

Module 2

Burden of Disease



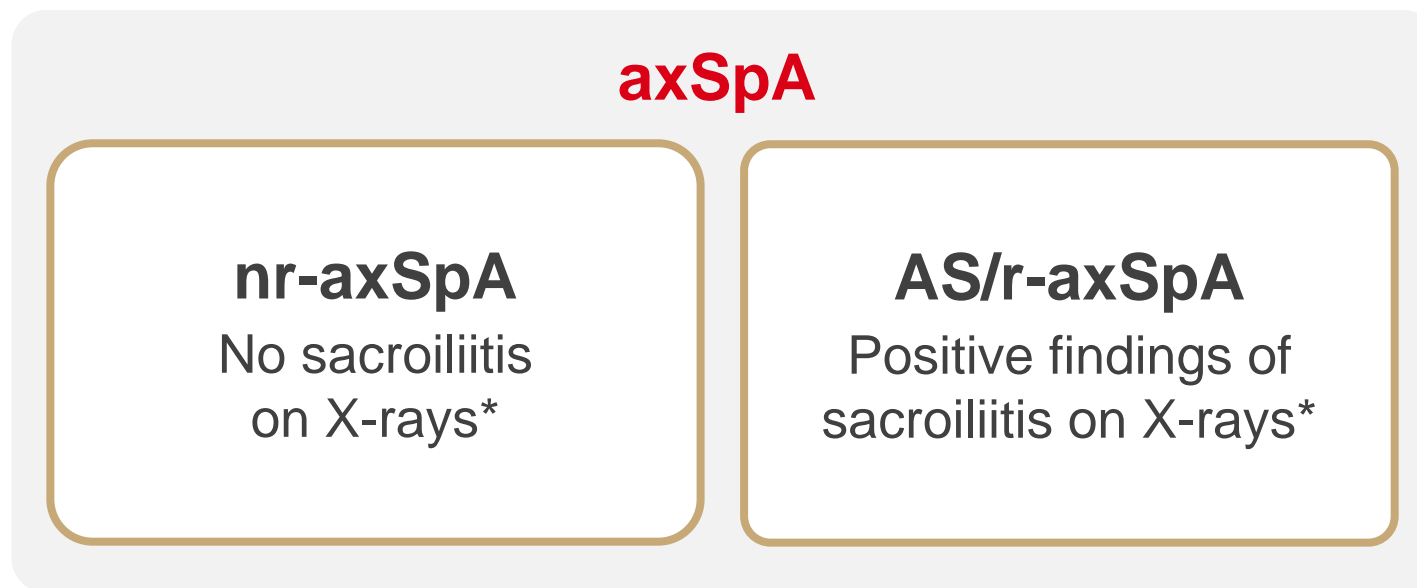
Content Flow



- Prevalence and classification of AS/r-axSpA and nr-axSpA
- Gender disparity in AS/r-axSpA and nr-axSpA
- Burden of AS/r-axSpA and nr-axSpA
 - Physical/disability
 - Quality of life
 - Psychological
 - Comorbidities
- Impact of treatment on AS/r-axSpA and nr-axSpA
- Summary

One Disease, Two Subtypes

axSpA encompasses two subtypes of the same disease¹⁻³



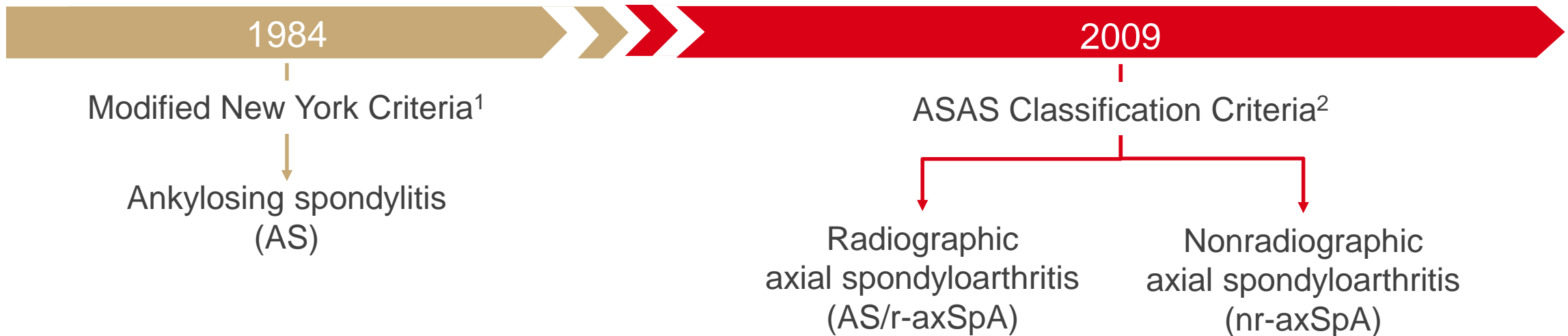
*Defined by specific criteria.

AS=Ankylosing Spondylitis; axSpA=Axial Spondyloarthritis; nr-axSpA=Nonradiographic Axial Spondyloarthritis; r-axSpA=Radiographic Axial Spondyloarthritis.

1. Ward MM, et al. *Arthritis Rheumatol.* 2016;68(2):282-298. 2. Taurog JD, et al. *N Engl J Med.* 2016;374(26):2563-2574. 3. van der Linden S, et al. *Arthritis Rheum.*1984;27(4):361-368.

AS/r-axSpA and nr-axSpA Classification

- Diagnosis and classification of AS has been based on the modified New York (mNY) criteria, which require the presence of radiographic sacroiliitis¹
- The ASAS criteria allow for the classification of patients without radiographic changes as nr-axSpA²
 - Positive MRI of the sacroiliac joints (based on specific definitions) is used to identify this subtype
 - The criteria also contains a clinical arm, which enhances the capability to identify patients without MRI findings as it requires the presence of positive HLA-B27 and two SpA features
- The imaging arm of the ASAS classification criteria includes sacroiliitis on X-rays (as per mNY criteria) as one of its criterion and therefore, identifies patients with AS/r-axSpA²



AS=Ankylosing Spondylitis; ASAS=Assessment of SpondyloArthritis International Society; axSpA=Axial Spondyloarthritis; mNY=modified New York; MRI=Magnetic Resonance Imaging; nr-axSpA=Nonradiographic Axial Spondyloarthritis; r-axSpA=Radiographic Axial Spondyloarthritis; SpA=Spondyloarthritis.

1. van der Linden S, et al. *Arthritis Rheum.*1984;27(4):361-368. 2. Rudwaleit M, et al. *Ann Rheum Dis.* 2009;68(6):777-783.

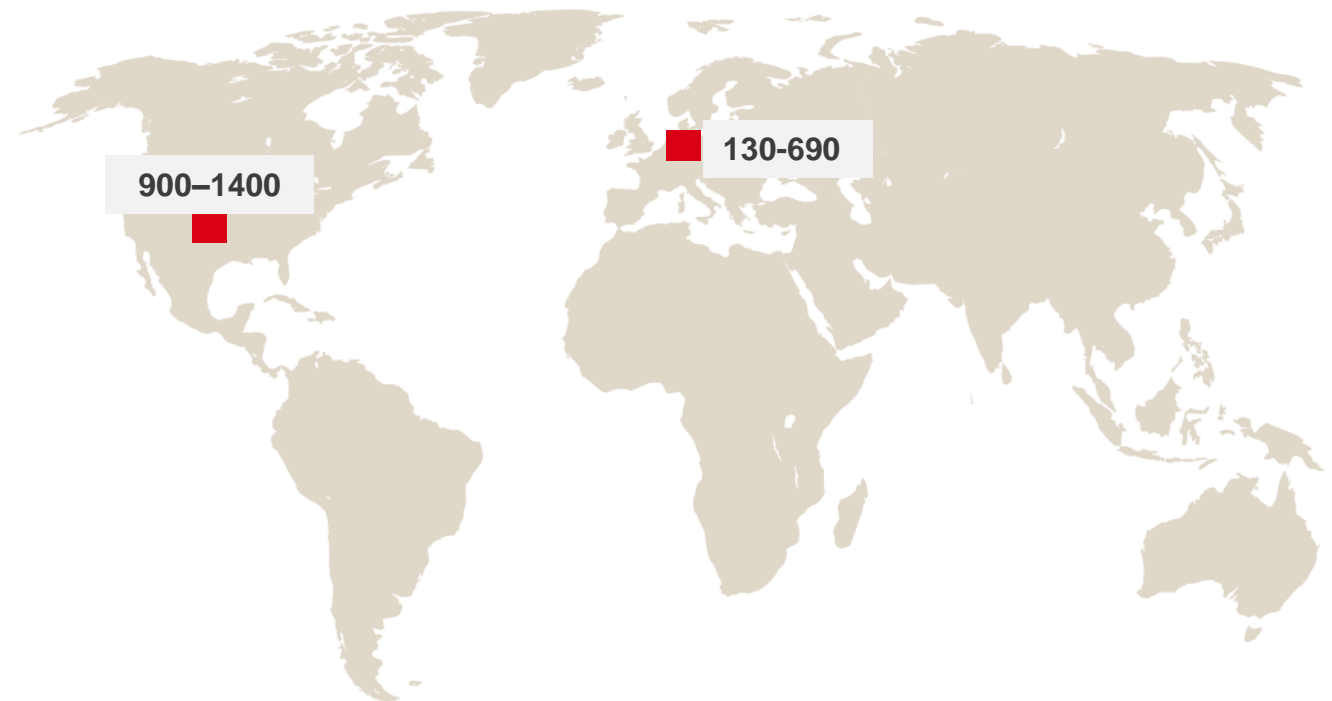
Prevalence of AS/r-axSpA and nr-axSpA



AS/r-axSpA and nr-axSpA Prevalence

- Estimated prevalence rates:
 - axSpA: 0.1 to 1.4%^{1,2}
 - AS/r-axSpA: 0.1 to 0.5%^{1,2}
 - nr-axSpA: 0.35%³
- Age of onset for majority of patients is within the third decade of life (<40 years)⁴
- <5% of patients present above the age of 45⁴

Prevalence rate per 100,000 patients for axSpA²



AS=Ankylosing Spondylitis; axSpA=Axial Spondyloarthritis; nr-axSpA=Nonradiographic Axial Spondyloarthritis; r-axSpA=Radiographic Axial Spondyloarthritis.

1. Reveille JD, Weisman MH. *Am J Med Sci*. 2013;345(6):431-436. 2. Bohn R et al. *Clin and Exp Rheumatol* .2018;36:263-274. 3. Strand V, et al. *Arthritis Care Res (Hoboken)*. 2013;65(8):1299-306. 4. Rudwaleit M, et al. *Ann Rheum Dis*. 2009;68:777-783.

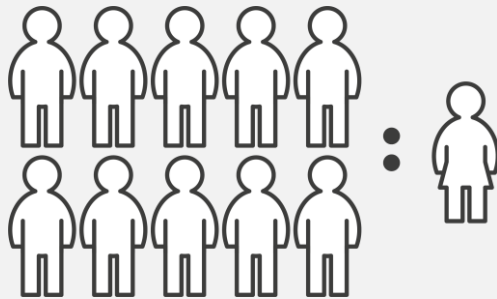
Gender Disparity in AS/r-axSpA and nr-axSpA



Gender Disparity in AS/r-axSpA and nr-axSpA

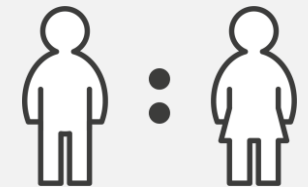
Differing reports exist on gender disparity in relation to the prevalence of axSpA

Historically the prevalence of **AS** has overestimated a greater male to female ratio (**10:1**)¹



Based on a G7 prevalence of 4.6 million:²⁻⁴

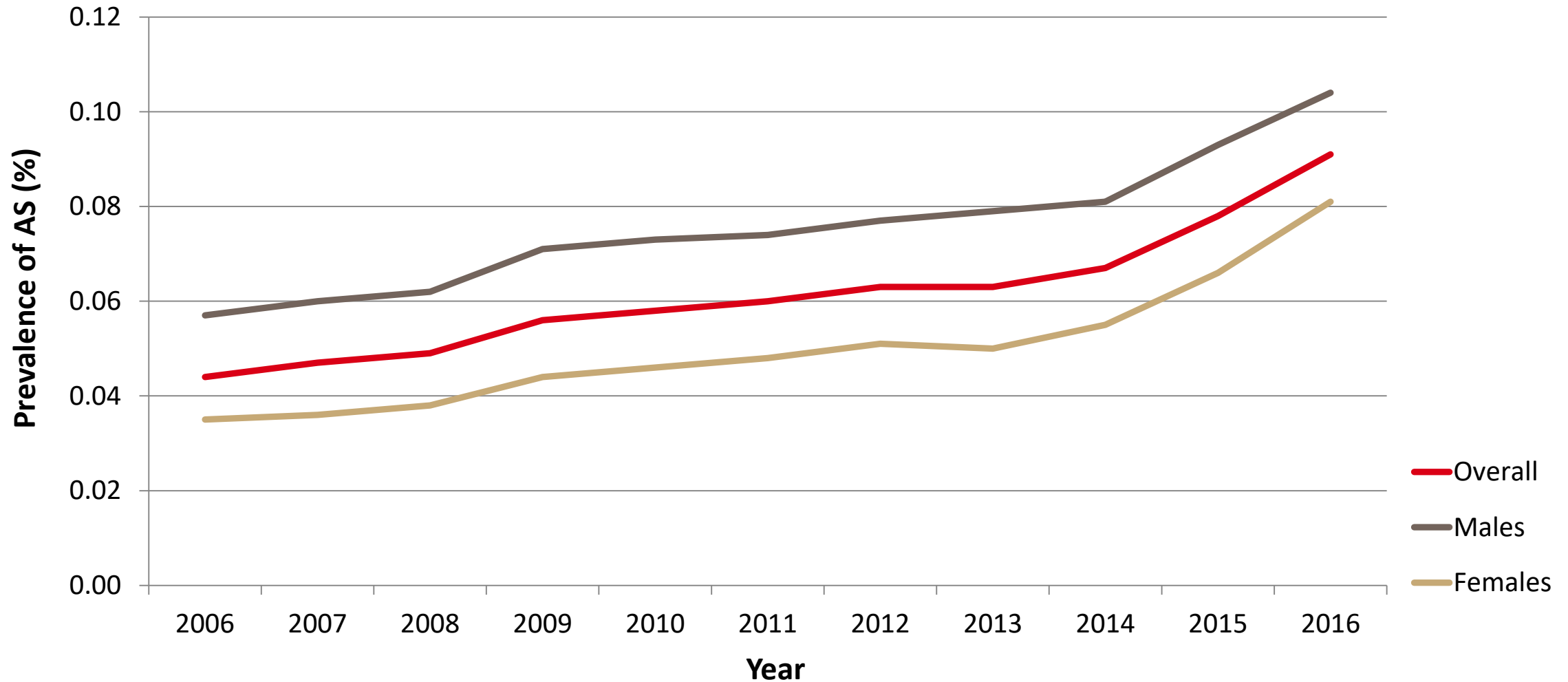
- In **axSpA** (AS/r-axSpA and nr-axSpA), the gender split is about **50/50**
- In **AS/r-axSpA**, the prevalence is higher in males (60–75% of cases)
- In **nr-axSpA**, the prevalence is lower in males (30–50% of cases)



AS=Ankylosing Spondyloarthritis; axSpA=Axial Spondyloarthritis; nr-axSpA=Nonradiographic Axial Spondyloarthritis; r-axSpA=Radiographic Axial Spondyloarthritis.

1. Polley HF, Slocumb CH. *Ann Intern Med.* 1947;26(2):240-9. 2. Sieper J, et al. *Ann Rheum Dis.* 2009;68(6):784-88. 3. Rudwaleit M, et al. *Arthritis Rheum.* 2009;60(3):717-27. 4. Reveille JD, Weisman MH. *Am J Med Sci.* 2013;345(6):431-436.

Prevalence of AS Diagnosis Codes More Than Doubled between 2006 and 2016 with a Male to Female Ratio of ~1.5:1



AS=Ankylosing Spondyloarthritis.



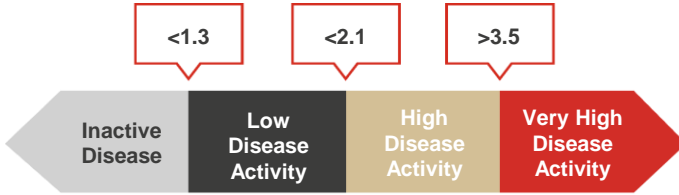
Walsh J, et al. ACR/ARHP Annual Meeting. October 2018. Abstract #910.

Comparison of AS/r-axSpA and nr-axSpA Disease Burden



Disease Activity Scores in Patients with AS and nr-axSpA

Patients with AS and nr-axSpA share a similar disease burden

Characteristic		AS (n=310), mean (SD)	nr-axSpA (n=97), mean (SD)	P-value
Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; 0-10)		4.2 (2.4)	4.6 (2.6)	0.16
Bath Ankylosing Spondylitis Functional Index (BASFI; 0-10)		3.6 (2.8)	3.3 (2.7)	0.34
Ankylosing Spondylitis Disease Activity Score (ASDAS)		2.0 (0.8) (active disease)	2.2 (0.8) (active disease)	0.65





US-based Corrona Psoriatic Arthritis/Spondyloarthritis Registry.

AS=Ankylosing Spondylitis; nr-axSpA=Nonradiographic Axial Spondyloarthritis; SD=Standard Deviation.

Mease PJ, et al. *Arthritis Care Res (Hoboken)*. 2018;70(11):1661-1670.

Quality of Life in Patients with AS and nr-axSpA

AS and nr-axSpA have similar impact on QoL

Characteristic		AS (n=310)	nr-axSpA (n=97)	P-value
Patient pain (VAS 0-100), mean (SD)		43.9 (29.8)	46.8 (29.7)	0.44
Patient-reported fatigue (VAS 0-100), mean (SD)		47.8 (29.4)	50.2 (28.7)	0.48
Morning stiffness, n (%)		277 (89.3)	91 (93.8)	0.95
EQ-5D (0-1), mean (SD) QoL measure across 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression		0.7 (0.2)	0.7 (0.2)	0.98

US-based Corrona Psoriatic Arthritis/Spondyloarthritis Registry.

AS=Ankylosing Spondylitis; EQ-5D=EuroQoL-5D; nr-axSpA=Nonradiographic Axial Spondyloarthritis; QoL=Quality of Life; SD=Standard Deviation; VAS=Visual Analog Scale.

Mease PJ, et al. *Arthritis Care Res (Hoboken)*. 2018;70(11):1661-1670.

Psychological Distress in Patients with AS and nr-axSpA

Patients with AS and nr-axSpA have a similar psychological burden

Parameter	AS (n=174)	nr-axSpA (n=142)	P-value
High risk of depression, HADS-D score ≥ 7 , n (%)	79 (45.4)	82 (42.3)	0.57
High risk of anxiety, HADS-A score ≥ 10 , n (%)	36 (20.7)	35 (24.6)	0.4




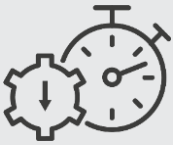
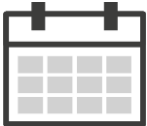
Study of 316 patients (142 nr-axSpA, 174 AS).

AS=Ankylosing Spondylitis; HADS-A=Hospital Anxiety Depression Scale-Anxiety; HADS-D=Hospital Anxiety Depression Scale-Depression; nr-axSpA=Nonradiographic Axial Spondyloarthritis.

Kilic G, et al. *Medicine (Baltimore)*. 2014;93:e337.

Workplace and Household Productivity in Patients with AS and nr-axSpA

Patients with AS and nr-axSpA experience similar reductions in productivity

WPS questions*		axSpA (n=324), mean (SD)	AS (n=178), mean (SD)	nr-axSpA (n=146), mean (SD)
# of days of work missed (absenteeism) [†]		2.0 (4.8)	1.6 (3.5)	2.5 (6.0)
# of days with productivity ≤50% at work (presenteeism) ^{†‡}		5.2 (7.6)	4.7 (7.1)	5.8 (8.0)
# of days of family, social or leisure activities missed		4.4 (6.9)	3.6 (6.1)	5.4 (7.8)

AS=Ankylosing Spondyloarthritis; axSpA=Axial Spondyloarthritis; nr-axSpA=Nonradiographic Axial Spondyloarthritis; SD=Standard Deviation; WPS=Workplace Productivity Survey.

*Recall period for Work Productivity Survey is 1 month.

[†]Assessed in employed patients only.

[‡]Days counted exclude those counted in previous question (full days missed).

Osterhaus JT, Pucaru O. *Arthritis Res Ther.* 2014;16(4):R164.

Peripheral and EAMs in Patients with AS and nr-axSpA






	AS (n=2236), % of patients ¹	nr-axSpA (n=1242), % of patients ¹
Peripheral disease		
Arthritis	29.7%	27.9%
Enthesitis	28.8%	35.4%
Dactylitis	6.0%	6.0%
Extra-articular disease		
Uveitis	23.0%	15.9%
Psoriasis	10.2%	10.9%
IBD	4.1%	6.4%

- AS is characterized by significantly higher C-reactive protein (CRP) levels compared to nr-axSpA²

AS=Ankylosing Spondyloarthritis; EAM=Extra-articular Manifestations; IBD=Inflammatory Bowel Disease; nr-axSpA=Nonradiographic Axial Spondyloarthritis.

1. de Winter JJ, et al. *Arthritis Res Ther.* 2016;18:196. 2. Proft F, Poddubnyy D. *Ther Adv Musculoskel Dis.* 2018; 10(5-6):129–139.

Comorbidities in Patients with AS and nr-axSpA

Comorbidity		AS (n=310), n (%)	nr-axSpA (n=97), n (%)	P-value
Hypertension and hyperlipidemia		118 (38.1)	34 (25.0)	0.59
Cardiovascular disease*		30 (9.7)	9 (9.2)	0.91
Diabetes mellitus		23 (7.4)	6 (6.2)	0.68
Any cancer†		16 (5.2)	5 (5.2)	1.00
Fibromyalgia		12 (3.9)	5 (5.2)	0.58

US-based Corrona Psoriatic Arthritis/Spondyloarthritis Registry.

AS=Ankylosing Spondyloarthritis; nr-axSpA=Nonradiographic Axial Spondyloarthritis.

*Combined histories of myocardial infarction, acute coronary syndrome, coronary artery disease, congestive heart failure, peripheral artery disease, cardiac revascularization procedure, ventricular arrhythmia, cardiac arrest, unstable angina, stroke, transient ischemic attack, pulmonary embolism, carotid artery disease, deep venous thrombosis, or other cardiovascular event.

†Excludes nonmelanoma of the skin.

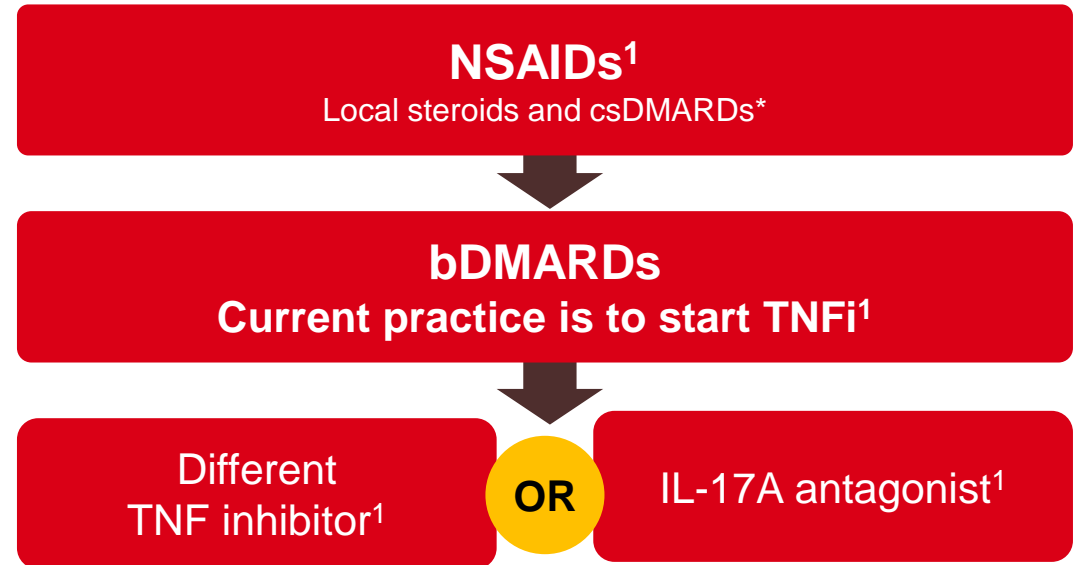
Mease PJ, et al. *Arthritis Care Res (Hoboken)*. 2018;70(11):1661-1670.

The Unmet Need in Treatment



Current ASAS-EULAR (2016) Treatment Algorithm for axSpA

Education, exercise, physical therapy, patient associations, self-help groups¹



ASAS-EULAR recommends treatment with bDMARDs if:¹

- Failure of ≥ 2 NSAIDs over 4 weeks,
 - In patients with predominant peripheral manifestations, failure of 1 local steroid injection (if appropriate) and normally a therapeutic trial of sulfasalazine, **AND**
- High disease activity: ASDAS ≥ 2.1 or BASDAI ≥ 4 , **AND**
- Positive rheumatologist's opinion

*In patients with peripheral arthritis.

ASAS=Assessment in Spondyloarthritis International Society; ASDAS=Ankylosing Spondylitis Disease Activity Score; axSpA = Axial Spondyloarthritis; bDMARD=Biological Disease Modifying Antirheumatic Drug; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; csDMARD=Conventional Synthetic Disease Modifying Antirheumatic Drug; EULAR=European League Against Rheumatism; IL=Interleukin; NSAID=Nonsteroidal Anti-inflammatory Drug; TNF=Tumor Necrosis Factor.

1. van der Heijde D, et al. *Ann Rheum Dis*. 2017;76:978-991.

Current ACR/SPARTAN (2019) Treatment Recommendations for AS

Education, exercise, physical therapy, patient associations, self-help groups¹

Recommendations updated in 2019²

NSAIDs¹

Local steroids and sulfasalazine may be considered*



TNF inhibitor¹

Switch to another TNFi in the event of a secondary nonresponse to first TNFi



Secukinumab/ixekizumab¹

Following primary nonresponse to TNFi

*Local steroids if active sacroiliitis or enthesitis; sulfasalazine if prominent peripheral arthritis.

ACR/SPARTAN=American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network; NSAID=Nonsteroidal Anti-Inflammatory Drug; TNF=Tumor Necrosis Factor.

1. Ward MM, et al. *Arthritis Rheumatol.* 2019;71(10):1599-1613. 2. <https://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice-Guidelines/Axial-Spondyloarthritis>. Accessed on March 17, 2019.

NSAID Efficacy in Patients with AS/r-axSpA and nr-axSpA

After 4 weeks of continuous NSAID treatment:

ASAS40 response:

40%

of patients with
AS/r-axSpA

30%

of patients with
nr-axSpA

**ASDAS clinically
important improvement:**

34%

of patients with
AS/r-axSpA

32%

of patients with
nr-axSpA

AS=Ankylosing Spondyloarthritis; ASAS40=Assessment in Spondyloarthritis International Society 40% response; ASDAS=Ankylosing Spondylitis Disease Activity Score; NSAID=Nonsteroidal Anti-inflammatory Drug; nr-axSpA=Nonradiographic Axial Spondyloarthritis; r-axSpA=Radiographic Axial Spondyloarthritis. Baraliakos X, et al. *Rheumatology (Oxford)*. 2017;56(1):95-102.

Summary



- Patients with AS/r-axSpA and nr-axSpA both have significant physical impairment, reduction in QoL and psychological burden
- The burden of the disease is the same for both AS/r-axSpA and nr-axSpA
- Under current treatment guidelines, a significant number of patients with either AS/r-axSpA or nr-axSpA fail to respond to NSAIDs or TNFi




Back-up Slides



Disease Burden of AS/r-axSpA







Disease Activity Scores in Patients with AS/r-axSpA

Assessment	AS (n=310) mean (SD)
<p>Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; measure of disease activity; 0, none to 10, very severe)</p> 	4.2 (2.4)
<p>Bath Ankylosing Spondylitis Functional Index (BASFI; degree of functional limitation with activities of daily living; 0, easy to 10, impossible)</p> 	3.6 (2.8)
<p>Ankylosing Spondylitis Disease Activity Score (ASDAS; composite index to assess disease activity)</p> 	2.0 (0.8) (active disease)

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Quality of Life in Patients with AS/r-axSpA


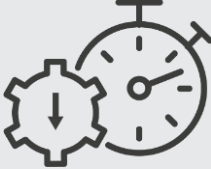
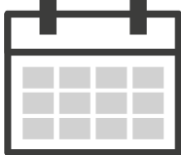
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Morning stiffness, n (%) 	277 (89.3)
EuroQoL-5D (0-1), mean (SD) QoL measure across 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression 	0.7 (0.2)

US-based Corrona Psoriatic Arthritis/Spondyloarthritis Registry.

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Mease PJ, et al. *Arthritis Care Res (Hoboken)*. 2018;70(11):1661-1670.

Workplace and Household Productivity in Patients with AS/r-axSpA

WPS questions	AS (n=178), mean (SD)
# of days of work missed (absenteeism)* 	1.6 (3.5)
# of days with productivity ≤50% at work (presenteeism)*† 	4.7 (7.1)
# of days of family, social or leisure activities missed 	3.6 (6.1)

AS=Ankylosing Spondyloarthritis; r-axSpA=Radiographic Axial Spondyloarthritis; SD=Standard Deviation; WPS=Workplace Productivity Survey.

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AS=Ankylosing Spondyloarthritis; EAMs=Extra-articular Manifestations; IBD=Inflammatory Bowel Disease; r-axSpA=Radiographic Axial Spondyloarthritis.
de Winter JJ et al. *Arthritis Res Ther.* 2016;18:196.

Comorbidities in Patients with AS/r-axSpA Compared to the General Population

For the US only.

Comorbidity		AS (n=6679), n (%)	Matched controls (n=19,951), n (%)	P value
Hypertension		1044 (15.6)	2736 (13.7)	<0.001
Cardiovascular disease		1080 (16.2)	2795 (14.0)	<0.001
Depression		686 (10.3)	1187 (6.0)	<0.001
Malignancies		294 (5.9)	879 (4.4)	<0.001
Osteoporosis		286 (4.3)	250 (1.3)	<0.001

AS=Ankylosing Spondylarthritis; r-axSpA=Radiographic Axial Spondylarthritis.
Walsh JA, et al. *Clin Rheumatol*. 2018;37(7):1869-1878.