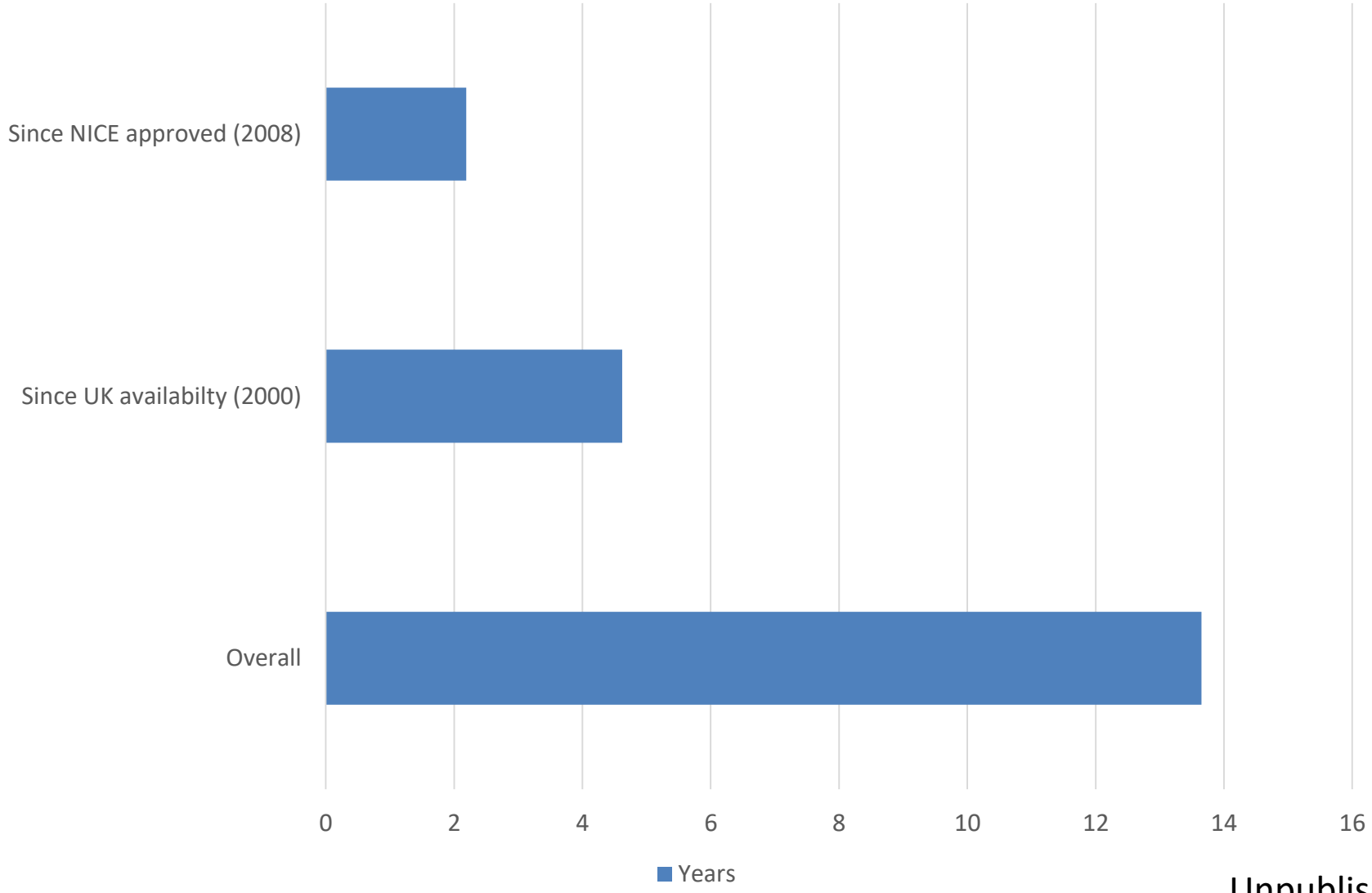


Image used with permission from Dr Raj Sengupta.

1. Haroon N, et al. *Arthritis Rheum.* 2013;65:2645–54; 2. Maksymowych WP. *Nat Rev Rheumatol.* 2010;6:75–81.

BMP, bone morphogenetic protein; DKK-1, Dickkopf-related protein 1; TNF, tumour necrosis factor

Time to first biologic - Bath and Norwich data



Unpublished data

Overall Summary

- Radiographic progression in axSpA is slow in the majority of patients
- Less than 2% patients change from nr-axSpA to AS over 5years
- Predictors of progression include HLA B27, raised CRP, baseline syndesmophytes, MRI osteitis and smoking
- The progression from fatty lesions to syndesmophyte formation appears to be fixed
- Radiographic damage has more impact on function and mobility in later disease
- Biologic therapy more likely to be effective in early disease