Opportunities and challenges in diagnosis and management of axSpA: 2023 update

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Conflicts of Interest

- **Consultancy / Speaker / Research grants from:** Abbvie, BMS, Fresenius Kabi, Galapagos, Janssen, Lilly, Moonlake, MSD, Novartis, Pfizer, Roche, UCB.
- **Grants:** SAR, SER, SORCOM, EULAR, ASAS
- **Membership:** ASAS (EC), ACR, GRESSER, SAR, SER, SORCOM

Diagnosis

Review > Curr Rheumatol Rep. 2023 Mar;25(3):47-55. doi: 10.1007/s11926-022-01096-0. Epub 2023 Jan 5.

Axial Spondyloarthritis and Diagnostic Challenges: Over-diagnosis, Misdiagnosis, and Under-diagnosis

Mohamad Bittar [1], Muhammad Asim Khan [2], Marina Magrey [3]

ASAS Quality Standards for axSpA: Referral and Diagnosis

< 3 days

QS1. Referral
(suspicion of axSpA)

< 3 weeks

QS2. Time to specialist
(rheumatologist and health professionals)

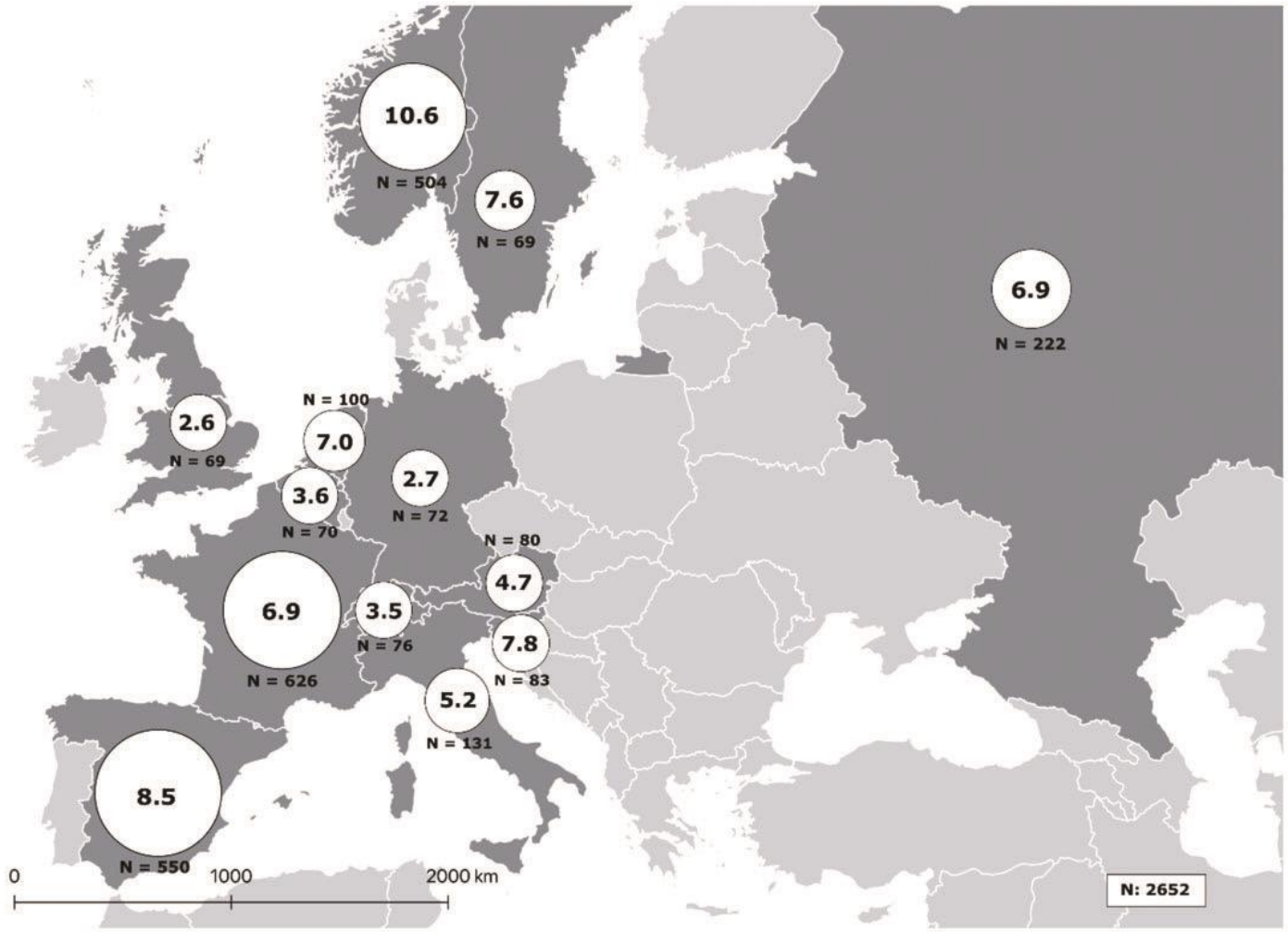
< 2 months

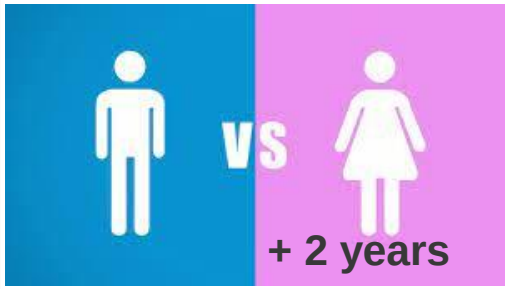
QS3. Assessment
(history taken, lab, imaging)

DIAGNOSIS

Kiltz U, et al. Ann Rheum Dis 2020;79:193–201
Navarro-Compán V and Sepriano A, et al. Ann Rheum Dis 2021;80:1511–21

Diagnostic delay: Data from the European map of spondyloarthritis (EMAS): 2652 patients in 13 countries

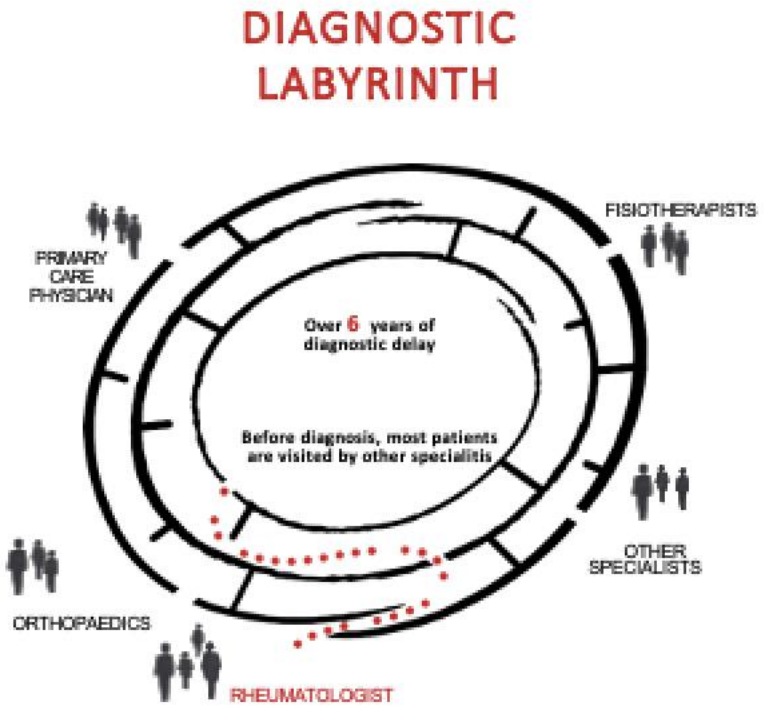




Garrido-Cumbrera M, et al. Rheumatology 2022;61:705–712

Reasons Associated with Diagnositic Delay in axSpA

GOLD STANDARD DIAGNOSTICS

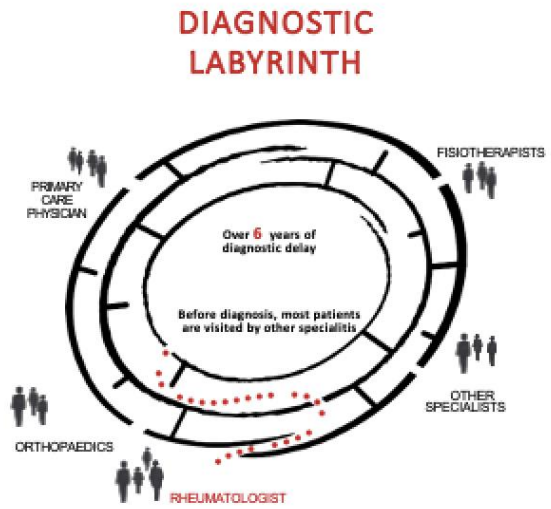


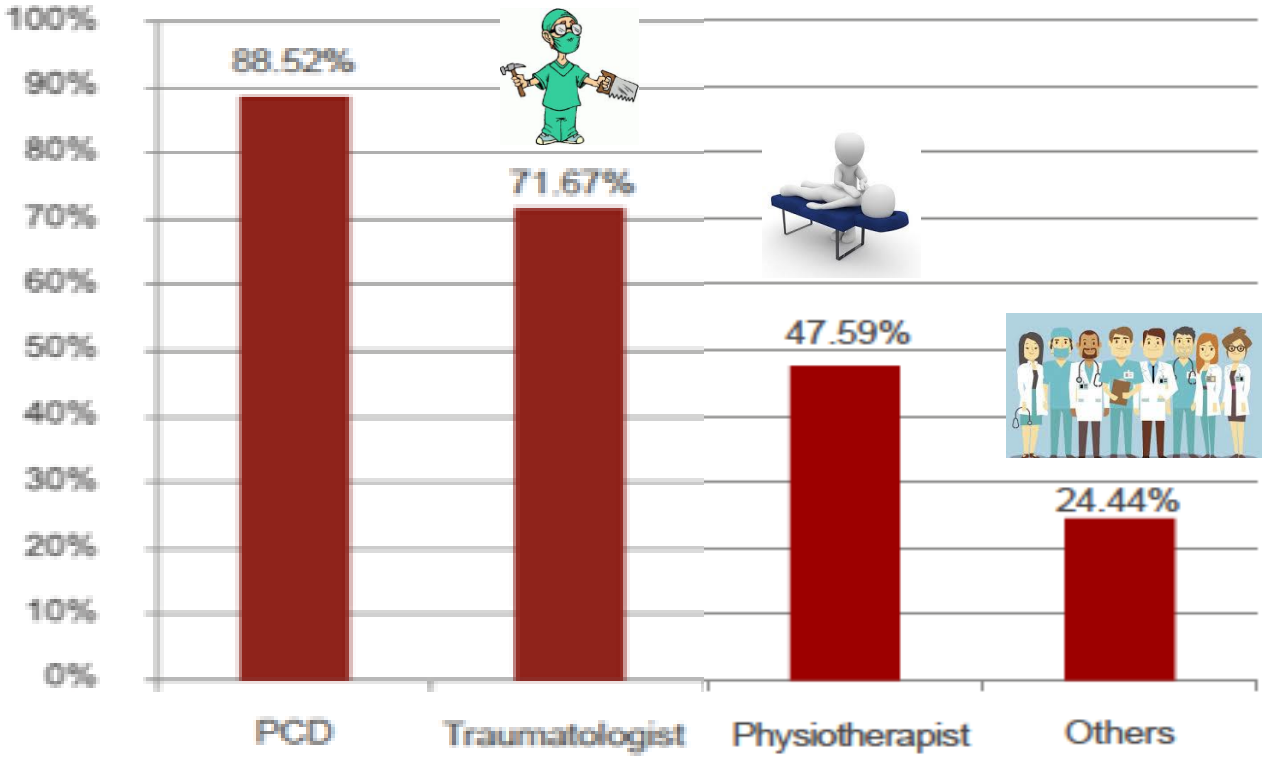
Garrido-Cumbrera M, et al. Rheumatology 2022;61:705–712

Atlas de Espondiloartritis Axial en España 2017

RADIOGRAFÍA DE LA ENFERMEDAD

The Patient Journey

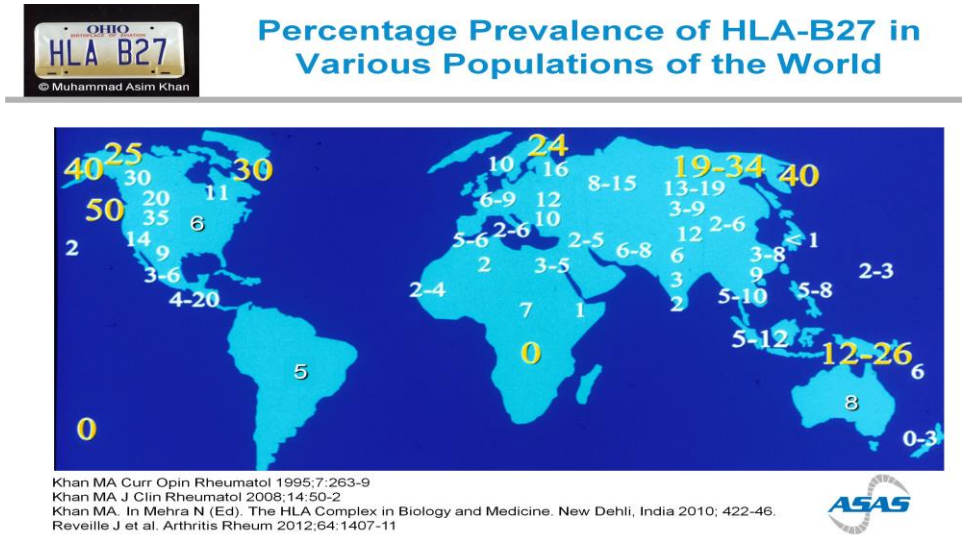




Source: 2017 Atlas patient survey

No gold standard tool to diagnose axSpA

HLA-B27

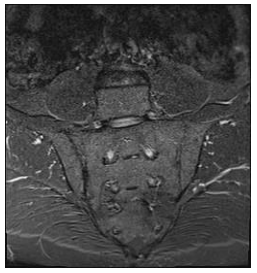


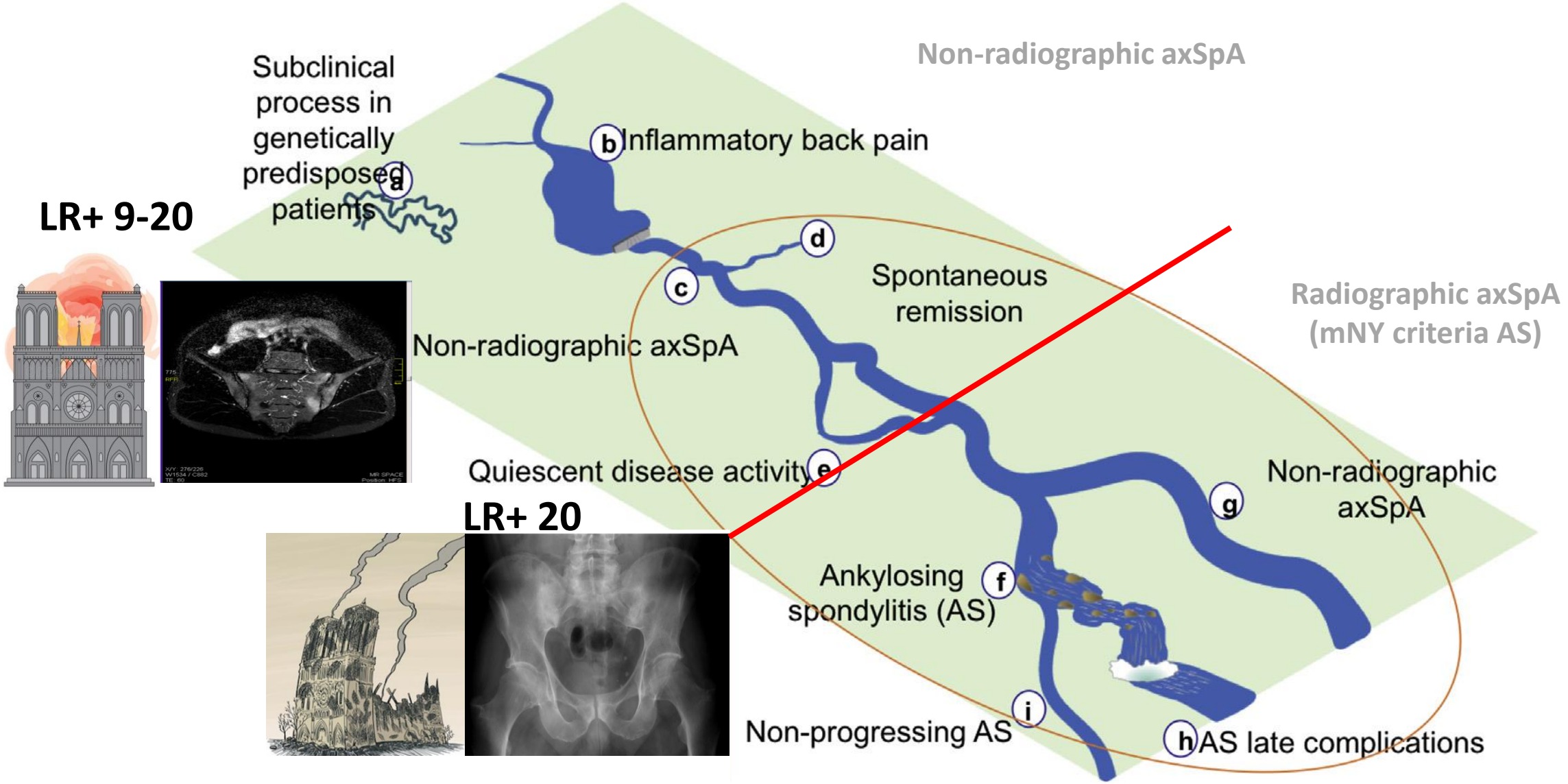
- 70-90%
- General population (0-50%)

Raised CRP/ESR

- Up to 40%
- Not very sensitive

Imaging

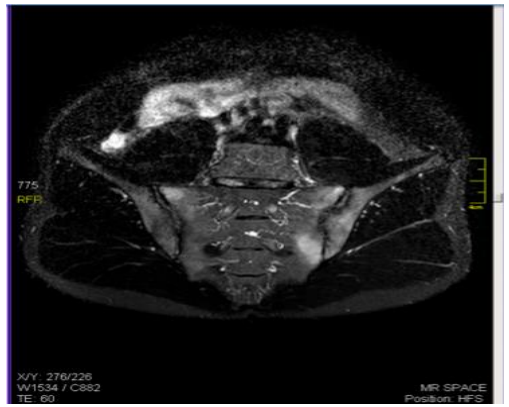


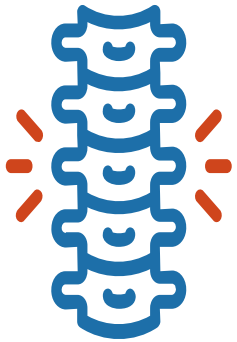


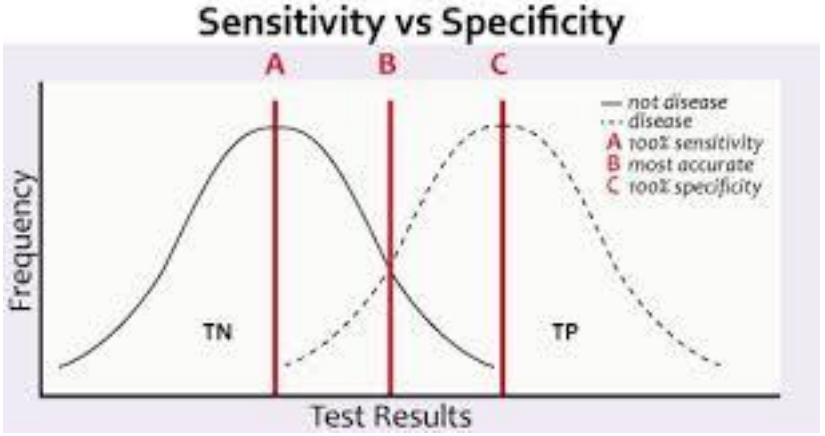
Garg N, et al. Best Pract Res Clin Rheumatol 2014;28(5):663-672

MRI Role in axSpA Diagnosis

Is MRI-SIJ the holy grail for diagnosis of axSpA?







Both, correct acquisition and interpretation of imaging are key for the diagnosis of axSpA

Caetano A, et al. Front Med (Lausanne). 2021;8:65853
Diekhoff T, et al. Skeletal Radiol. 2022;51(9):1721-30

Sacroiliitis on report ≠ axSpA

Pregnancy

- At Birth – 60%
- Month 6 – 15%

Physical Training

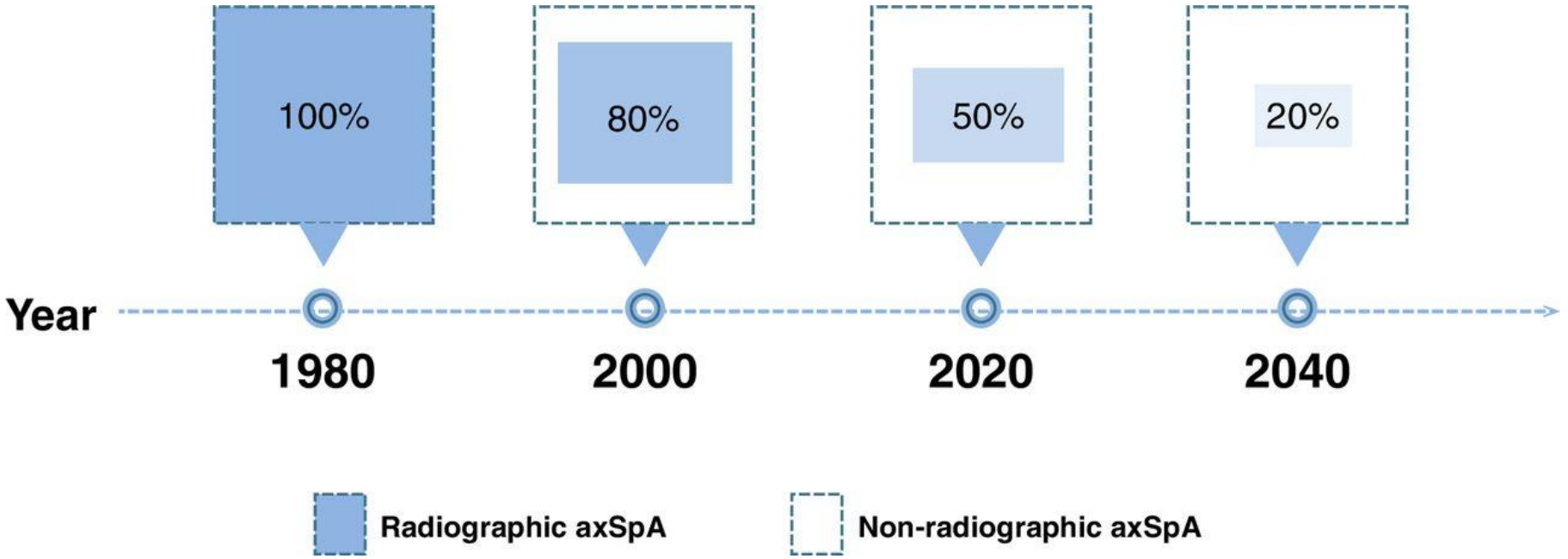
- Before training-22.7%
- After 6 wks training – 36.4%

Age

- 20-29 years – 2.8%
- 30-39 years – 16.1%
- 40-49 years – 17.9%

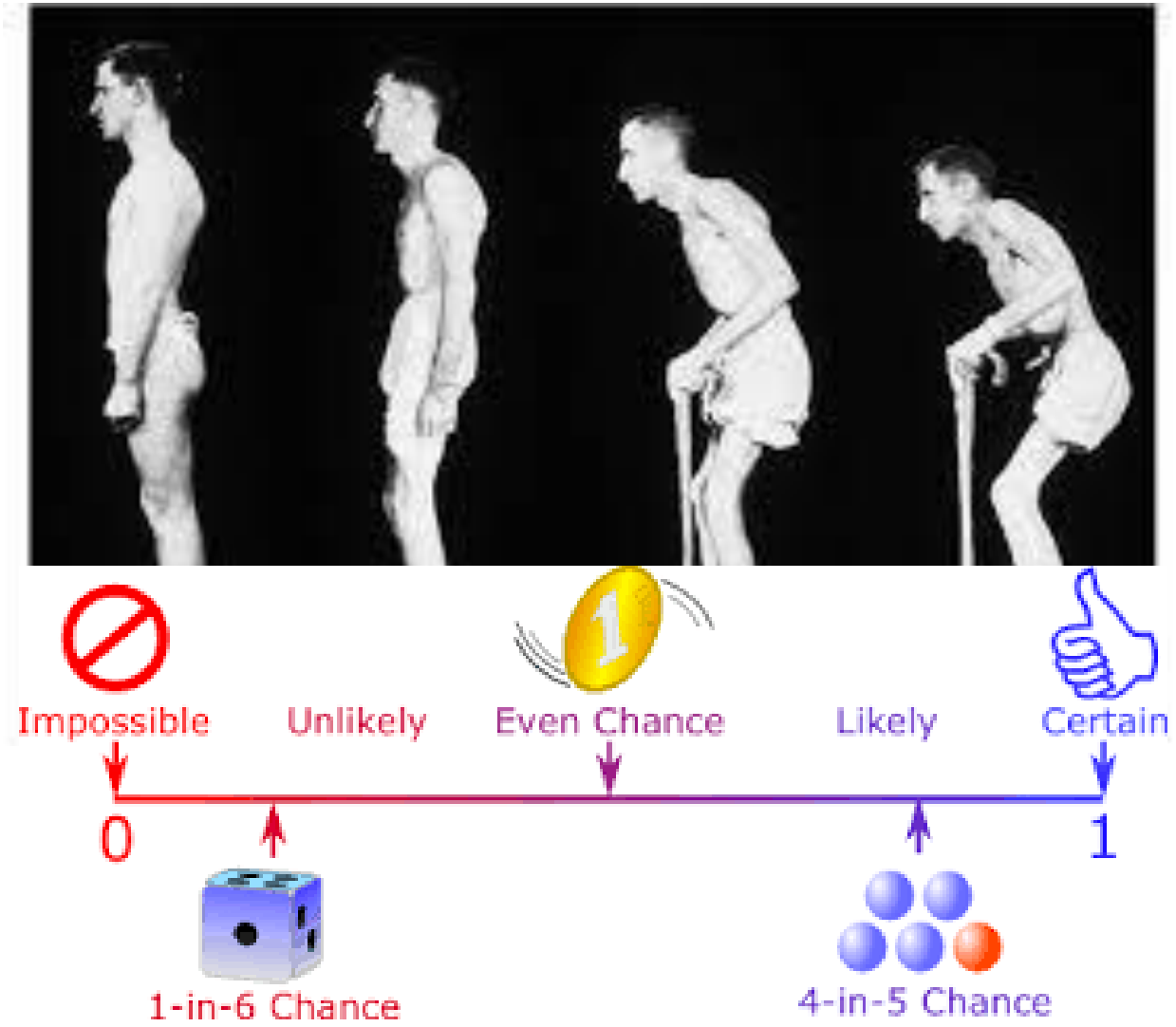
De Winter et al. Arthritis Rheumatol. 2018;70:1042–8

AxSpA Subtype at Diagnose Estimate



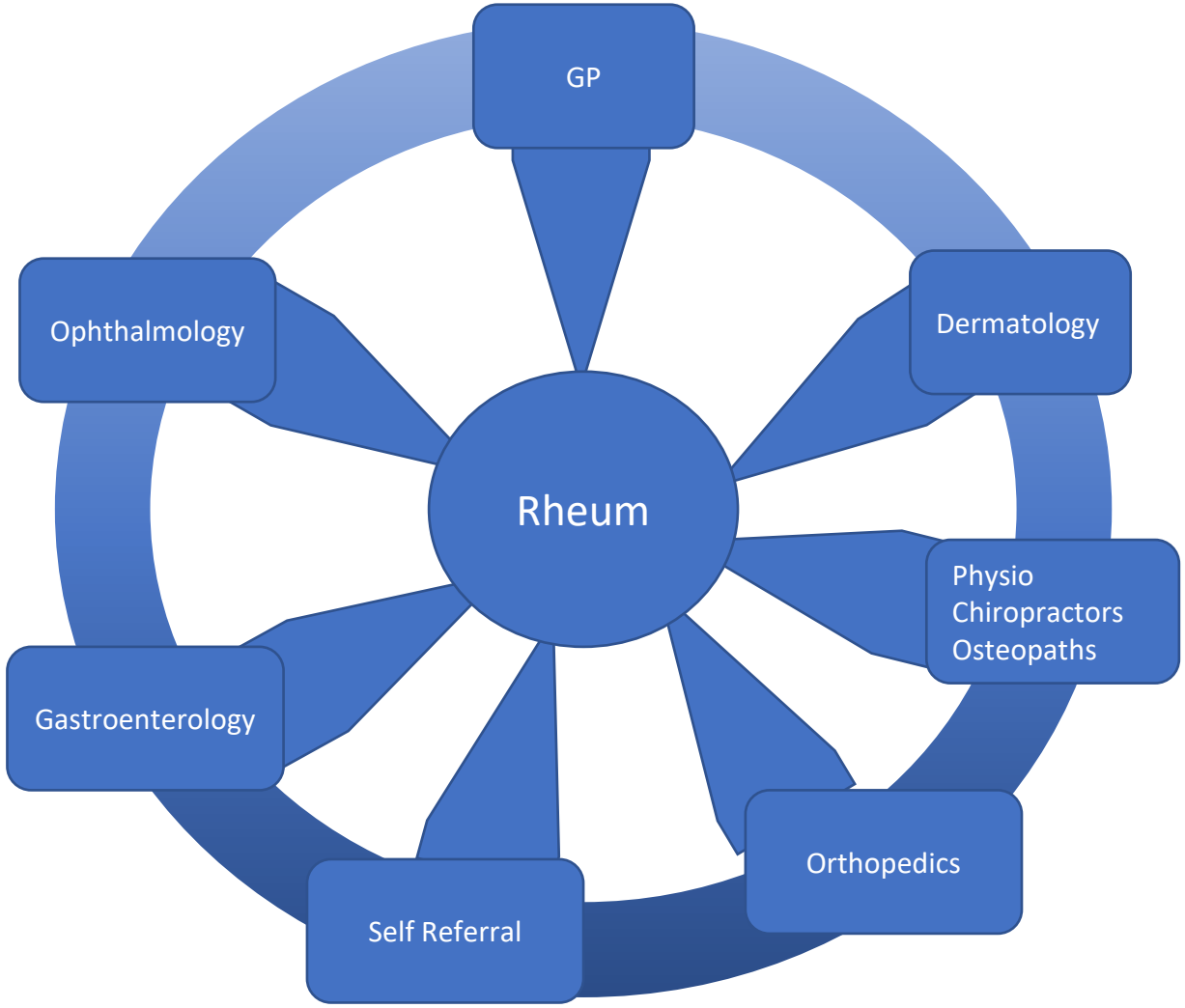
Benavent D et al. Clin Rheumatol 2021 Feb;40(2):501-512
Navarro-Compán V et al. Ann Rheum Dis 2021;80:1511-1521

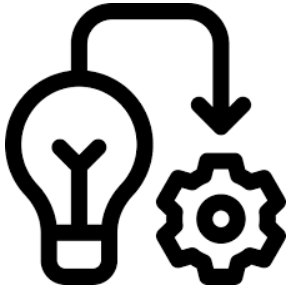
Certainty around Diagnosis of axSpA



Opportunity

Efficient and feasible referral strategies

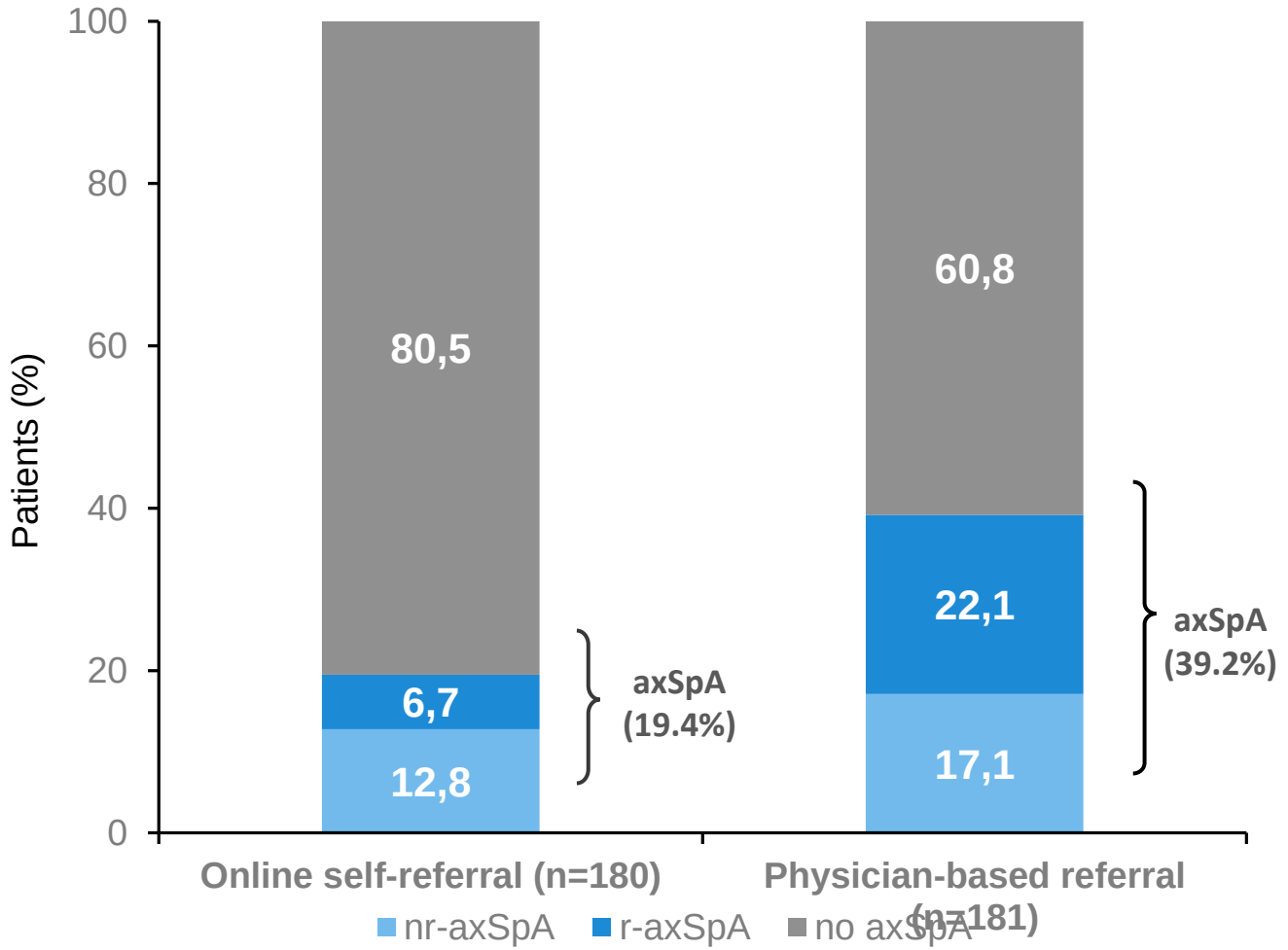




Navarro-Compán V, et al. her Adv Musculoskelet Dis. 2022 Jul 22;14

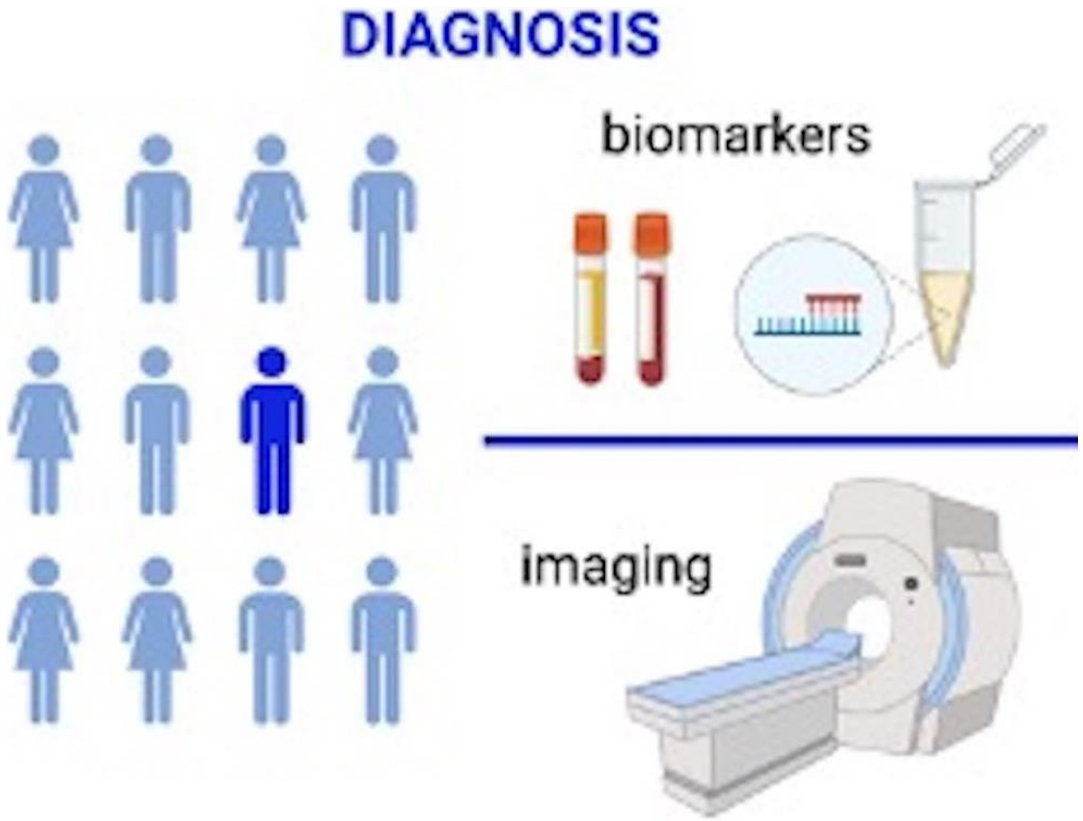
Online/ SM self-referral tools can be an effective for early diagnosis

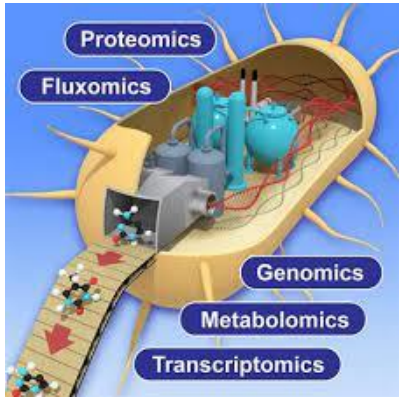
HLA- B27 negative
Females
Non-radiographic stage

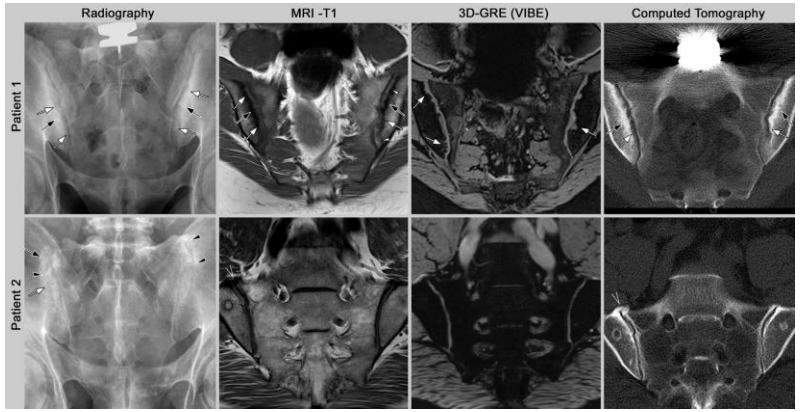


Proft F, et al. Semin Arthritis Rheum. 2020;50:1015–21

Tools for a precise diagnosis

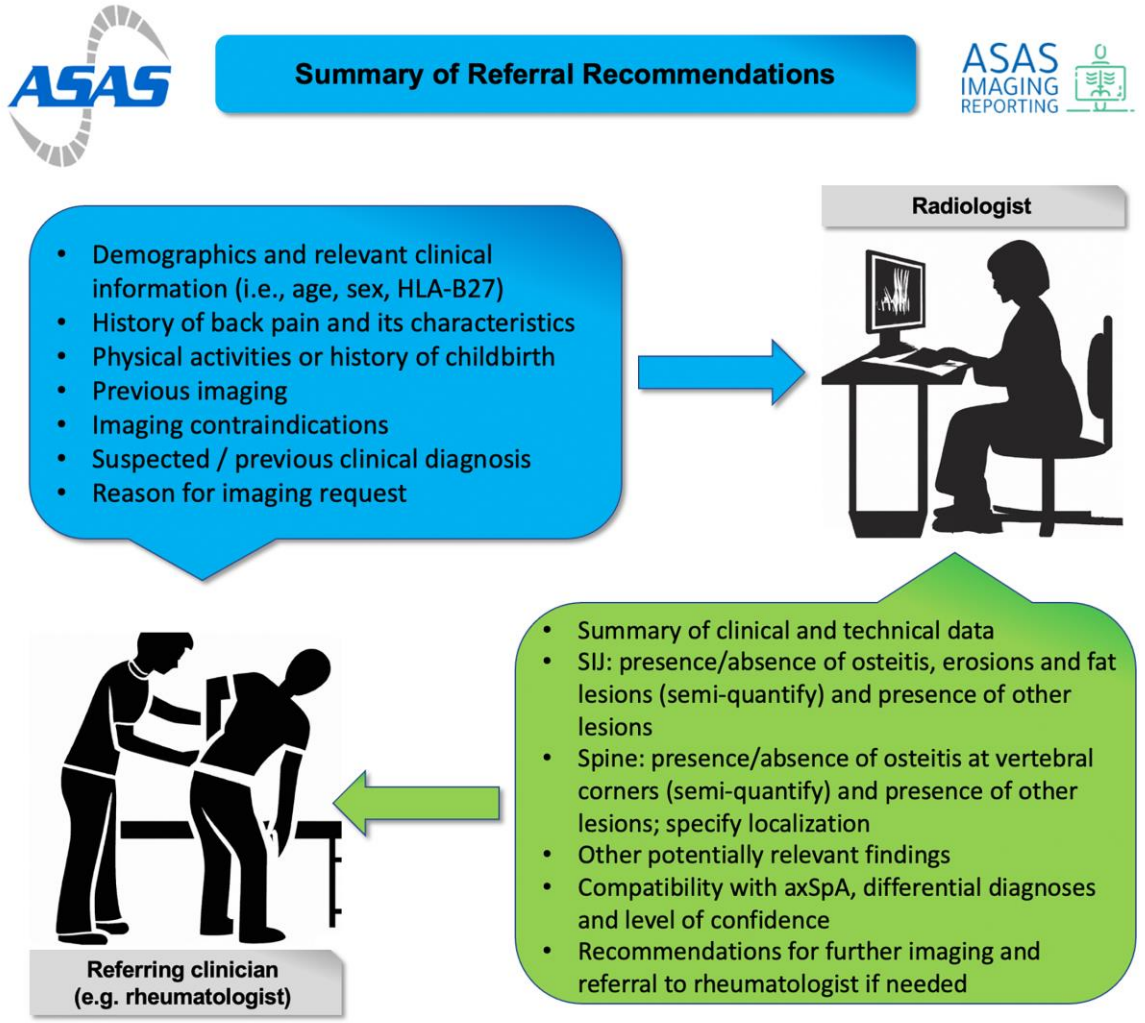






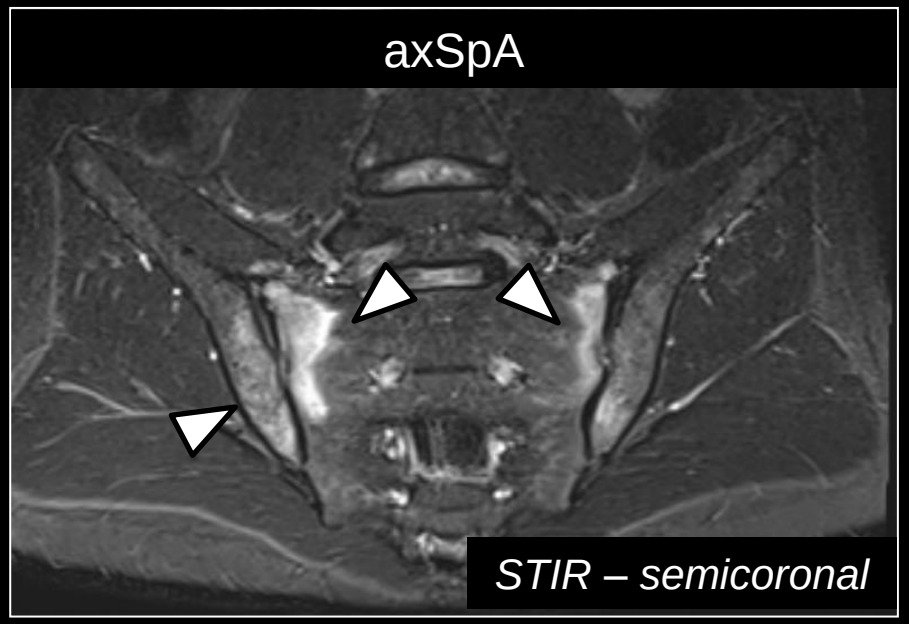
Navarro-Compán V, et al. Ther Adv Musculoskelet Dis. 2022 Jul 22;14:1759720X221111611
Poddubnyy D, et al. Ann Rheum Dis 2022;81:1486–1490

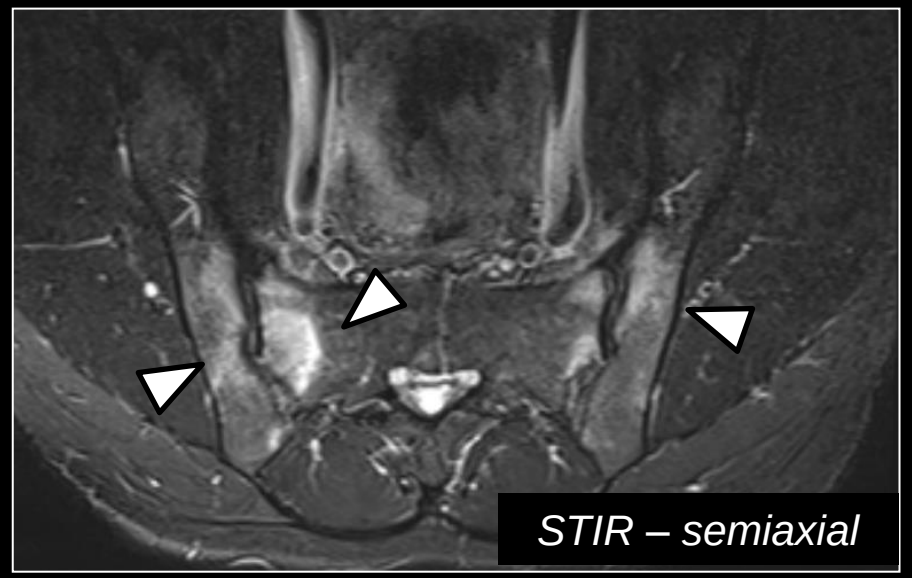
ASAS recommendations for requesting and reporting imaging examinations in patients with known or suspected axSpA

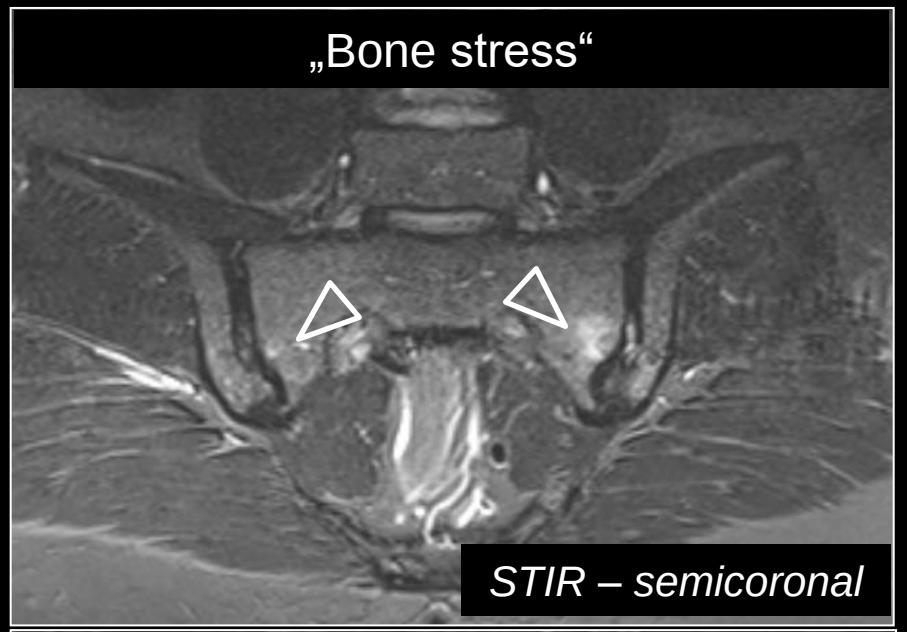


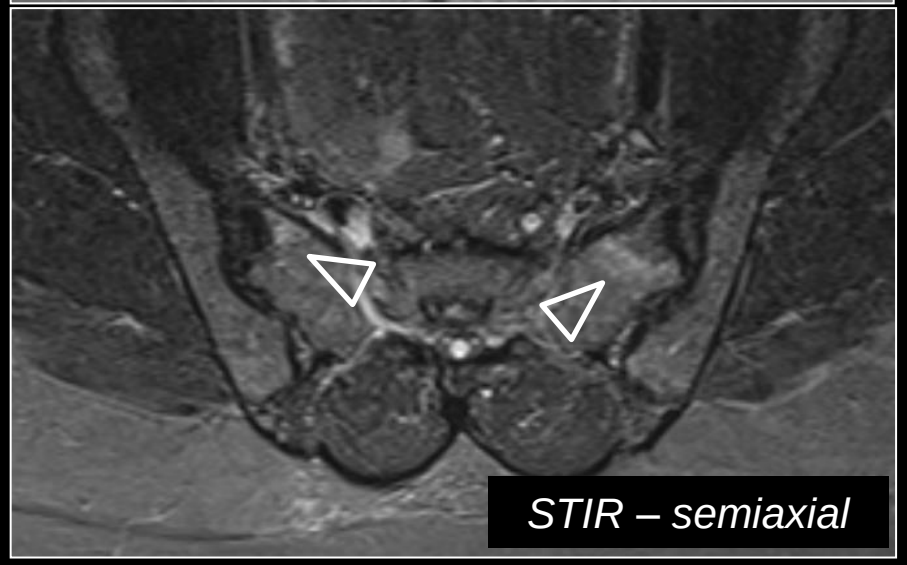
Diekhoff T, et al. Ann Rheum Dis 2022;81:97

The ability to distinguish between imaging lesions suggestive of axSpA and other diseases / artifacts is critical for accurate diagnosis[1]





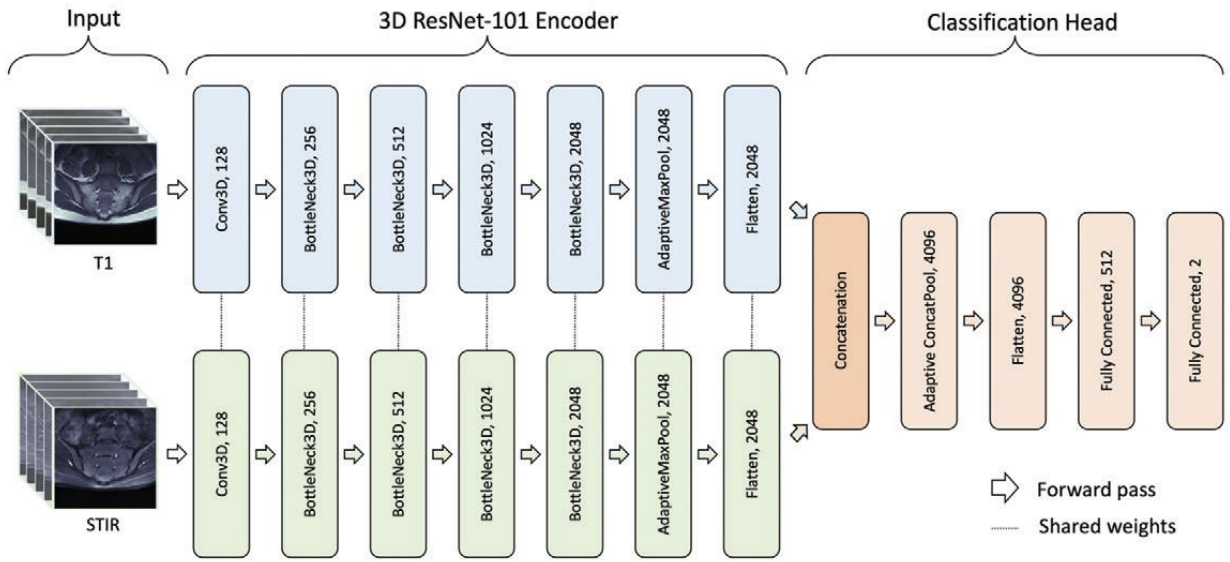


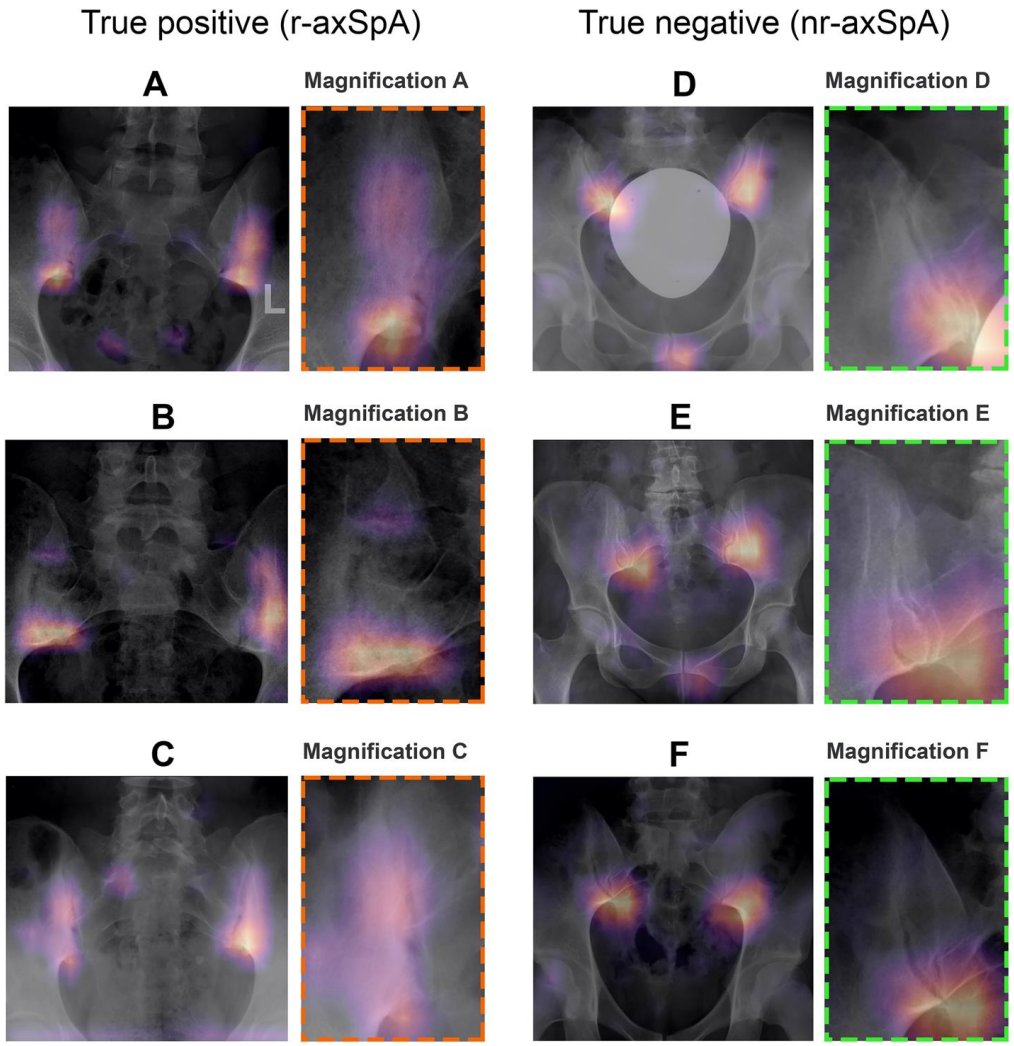


Caetano A, et al. Front Med (Lausanne). 2021;8:65853. Diekhoff T, et al. Skeletal Radiol. 2022;51(9):1721-30

Braun/Baraliakos 2018 and 2019

Deep learning for detection of sacroiliitis (xRay & MRI)

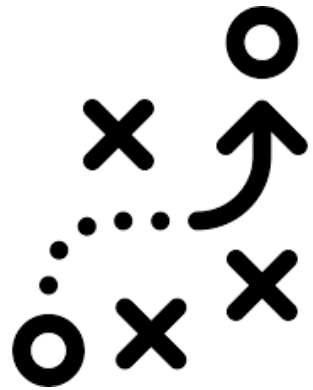




Bressem KK, et al. rthritis Res Ther. 2021 Apr 8;23(1):106
Bressem KK, et al. Radiology 2022; 305:655–665

wikiHow

Management



Management in axSpA: Goal and Target

Goal of therapy include:

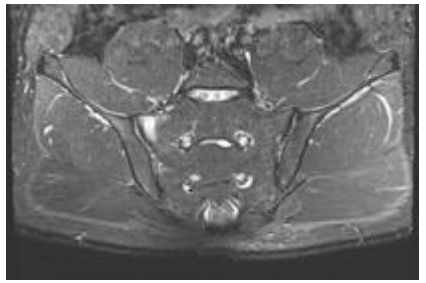
- Maximize health-related quality of life
- Control symptoms and inflammation
- Prevent structural damage
- Normalize/preserve function and social participation

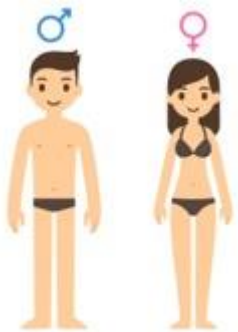
Treatment targets:

- Treatment should be guided according to a predefined treatment target
- Recommended target: sustained remission / LDA according to ASDAS
- A target should be a shared decision between patient and rheumatologist

Ramiro S, et al. Ann Rheum Dis. 2023 Jan;82(1):19-34
Smolen JS, et al. Ann Rheum Dis. 2018;77:3–17

Factors Associated with Radiographic Progression

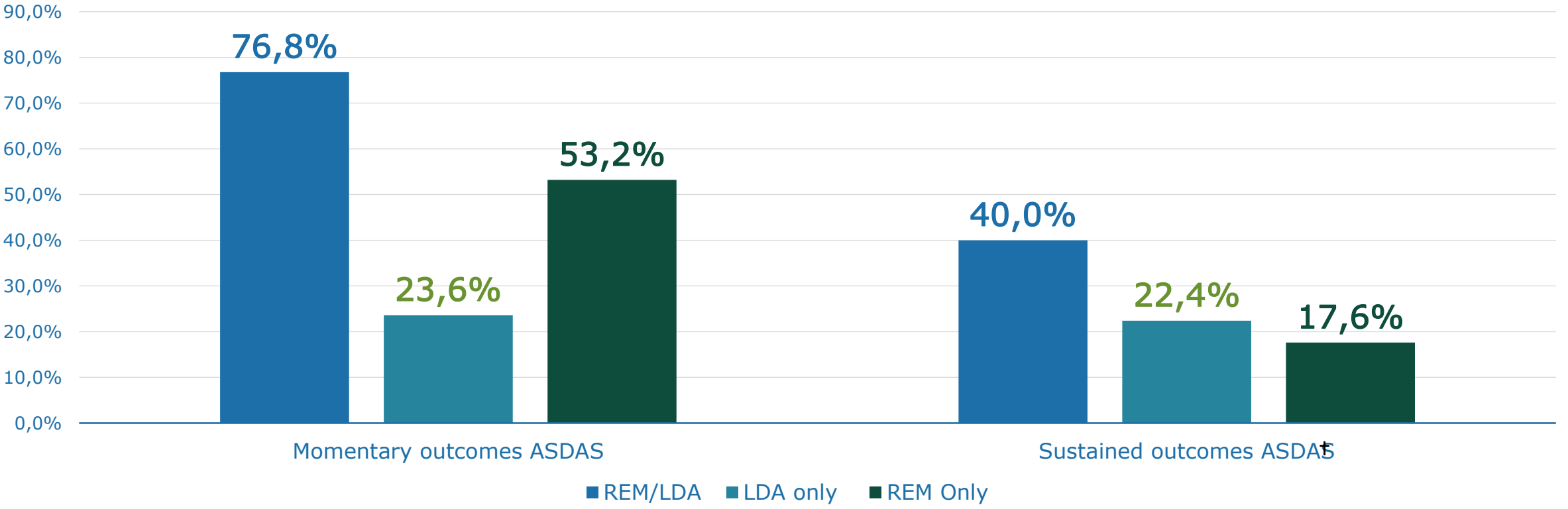




RADIOGRAPHIC PROGRESSION

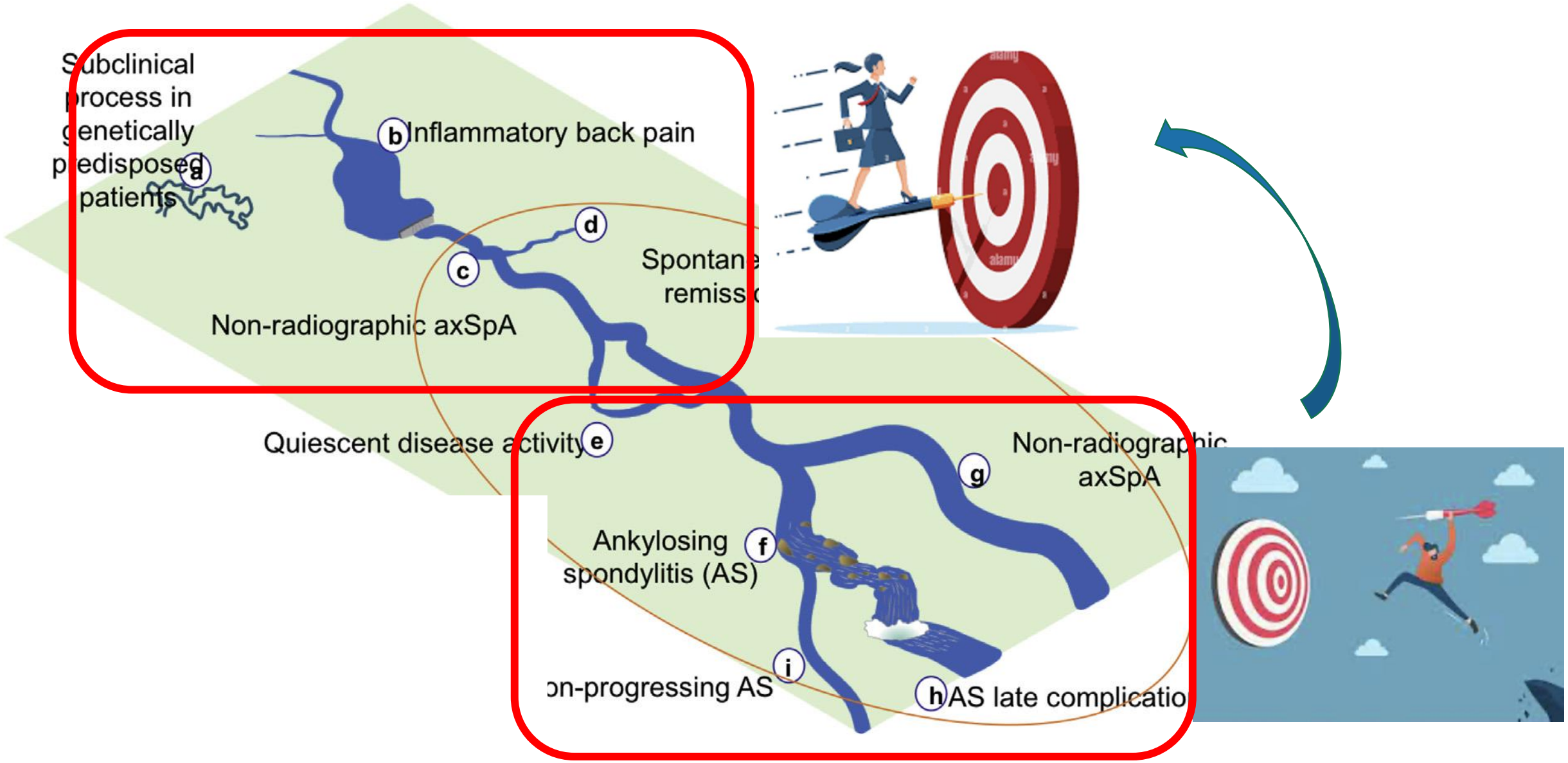
Less than half of axSpA patients on bDMARDs achieve sustained LDA/REM status in clinical practice

axSpA momentary and sustained ASDAS outcomes



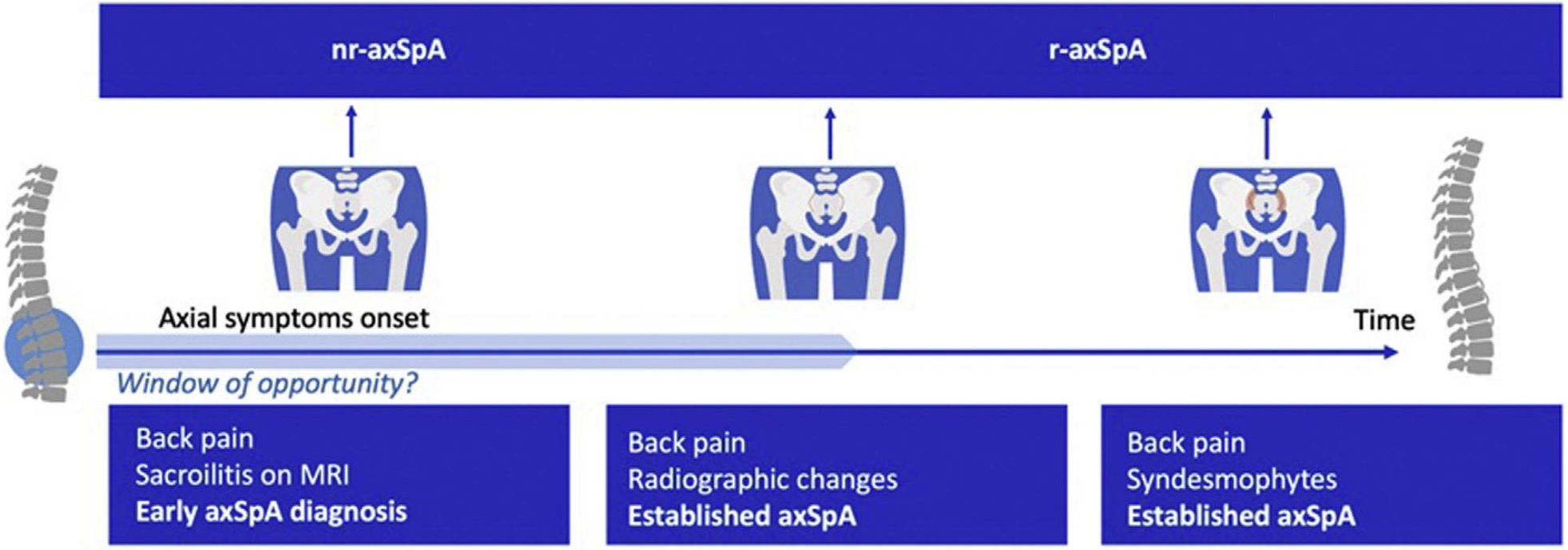
Benavent D et al. BMJ Open 2022; Apr 29;12(4):e057850

† Sustained REM was defined as ASDAS<1.3 and/or BASDAI <2 and normal CRP while sustained LDA was defined as ASDAS <2.1 and/or BASDAI <4 and normal CRP on at least three consecutive visits



Garg N, et al. Best Pract Res Clin Rheumatol 2014;28(5):663-672

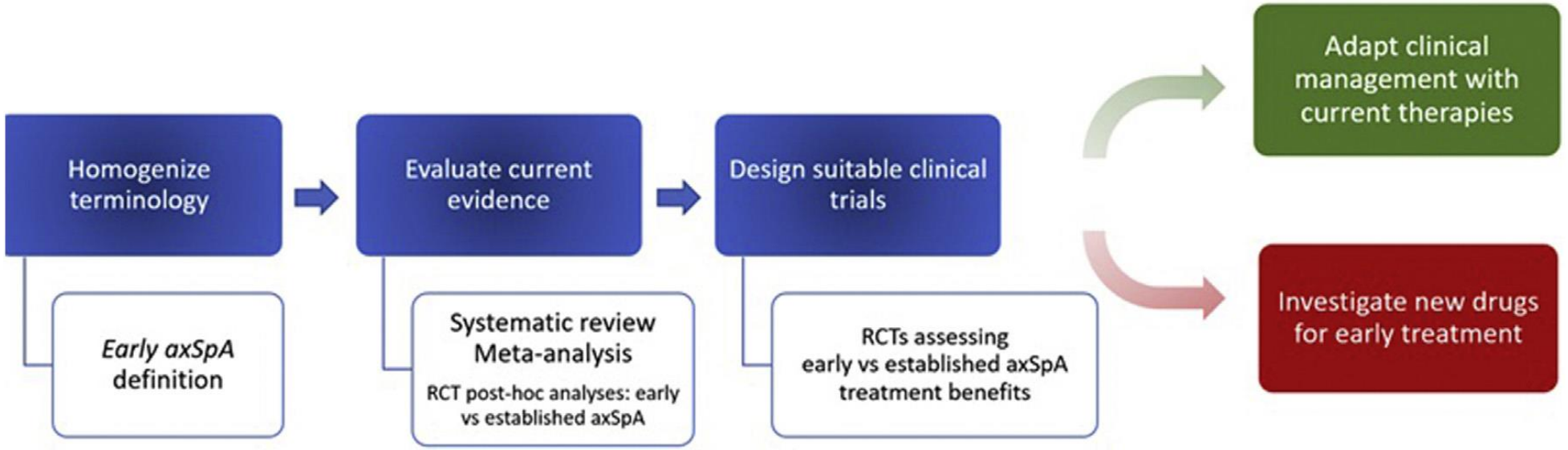
Window of Opportunity



axSpA, axial spondyloarthritis; nr-axSpA, non radiographic axSpA; r-axSpA, radiographic axSpA

Benavent D, et al. Joint Bone Spine. 2023 Jun 22;90(6):105603. doi: 10.1016/j.jbspin.2023.105603

Unmet needs and critical actions to investigate a potential window of opportunity in axSpA



axSpA, axial spondyloarthritis; RCT, randomized controlled trial

Benavent D, et al. Joint Bone Spine. 2023 Jun 22;90(6):105603. doi: 10.1016/j.jbspin.2023.105603

ASAS definition of early axial spondyloarthritis

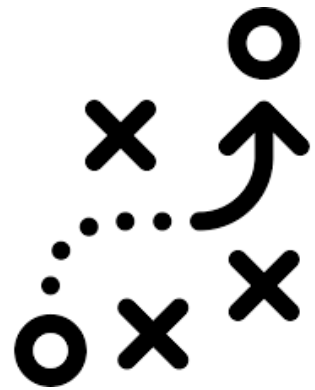
ASAS SPEAR
SPondyloarthritis: EARly definition

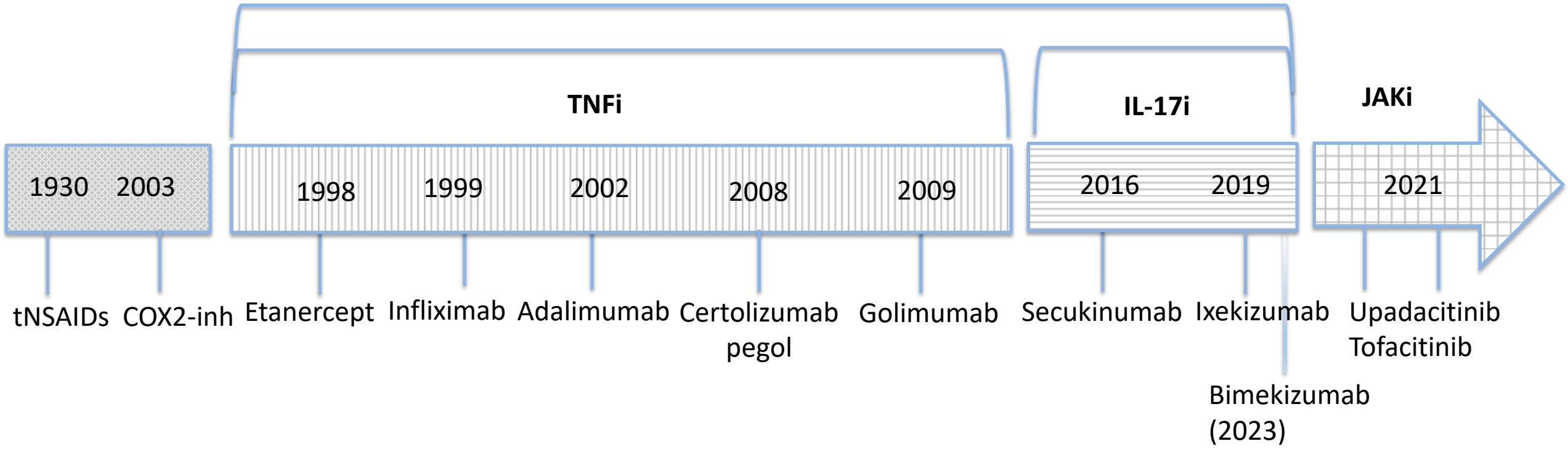
Patients with a diagnosis of axSpA with duration of axial symptoms of ≤2 years*

*Axial symptoms should include spinal/buttock pain or morning stiffness and should be considered by a rheumatologist as related to axSpA.

Navarro-Compán V, et al. Ann Rheum Dis. 2023 Jun 15:ard-2023-224232

ASAS Assessment of SpondyloArthritis international Society

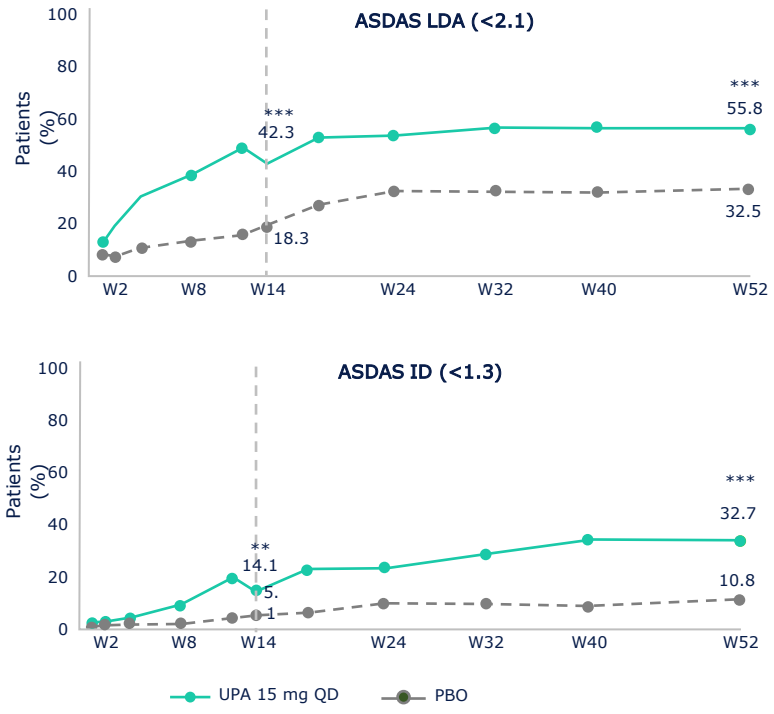



NSAIDs
bDMARDs
tsDMARDs
TNFi
IL-17i
JAKi
1930
2003
1998
1999
2002
2008
2009
2016
2019
2021
tNSAIDs
COX2-inh
Etanercept
Infliximab
Adalimumab
Certolizumab pegol
Golimumab
Secukinumab
Ixekizumab
Upadacitinib
Tofacitinib
Bimekizumab (2023)

tsDMARDs (JAKi)
Target achievement: sustained LDA/remission

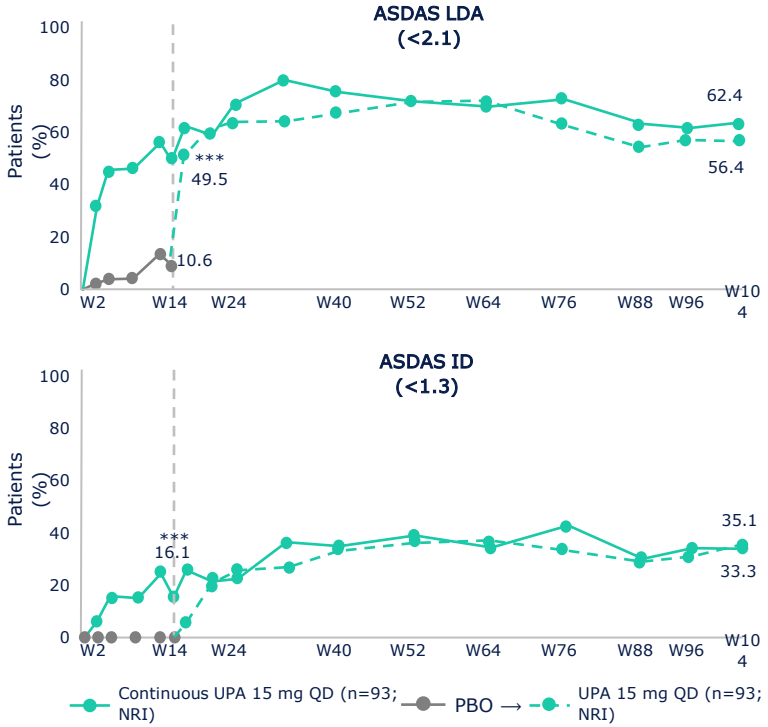
nr-axSpA

SELECT-AXIS 2
bDMARD-naïve/bDMARD-IR

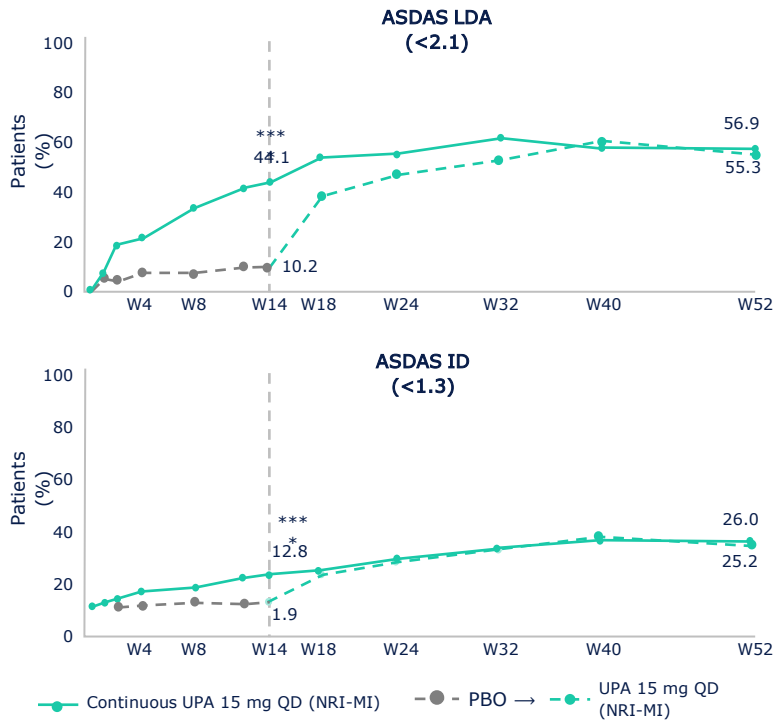


r-axSpA

SELECT-AXIS 1
bDMARD-naïve (up to week 104)



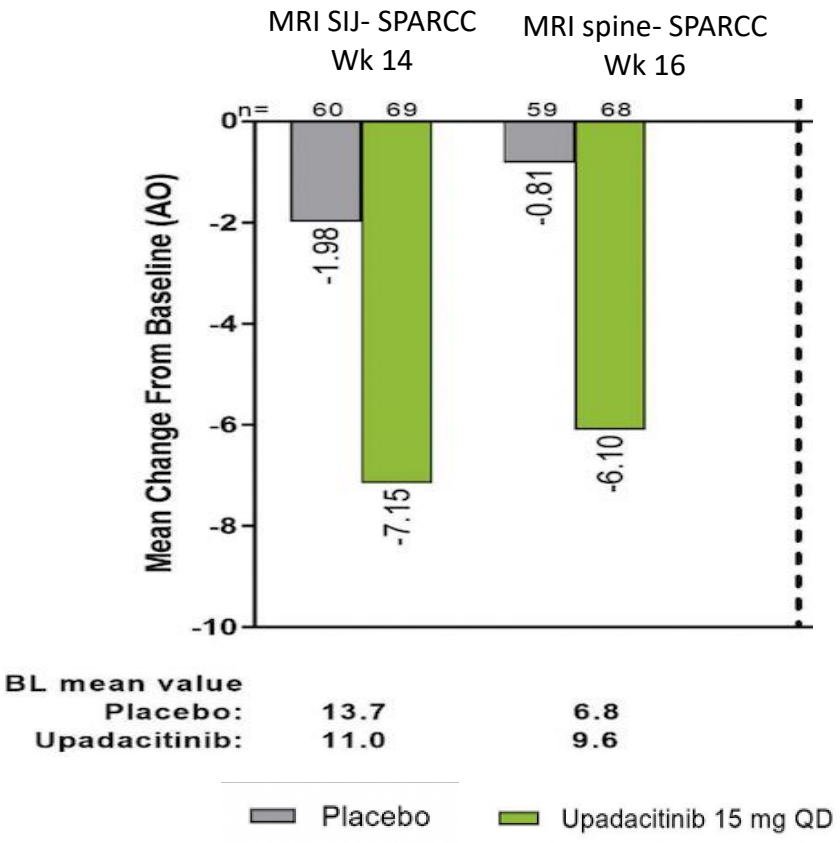
SELECT-AXIS 2
bDMARD-IR



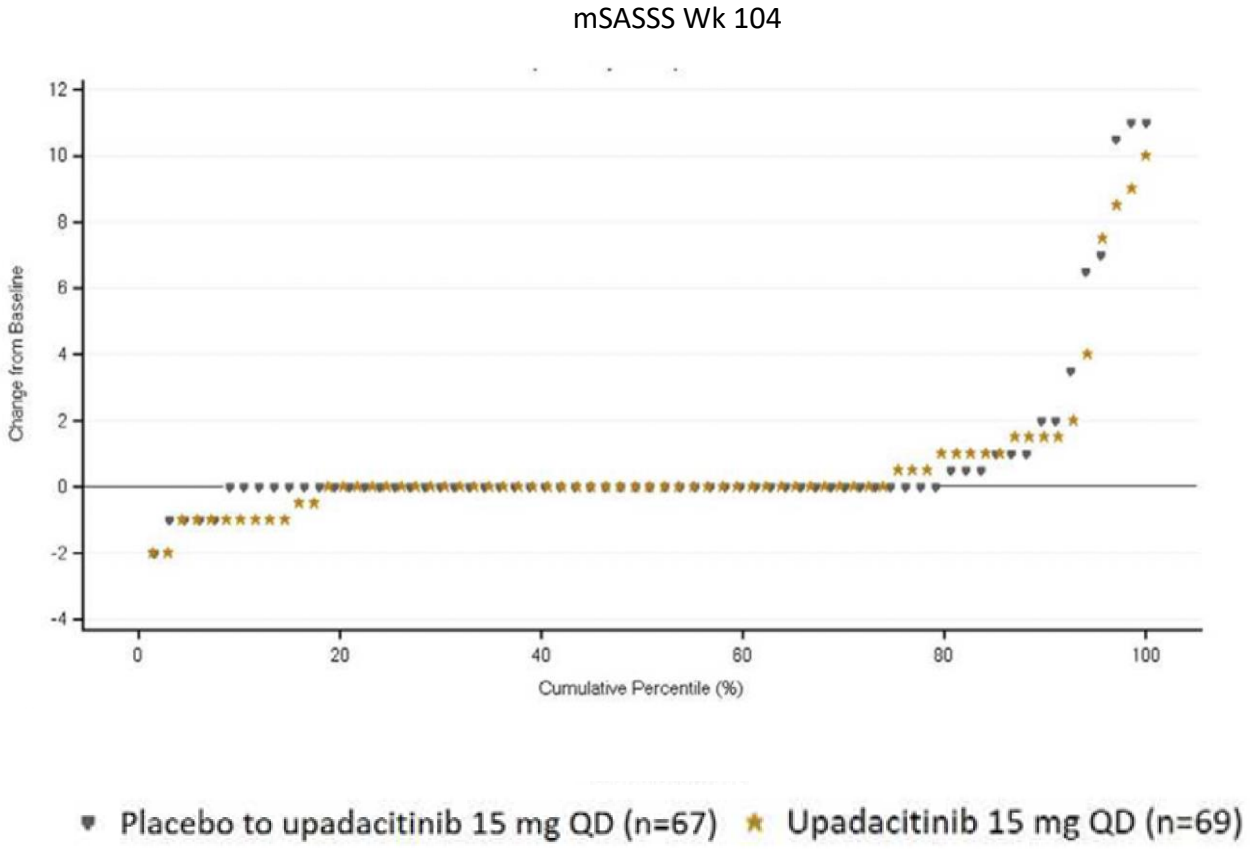
Deodhar A, et al. Lancet. 2022;400(10349):369-79; van den Bosch F, et al. EULAR 2023. Milan, Italy; van der Heijde D, et al. RMD Open. 2022;8(2):e002280 van der Heijde D, et al. Ann Rheum Dis. 2022;81(11):1515-23, Baraliakos X, et al. EULAR 2023. Milan, Italy.

tsDMARDs (JAKi): Objective signs of inflammation and structural damage

Inflammatory lesions on MRI



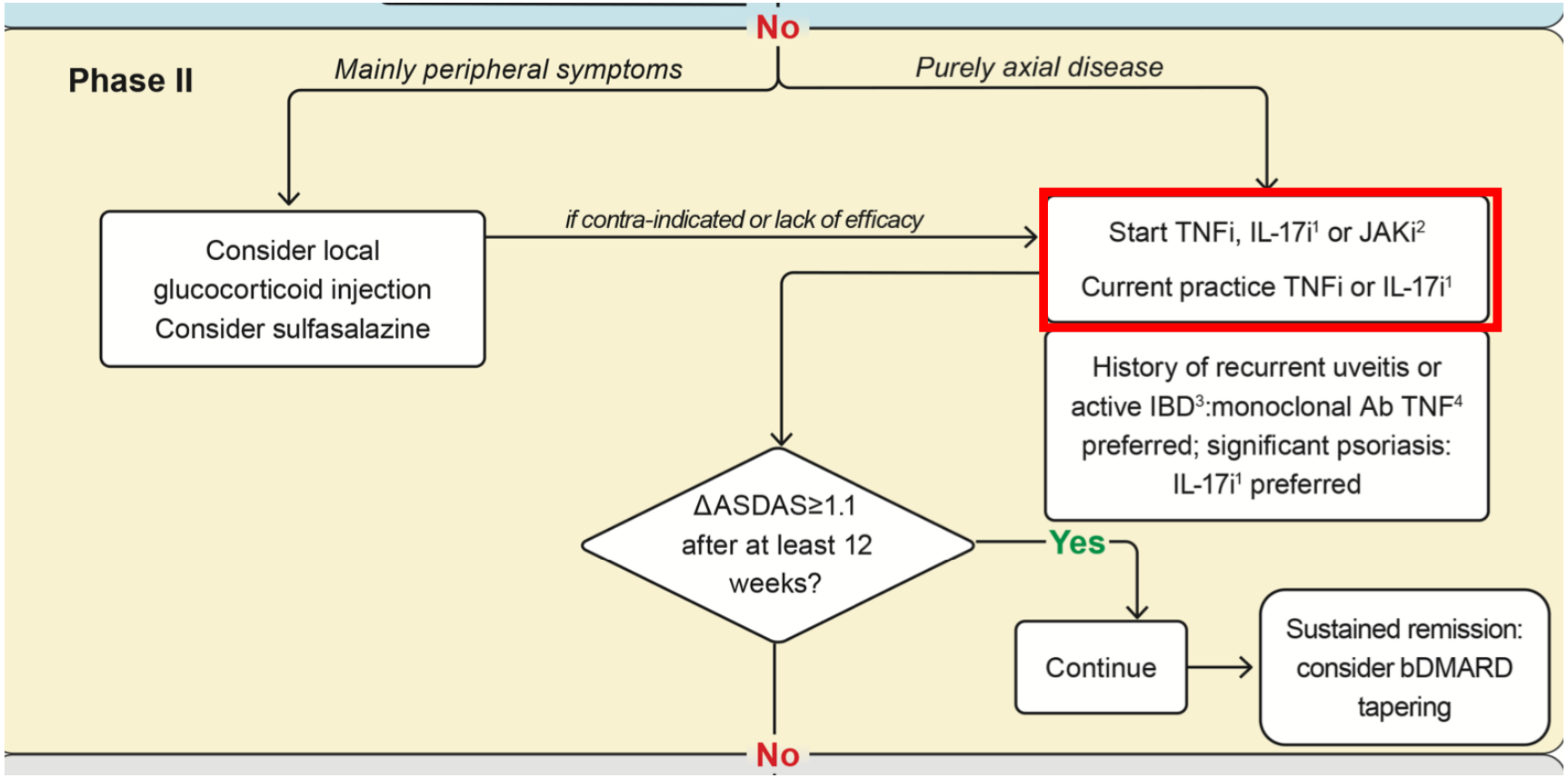
Radiographic progression (xRay)



van der Heijde D, et al. RMD Open 2022; 8:e002280

Re-phrased

ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update

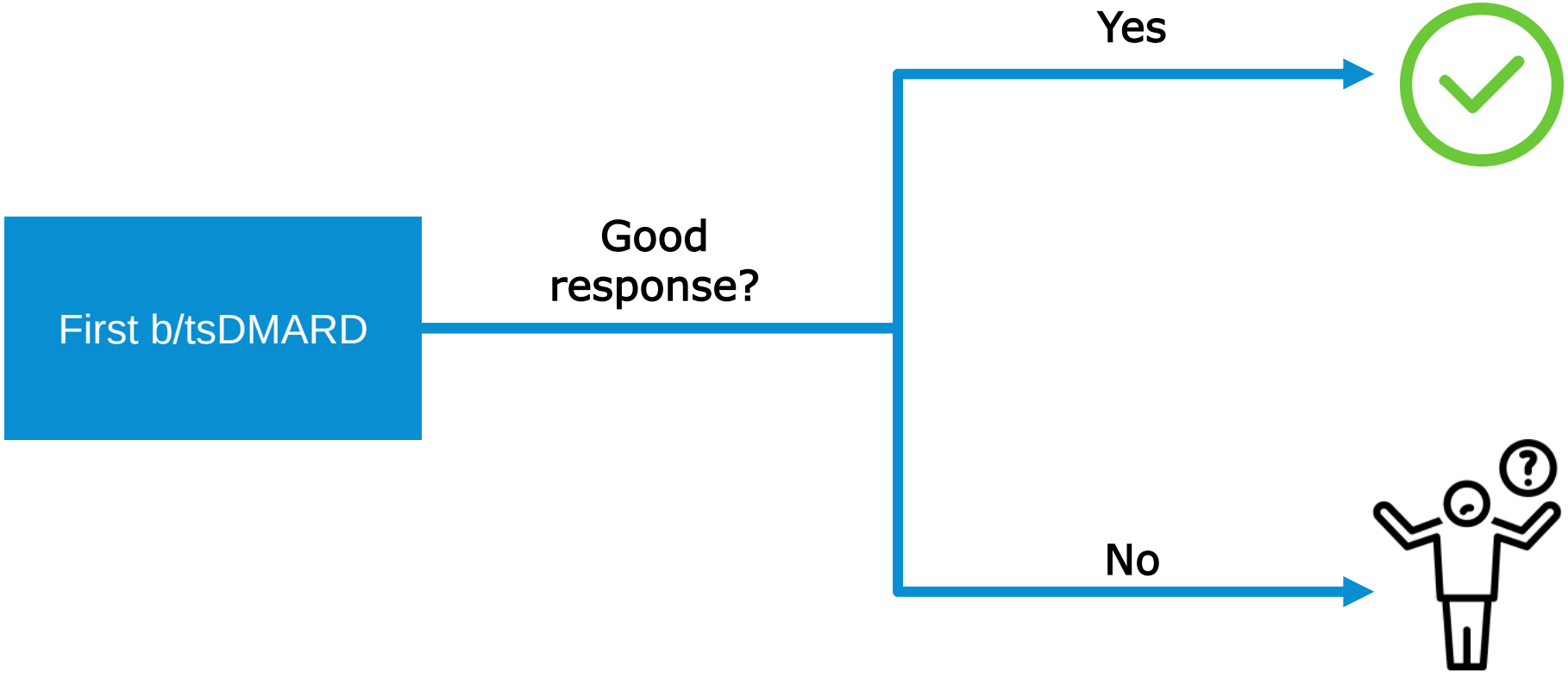


Recommendation 9
bDMARDs should be considered in patients with persistently high disease activity despite conventional treatments (figure 1); current practice is to start with TNFi therapy

TNFi, IL-17i*or JAKi should be considered in patients with persistently high disease activity despite conventional treatments; **current practice is to start a TNFi or IL-17i*.**
**IL17i: refers only to IL-17A-inhibitors*

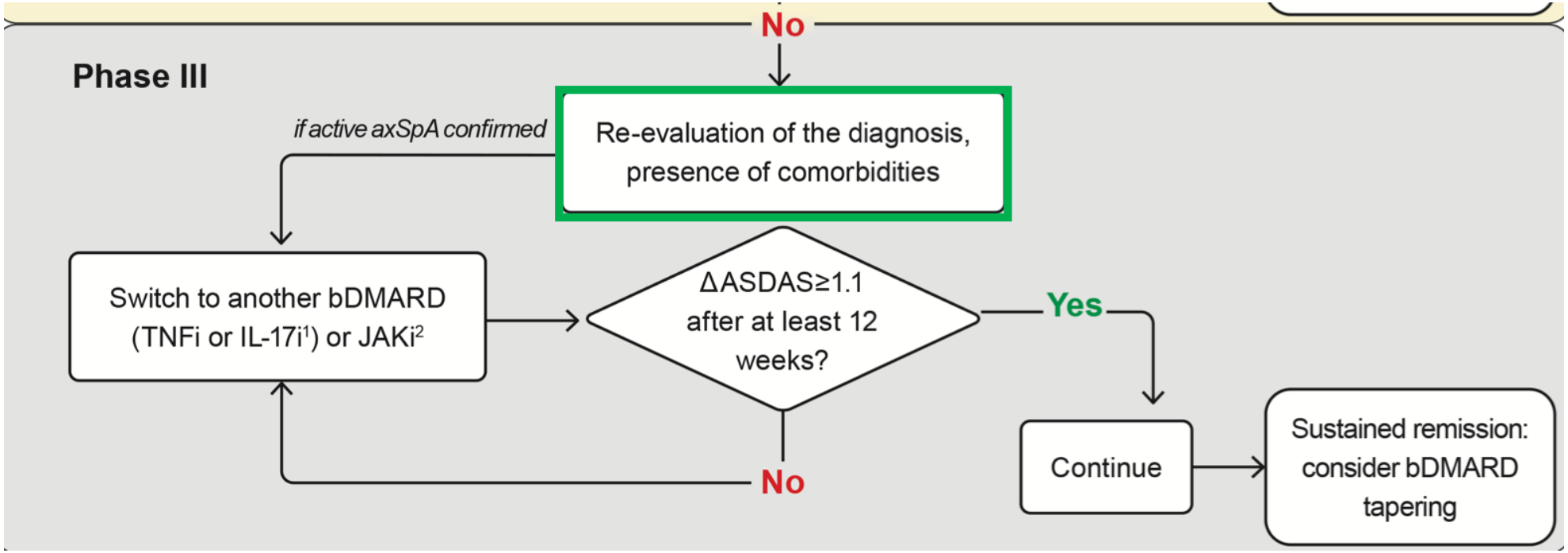
Ramiro S, , *et al.* Ann Rheum Dis. 2023 Jan;82(1):19-34

Strategy to manage D2T axSpA



New

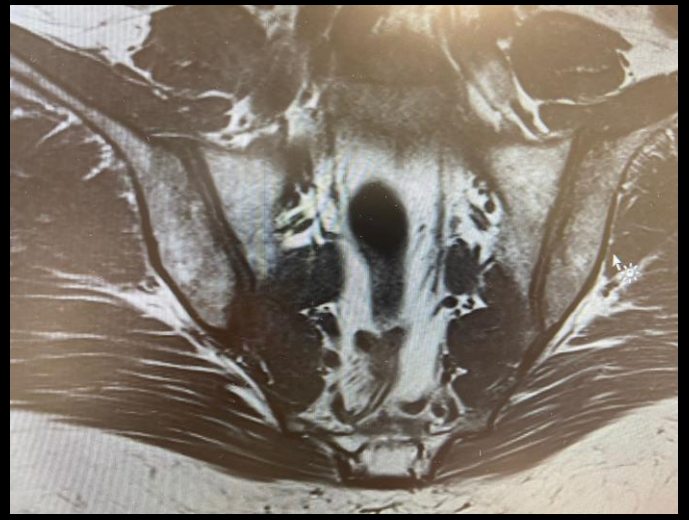
ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update



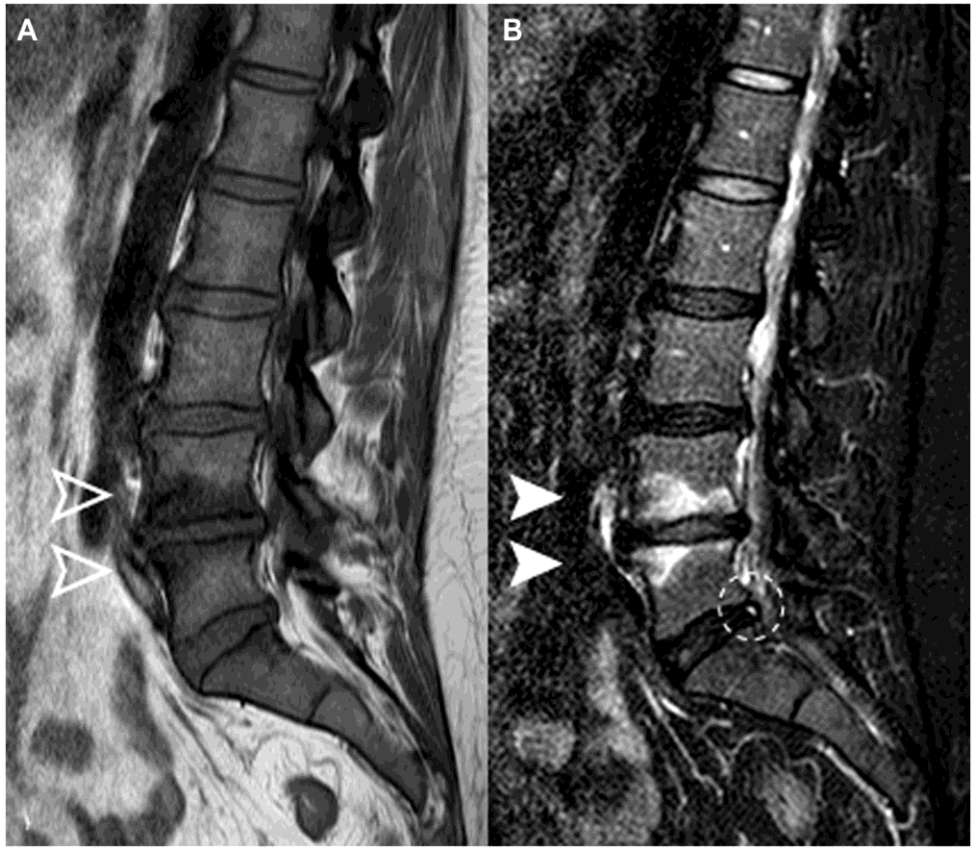
Recommendation 11
Absence of response to treatment should trigger **re-evaluation of the diagnosis** and consideration of the presence of **comorbidities**.

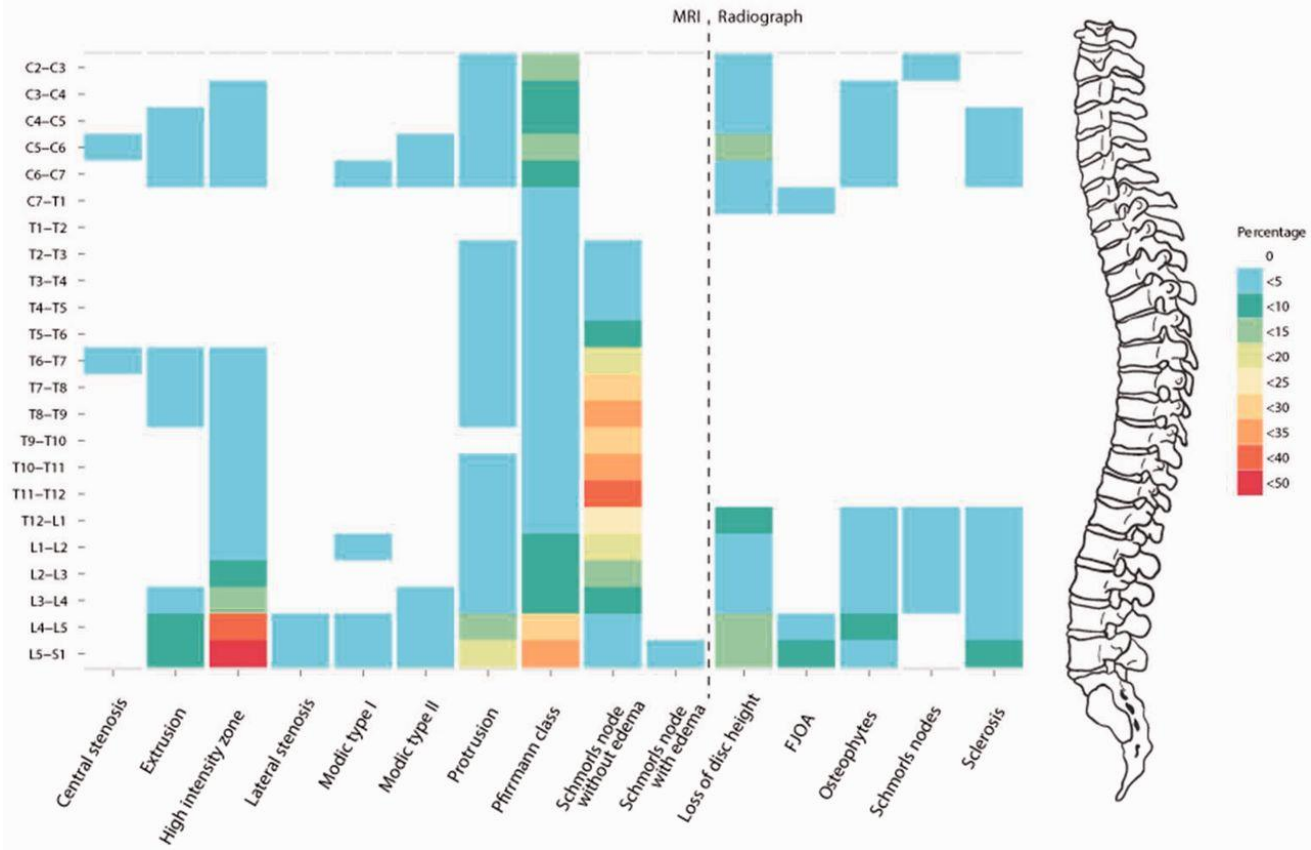
Ramiro S, , *et al.* Ann Rheum Dis. 2023 Jan;82(1):19-34

MRI Report: Sacroiliitis



Comorbidities: Degenerative spinal changes in axSpA

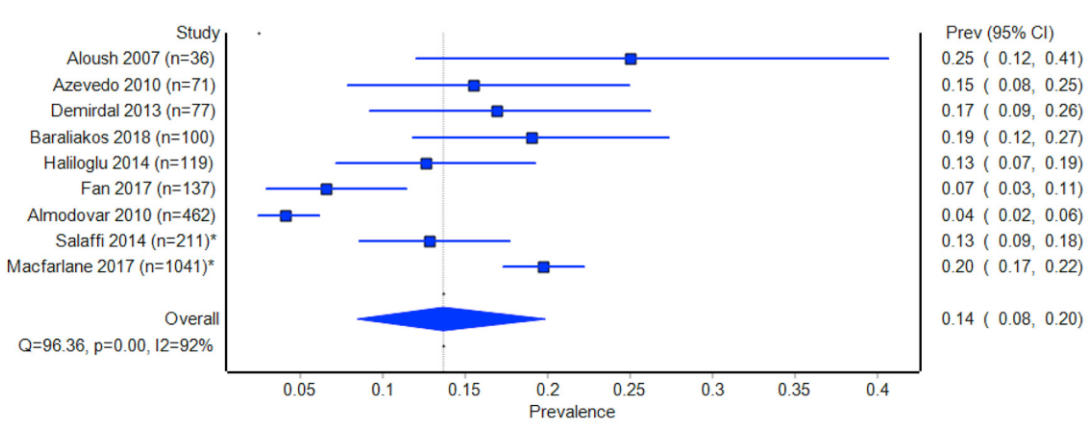




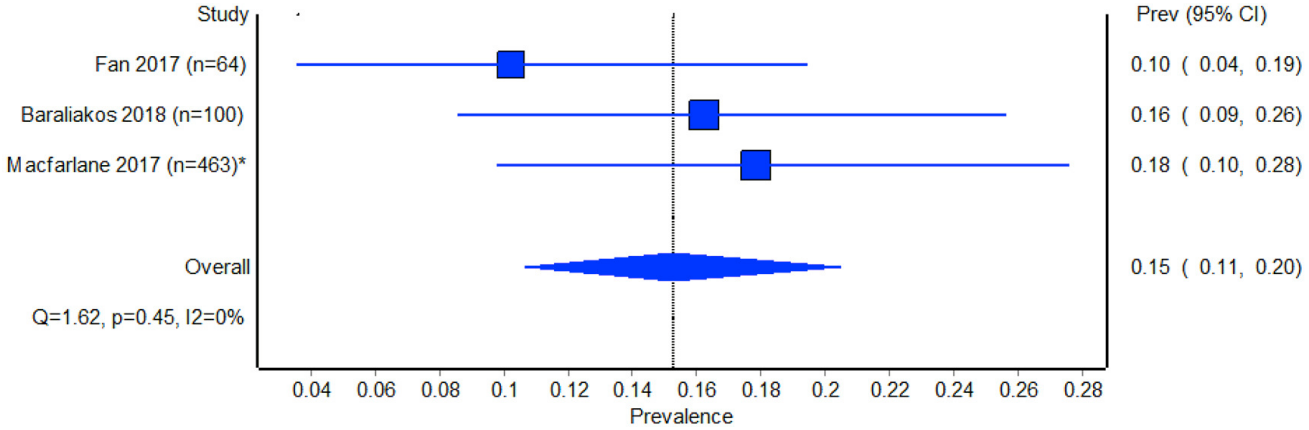
De Bruin F, et al. Rheumatology (Oxford). 2023 Apr 24:kead162. doi: 10.1093

Comorbidities: Concomitant Fibromyalgia

14% of Ankylosing Spondylitis Patients have Comorbid FM



15% of Non-Radiographic Axial Spondylitis Patients have Comorbid FM



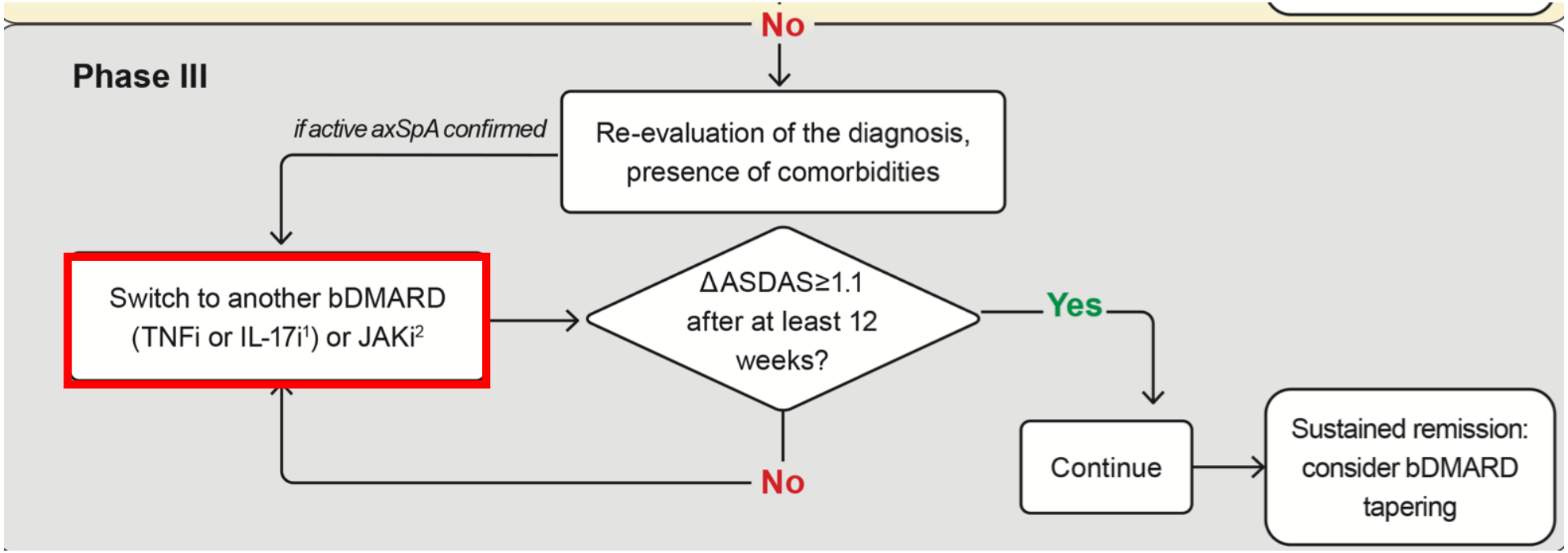
Registry data has found that the prevalence of FM is much more common in women (10.5%) with axSpA compared to men (1.0%)

1.

Zhao SS, et al. Best Practice & Research Clinical Rheumatology. 2019;33(3):101423
Mease PJ, et al. The Journal of Rheumatology. 2021;48(10):1528-1536

Re-phrased

ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update



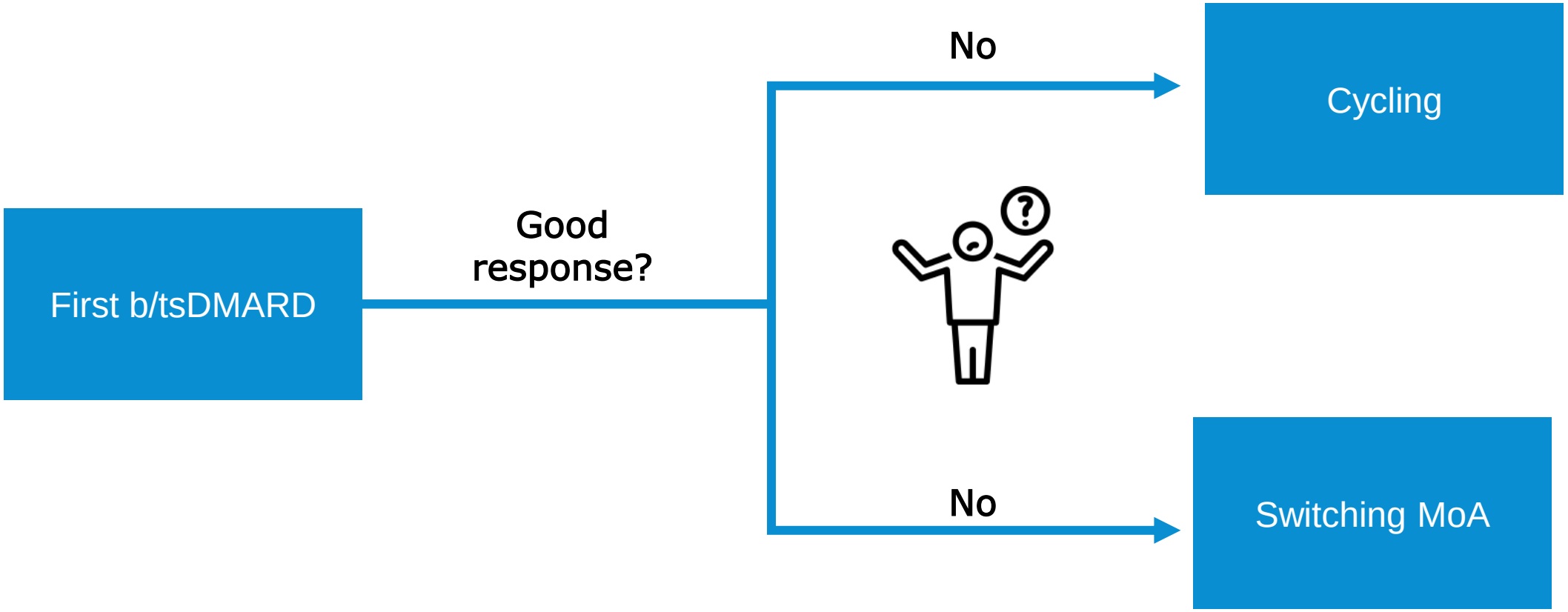
Recommendation 10
If TNFi therapy fails, switching to another TNFi or an anti-IL-17 therapy should be considered

Following a first b/tsDMARD failure, **switching to another bDMARD (TNFi or IL-17i*) or a JAKi** should be considered.

**IL17i: refers only to IL-17A-inhibitors*

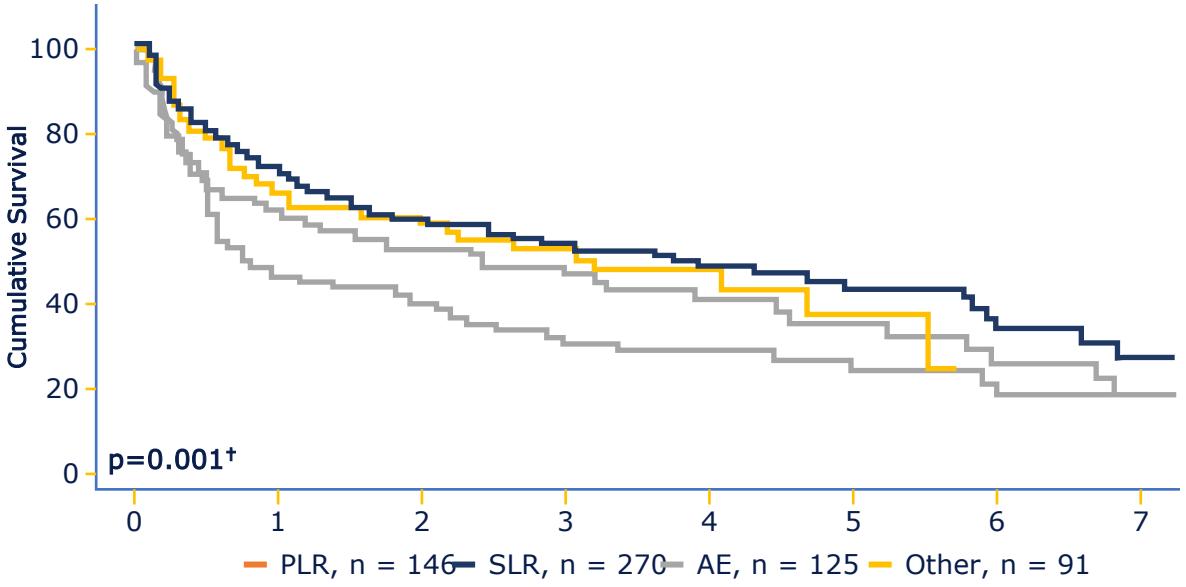
Ramiro S , et al. Ann Rheum Dis. 2023 Jan;82(1):19-34

Strategy to manage D2T axSpA



Cycling TNFi - Data from Swiss Registry

Persistence to 2nd TNFi following prior TNFi failure

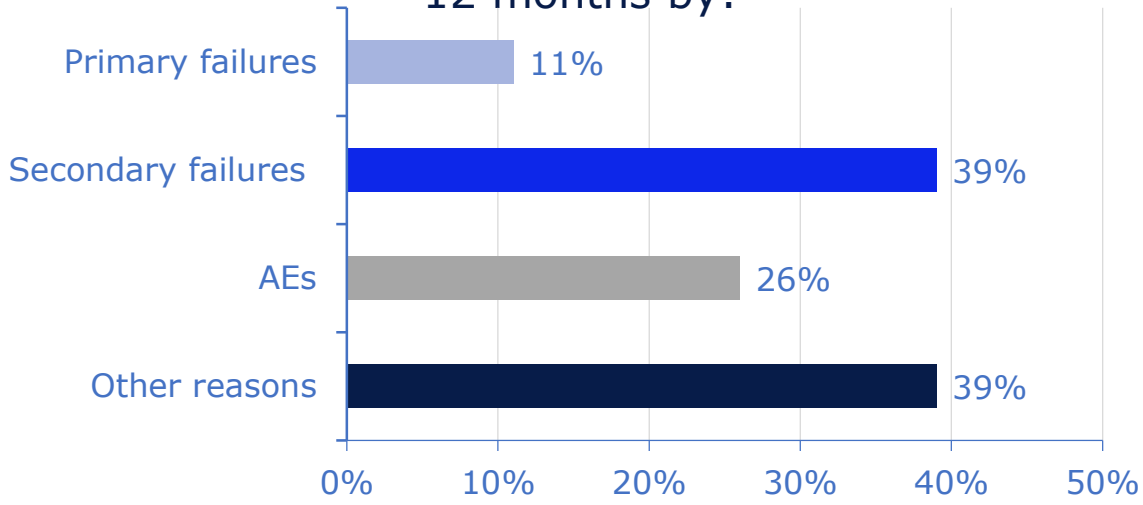


Median survival of a second TNFi was (N=632)

- 1.1 years after primary failure
- 3.8 years after secondary failure (p=0.003)

Target achievement after TNFi failure

ASDAS-LDA was significantly achieved after 12 months by:

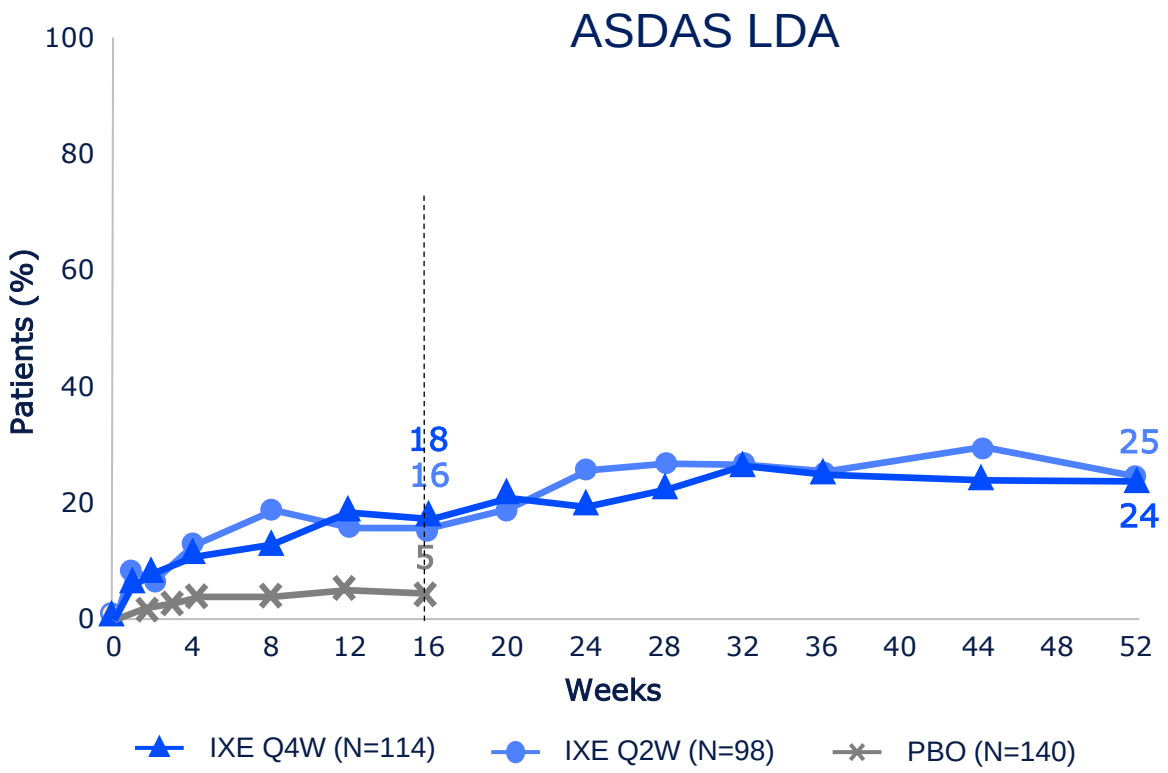


ASDAS-ID was achieved only in 4% of the primary failure patients,
in comparison to 22 % of those after secondary failure.

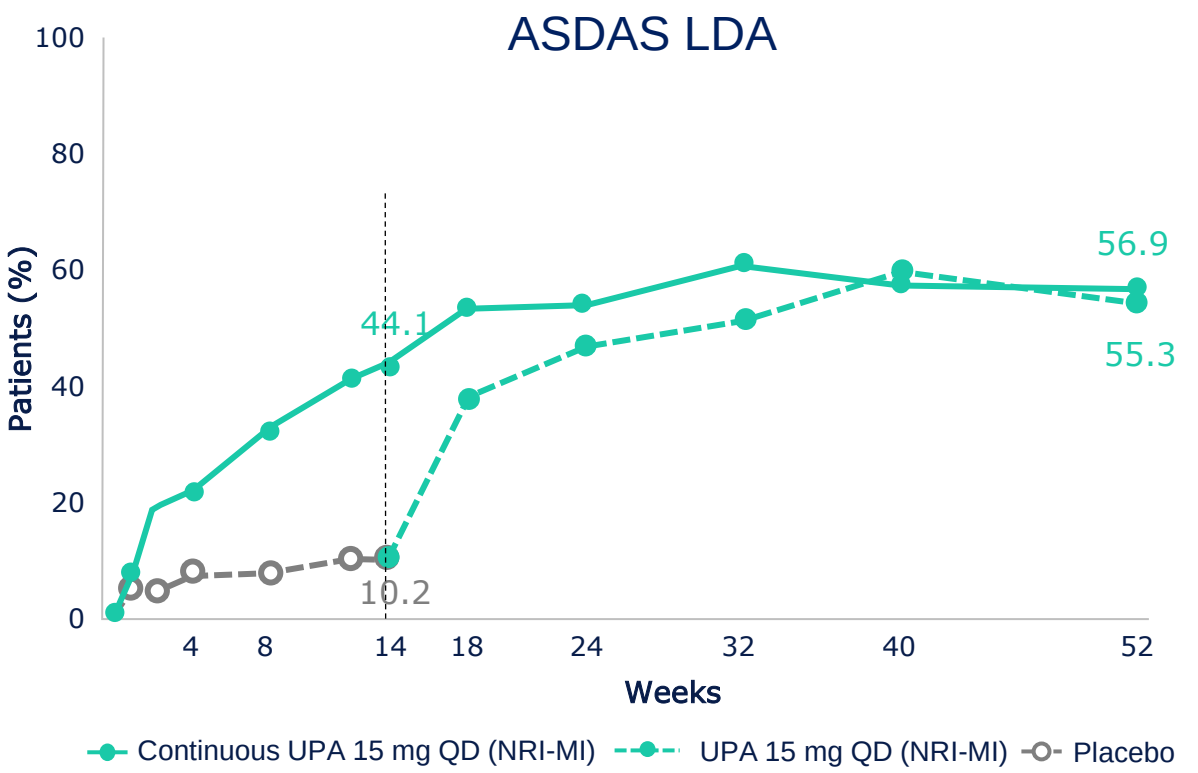
Ciurea A, et al. Arthritis Res Ther. 2016 Mar 22;18:71

Switching from TNFi to IL-17i or JAKi

IL-17 inhibitor (IXE): COAST-W in r-axSpA TNFi-IR

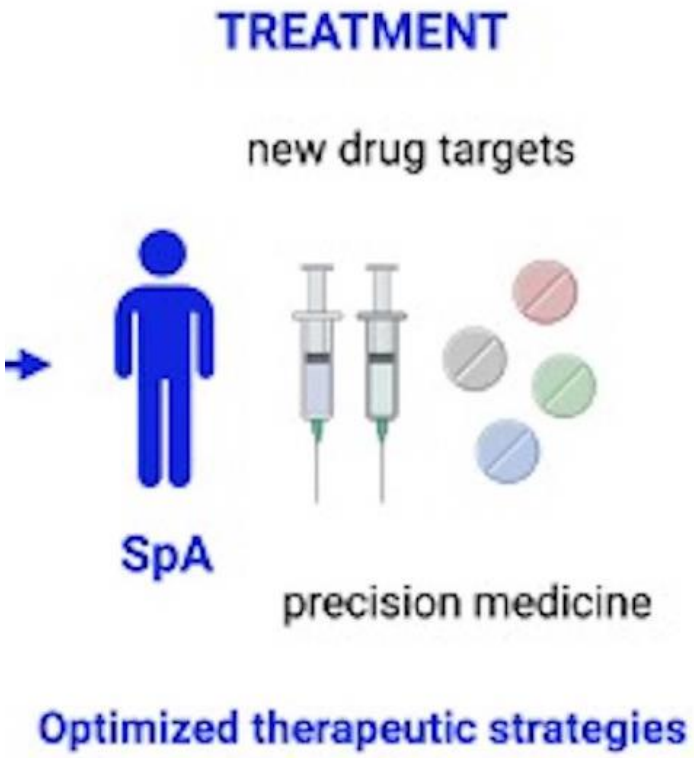


JAK inhibitor (UPA): SELECT AXIS 2 in r-axSpA bDMARD-IR



Dougados M, et al. Ann Rheum Dis. 2020;79(2):176-85
Baraliakos X, et al. EULAR 2023 Meeting. Milan, Italy.

A Glance into the future…



Navarro-Compán V, et al. Ther Adv Musculoskelet Dis. 2022 Jul 22;14:1759720X221111611

Take Home Messages

Diagnosis

Opportunity

- **<u>Diagnosis challenges:</u>** underdiagnosis, misdiagnosis and overdiagnosis:
  - **Diagnostic delay** is nowadays unacceptable, explained by several factors
    - Increase awareness of the disease
    - Implementation of efficient referral strategies
  - Overtime, **accurate diagnosis** of axSpA is becoming more and more challenging. The earlier the diagnosis, the more challenging can be.
    - Correct acquisition and interpretation of imaging (AI)
    - New biomarkers

Management

Opportunity

- **<u>Management challenges:</u>** achieving target/goal and selecting the optimal strategy:
  - **Recommended target** is achieved by less than 50% of patients in clinical practice.
    - It is early to confirm a window of opportunity in axSpA
    - Further evidence on early vs established axSpA diagnosis and treatment benefits is required.
    - Early axSpA definition has for the first time been defined based on expert consensus.
  - The **optimal strategy** is still to be defined.
    - TNFi, IL-17i and JAKi have shown disease activity control (target and objective signs).
    - Swicthing MoA seems more efficacious in case of primary failure.
    - Strategy trials are required to guide the best management decision for clinical practice.