bpacnz
PRIMARY CARE
UPDATE SERIES

04

AXIAL SPONDYLOARTHRITIS

AN UNCOMMON CAUSE OF A COMMON SYMPTOM

JULY 2021
VER 1.1

Axial spondyloarthritis (axial SpA) describes a continuum of disease

Umbrella term:

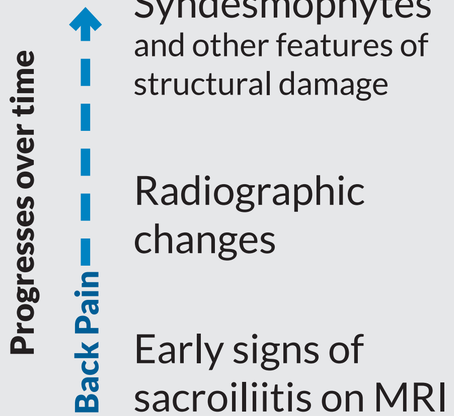
Axial SpA

…for chronic inflammatory arthritis primarily affecting the spine and the sacroiliac joints

Two main clinical subtypes:

Ankylosing spondylitis
also known as radiographic axial SpA

Non-radiographic axial SpA



In practice, the distinction between these clinical subtypes does not change the initial approach to management

Strong genetic basis

~50% of the total risk is associated with genetics

Having a **first degree relative** with ankylosing spondylitis **increases a persons relative risk** by **94 times** versus the general population

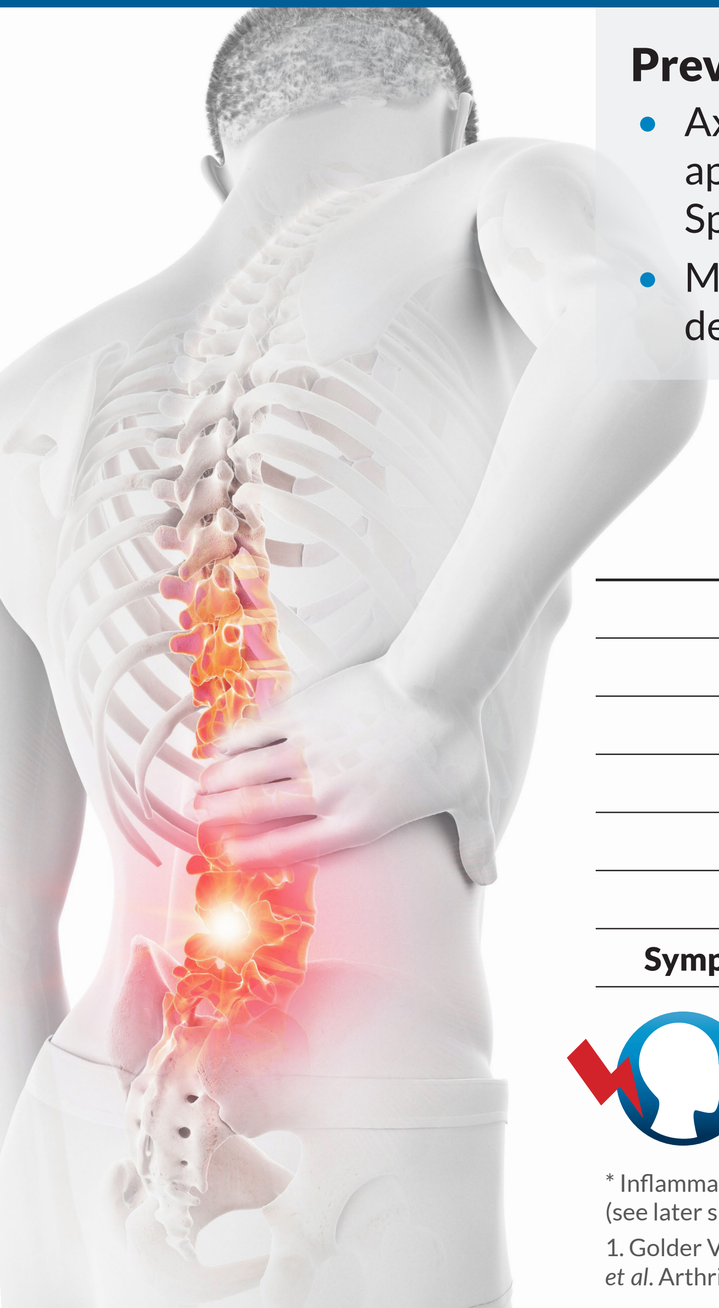
Multiple risk genes have been identified, but the ***HLA-B27* allele is present in most patients**

- Not all people with *HLA-B27* develop axial SpA

The **gut microbiota** is an important environmental determinant of developing axial SpA

1. Magrey MN, Danve AS, Ermann J, *et al*. Mayo Clin Proc. 2020;95:2499–508; 2. Morin M, Hellgren K, Frisell T. Rheumatology (Oxford). 2020;59:1695–702; 3. Gill T, Asquith M, Rosenbaum JT, *et al*. Curr Opin Rheumatol. 2015;27:319–325.

Differentiating inflammatory and mechanical back pain



Prevalence estimates vary:

- Axial SpA affects ~1% of the population in NZ; approximately one-third of patients with axial SpA eventually develop ankylosing spondylitis
- More common in people of European or Asian descent

Ankylosing spondylitis — More common in males

Non-radiographic axial SpA — Equal sex distribution

	Inflammatory back pain*	Mechanical back pain
Age at symptom onset	<40-45 years (peak onset 20 –30 years)	Any age
Onset	Insidious, persists for >3 months	Variable, may have an acute onset
Effect of activity	Improves with exercise	Improves with rest
Nocturnal back pain	Commonly present at night	Generally improves at night
Morning stiffness	Moderate-severe, persists for >30 min	Mild, short lived
Inflammatory markers	CRP sometimes elevated	Normal
Symptoms improves with NSAIDs	Frequently	Variably

Neck pain may be an early presenting symptom in patients with ankylosing spondylitis, and becomes a prominent issue in half of patients with established disease

Alternating buttock pain (between the left and right gluteal regions) may occur – usually does not radiate into legs

* Inflammatory back pain may be caused by axial SpA, or other related conditions such as psoriatic arthritis, reactive arthritis, and arthritis associated with inflammatory bowel disease (see later slide on spondyloarthropathies). Axial SpA, axial spondyloarthritis; CRP, C-reactive protein.

1. Golder V, Schachna L. Aust Fam Physician. 2013;42:780–4; 2. Magrey MN, Danve AS, Ermann J, *et al*. Mayo Clin Proc. 2020;95:2499–508; 3. Winter JJ, van Mens LJ, van der Heijde D, *et al*. Arthritis Res Ther. 2016;18:196.

Differentiating inflammatory and mechanical back pain

Questions about the patient's history to consider:

The duration and pattern of back pain

The efficacy of any previous analgesic use, particularly NSAIDs

As per previous slide

Any previous back injuries, surgery or radiculopathy

Other factors that may affect clinical suspicion, such as:

- Family history of axial SpA or any conditions associated with the *HLA-B27* allele **(see next slide)**
- Age (i.e. do they fit the expected demographic of axial SpA?)

Consider these differential diagnoses in people with low back pain:

- **Muscular pain** – from poor posture and core muscle weakness – may be exacerbated by injury
- **Fracture** – risk factors include a history of significant injury, older age, osteoporosis, osteopenia or the use of oral corticosteroids
- **Herniated disc** – characterised by leg pain with lower lumbar nerve root distribution
- **Spinal stenosis** – can result in radiating leg pain, numbness and weakness; more common in older adults
- **Referred pain from other structures/organs** – causes include abdominal aortic aneurysm, pelvic inflammatory diseases, endometriosis, prostatitis, renal or gastrointestinal disease
- **Vertebral infection** – assess whether patients have indicative symptoms, e.g. fever, or have had a recent documented infection
- **Cauda equina syndrome** – features include urinary retention, motor deficits in the lower limbs, faecal incontinence and "saddle" anaesthesia –the most frequent finding is urinary retention (sensitivity of 90%); the probability of cauda equina syndrome without urinary retention is ~1/10,000 patients
- **Cancer** – consider in patients with a personal or family history of cancer, unexplained weight loss, older age
- **Biopsychosocial factors**– these may become evident during discussions with the patient or when reviewing their history
- **Other** – Diffuse Idiopathic Skeletal Hyperostosis (DISH), Scheuermann's disease of the spine, biopsychosocial causes

1. Maher CM, Underwood M, Buchbinder R. Lancet. 2017;389:18–24; 2. Bezalel T, Carmeli E, Been E, *et al.* J Back Musculoskelet Rehabil. 2014;27:383–90.

(see later slide on spondyloarthropathies). Axial SpA, axial spondyloarthritis; CRP, C-reactive protein.

1. Golder V, Schachna L. Aust Fam Physician. 2013;42:780–4; 2. Magrey MN, Danve AS, Ermann J, *et al.* Mayo Clin Proc. 2020;95:2499–508; 3. Winter JJ, van Mens LJ, van der Heijde D, *et al.* Arthritis Res Ther. 2016;18:196.

Specific tests for patients with suspected axial SpA

Sacroiliac joint stress test

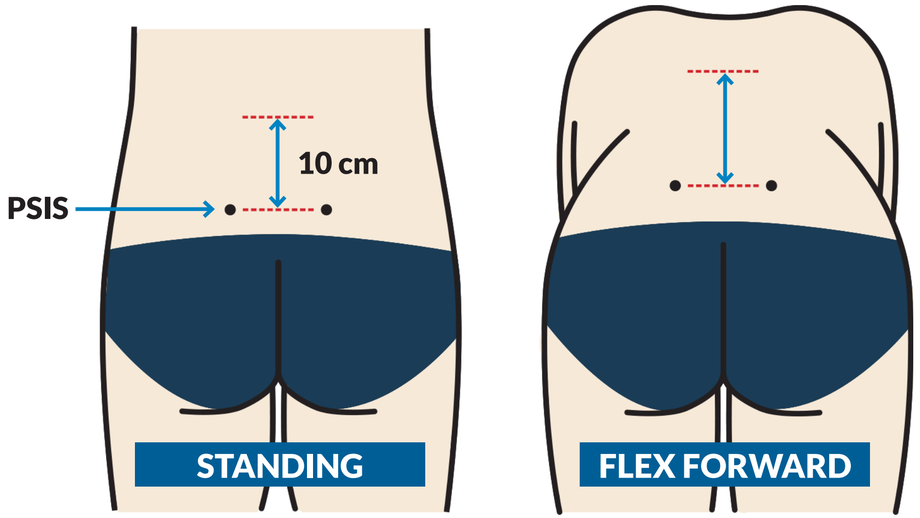
(sacroiliac distraction test) – assessing pain

1. Patient lies supine
2. Examiner applies downwards force to the anterior superior iliac spines (ASIS)
3. Initially apply force continuously for up to 30 seconds in an attempt to reproduce the patient's reported symptoms (a positive test)
4. If negative, apply a repeated vigorous force in an attempt to reproduce the patient's pain

Schober test

– assessing spinal mobility

Other methods of assessing spinal mobility include lumbar side flexion or occiput-to-wall distance*



1. Patient is standing
2. Examiner marks both the posterior superior iliac spines (PSIS) and then draws a horizontal line at the centre of the marks
3. A line is marked 10 cm above this line
4. The patient then flexes forward (as if attempting to touch their toes), and the examiner re-measures the distance between the top and bottom line
5. An increase of less than 4.5 cm is a positive test and may indicate axial SpA (although for some people this could be their normal range of motion)

* This test measures the degree of flexion deformity in the neck, which is more common in patients with advanced ankylosing spondylitis. Features such as osteoporosis or vertebral fractures may also affect neck mobility.

Axial SpA, axial spondyloarthritis

1. Sacroiliac Distraction Test. Physiopedia. 2021. Available at: https://www.physio-pedia.com/Sacroiliac_Distraction_Test (Accessed July, 2021); 2. Schober Test. Physiopedia. 2021. Available at: https://www.physio-pedia.com/Schober_Test (Accessed July, 2021)

Peripheral and extra-articular conditions may also be present

Axial SpA belongs to a group of related conditions (spondyloarthropathies) with many overlapping features

		Prevalence of peripheral conditions						Prevalence of extra-articular conditions					
		Peripheral arthritis		Enthesitis		Dactylitis		Uveitis		Psoriasis		Inflammatory bowel disease (IBD)	
		Past History	Current	Past History	Current	Past History	Current	Past History	Current	Past History	Current	Past History	Current
Axial SpA	Ankylosing spondylitis	30%	23%	29%	14%	6%	6%	23%	6%	–	10%	–	4%
	Non-radiographic axial SpA	28%	25%	35%	20%		5%	16%	6%		11%		6%
	Therefore, **a physical examination in patients with suspected axial SpA should also look for:**	Signs of arthritis in other locations, particularly the knees or ankles		Plantar fasciitis or Achilles tendonitis (usually tenderness on palpation or stiffness rather than visible swelling)		Sausage-like swelling/ inflammation of fingers/toes, involving the entire digit **N.B**. Although dactylitis is not a hallmark feature of rheumatoid arthritis (RA), the swelling from inflammation in RA can also sometimes be sausage-like in appearance.		Acutely inflamed red eye with redness around the edge of the cornea, eye pain, light sensitivity, visual impairment If present, refer patients for ophthalmology assessment		Scaly skin, dry/cracked skin particularly in the scalp line, behind the ears, extensor surfaces of elbows and knees, natal cleft and umbilicus; also look for thickened nails		Abdominal tenderness/ masses or any perianal features *(only if the history first indicates IBD may be possible, e.g. in patients that also experience diarrhoea with urgency)*	

Axial SpA, axial spondyloarthritis

1. Winter JJ, van Mens LJ, van der Heijde D, *et al*. Arthritis Res Ther. 2016;18:196.

Further investigations to arrange

Laboratory investigations to consider:

- CRP levels; if elevated, levels may range from >6 mg/L (slightly elevated) to 20–30 mg/L
- *HLA-B27* genetic testing
- Stool culture and chlamydia PCR if there is a suspicion of reactive arthritis due to underlying infection
- Testing for autoantibodies if there is suspicion of other rheumatic conditions – patients with axial SpA will typically be seronegative for rheumatoid factor, anti-CCP and anti-nuclear antibody

X-rays are rarely useful early on (radiographic changes usually occur long after symptom onset)

- Request if there is significant pain with sacroiliac stress test and symptoms have been present for >6 months
- Findings of sacroiliitis include joint space narrowing, sclerosis, erosive changes, and fusion of the joint (in late stages)

Additional imaging modalities, e.g. MRI, may pick up on early signs of sacroiliitis and add to the clinical picture, if available; these are usually requested the rheumatologist once the patient has been referred

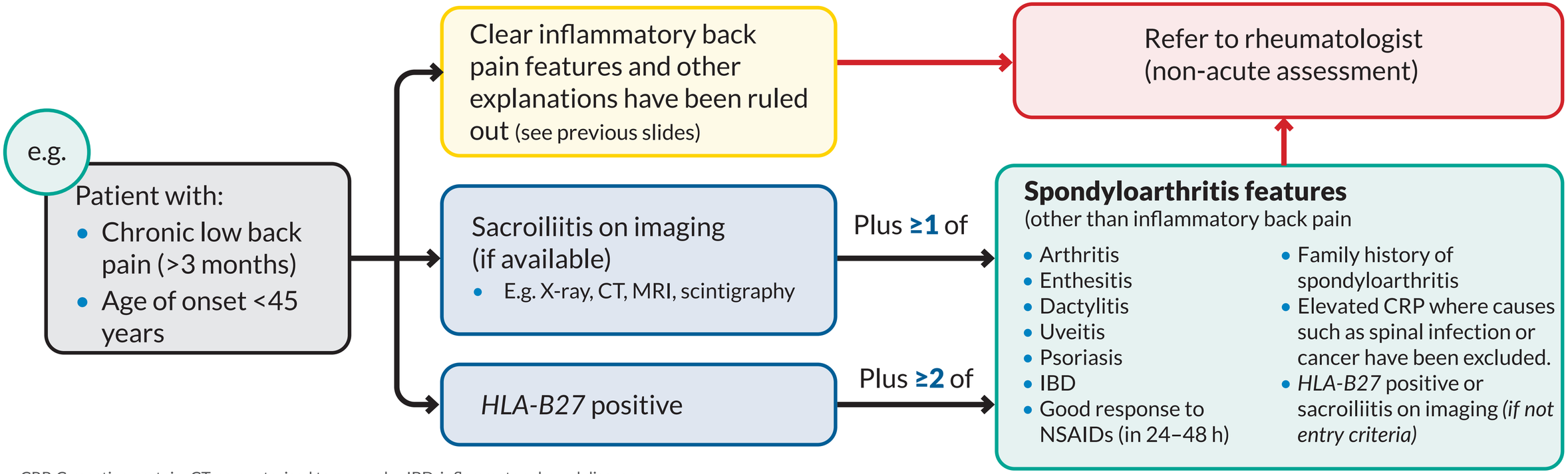
Anti-CCP, anti-cyclic citrullinated peptide; Axial SpA, axial spondyloarthritis; CRP, C-reactive protein; MRI, magnetic resonance imaging; PCR, polymerase chain reaction.

1. Magrey MN, Danve AS, Ermann J, *et al*. Mayo Clin Proc. 2020;95:2499–508.

Diagnosis is often delayed – refer suspected cases to Rheumatology

Early diagnosis and intervention = better patient outcomes, e.g. reduced skeletal damage

However: *"The average delay between symptom onset and diagnosis of axial SpA is estimated to be 5 to 7 years, with evidence that the delay can be significantly longer in women than in men"*– **Magrey *et al*, 2020**



CRP, C-reactive protein; CT, computerised tomography, IBD, inflammatory bowel disease; MRI, magnetic resonance imaging; PCR, polymerase chain reaction.

1. Magrey MN, Danve AS, Ermann J, *et al.* Mayo Clin Proc. 2020;95:2499–508.

Treatment for patients with axial SpA

The goals of treatment are to:

- Control pain
- Improve or maintain quality of life
- Improve mobility
- Keep people in employment or education

Pharmacological options – the choices are limited

NSAIDs – first-line

- No particular NSAID is preferred. Examples include:

	Dosing for patients with Axial SpA
Naproxen (immediate release)	Initially 250–500 mg twice daily, usual maintenance 250 mg twice daily (or 500 mg once daily); maximum 1 g daily
Naproxen (modified release)	Maintenance dose may be administered using modified release tablets as 750–1000 mg once daily; maximum 1 g daily
Celecoxib	200 mg daily in 1–2 divided doses, increased if necessary to maximum 400 mg daily in 1–2 divided doses

While awaiting rheumatology consultation, the patient should be given a prescription for a NSAID up to the maximum dose unless there are contraindications

- For patients with **active symptomatic** disease – regular use
- For patients with **stable** disease – use as-needed if symptoms return
- If there is an inadequate response after ~4 weeks, then trial another NSAID
- Long term treatment decisions should balance possible benefits against the risk of NSAID-related adverse effects

Biologic treatment

- Usually only considered for patients with severe disease who have had an **inadequate response to at least two different NSAIDs** (in combination with a PPI if indicated) while also undertaking a regular exercise regimen and other lifestyle interventions (see next slide)
- Various options are available **fully funded with Special Authority approval** for patients with ankylosing spondylitis
  - Check the NZF or PHARMAC websites to confirm the current criteria for funded access with Special Authority approval – initial applications must be made by a rheumatologist

Which biologics are recommended?

- TNF-inhibitors are first-line*
- As of July, 2021, funded access with Special Authority approval requires adalimumab or etanercept to be trialled first; infliximab or secukinumab can then be considered if at least one of these biologics is ineffective/not tolerated (secukinumab may be preferred in patients with co-morbid psoriasis)

Traditional disease modifying medicines, e.g. methotrexate, and **corticosteroids** are not recommended for patients with axial features due to a lack of evidence for efficacy, but may be suitable in those with peripheral features

* TNF inhibitors are also indicated for patients with severe non-radiographic axial SpA, however, there is no specific Special Authority category that would qualify patients for funded treatment in New Zealand.

Axial SpA, axial spondyloarthritis; CT, computed tomography; MRI, magnetic resonance imaging; NSAIDs, non-steroidal anti-inflammatory drugs; PPI, proton pump inhibitor.

1. Ward MM, Deodhar A, Gensler LS, *et al*. Arthritis Care Res. 2019;71:1285–99; 2. Magrey MN, Danve AS, Ermann J, *et al*. Mayo Clin Proc. 2020;95:2499–508; 3. NZ formulary (NZF). V107. Available at: https://nzf.org.nz/ (Accessed July, 2021).

Treatment for patients with axial SpA

Non-pharmacological considerations for all patients with newly diagnosed axial SpA:

Smoking cessation is important – smoking can worsen symptoms and has been associated with radiographic spinal damage

Exercise – physical activity improves disease activity in patients with axial SpA

- Exercise can be directed at postural training (e.g. through yoga), improving range of motion (e.g. performing a daily stretching routine), or general fitness (e.g. daily walks or aqua jogging)
- Home-based exercise can be effective, but studies suggest that supervised exercise or physiotherapy has greater benefits

⚠ Avoid spinal manipulation in patients with spinal fusion or advanced spinal osteoporosis

Weight loss (if applicable) – obesity is associated with increased disease activity and spinal stiffness

Psychological support – regularly assess the patient's mental health and wellbeing, and consider if there are features of depression or anxiety present

- Consider whether support is in place at home or if further help is required

1. Ward MM, Deodhar A, Gensler LS, *et al*. Arthritis Care Res. 2019;71:1285–99; 2. Poddubnyy D, Haibel H, Listing J, *et al*. Ann Rheum Dis;72:1430–2; 3. Millner JR, Barron JS, Beinke KM, *et al*. Semin Arthritis Rheum. 2016;45:411–27; 4. Bindesbøll C, Garrido-Cumbrera M, Bakland G, *et al*. Curr Rheumatol Rep. 2020;22:43

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Monitoring the effectiveness of treatment (#1)

Monitoring using an activity score is conditionally recommended in the 2019 ACR guidelines

- However, activity scores may have minimal/no benefit for some patients, e.g. those with symptoms not encompassed within the scoring criteria
- If **TNF inhibitor treatment** (with adalimumab/etanercept) is being considered for patients with **ankylosing spondylitis**, use of the **BASDAI tool** (below) is required for Special Authority (SA) initial applications and renewals*

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

Question:		Scale	Score
1	How would you rate your **level of fatigue?**	**0–10, where:** • 0 = none • 10 = very severe	
2	How would you describe the overall **level of neck, back, or hip pain** you have had?		
3	How would you describe the overall **level of pain/swelling in joints other than the neck, back or hip?**		
4	How would you describe the **level of discomfort you have had from an area tender to touch or pressure?**		
5	How would you describe the **level of morning stiffness you have had from the time you wake up?**		
6	**How long does your morning stiffness last** from the time you wake up?	**0–10, where:** • 0 = 0 hours • 5 = 1 hours • 10 = ≥2 hours	

Final BASDAI score =

Sum(Q1 to Q4) + ((Q5+Q6)/2) divided by 5

- A score of ≥4 suggests sub-optimal disease control

*** As of July, 2021:**

- **SA Initial application:** patients with a BASDAI score ≥6 may be eligible for TNF inhibitor treatment
- **SA renewal:** following 12 weeks of treatment, patients must have improved by ≥4 points, or ≥50% (whichever is less) from pre-treatment level

ACR, American College of Rheumatology.

1. Ward MM, Deodhar A, Gensler LS, *et al*. Arthritis Care Res. 2019;71:1285–99; 2. Zochling J. Arthritis Care Res. 2011;63:S47–58

Monitoring the effectiveness of treatment (#2) – alternatives to BASDAI

Bath Ankylosing Spondylitis function index (BASFI) – an alternative scoring tool focusing on assessing functional impairment/disability

Question: How much difficulty do you have performing the following daily activities?		**Scale**	**Score**
1	Putting on your socks or tights without help or aids, e.g. sock aids	**0–10, where:** • 0 = easy • 10 = impossible	
2	Bending forward from the waist to pick up a pen from the floor without an aid		
3	Reaching up to a high shelf without help or aids, e.g. helping hand		
4	Getting up from an armless chair without using your hands or any other help		
5	Getting up off the floor without any help from lying on your back		
6	Standing unsupported for ten minutes without discomfort		
7	Climbing 12–15 steps without using a handrail or walking aid (one foot on each step)		
8	Looking over your shoulder without turning your body		
9	Doing physically demanding activities, e.g. physiotherapy exercises, gardening or sports		
10	Doing a full day activities whether it be at home or work		

Final BASFI score =

Total points divided by 10

- Used to monitor treatment response over time
- More useful in patients displaying obvious physical impairment to detect change over time
- May not be sensitive enough to detect subtle changes in patients that only have mild impairment

Or

Monitoring CRP may be useful in patients who present initially with elevated levels

This can then be used to calculate their **ASDAS score**, which is similar to BASDAI but incorporates acute phase reactants (See Machado *et al*, 2018)

ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis function index; CRP, C-reactive protein.

1. Ward MM, Deodhar A, Gensler LS, *et al*. Arthritis Care Res. 2019;71:1285–99; 2. Zochling J. Arthritis Care Res. 2011;63:S47–58; Machado PM, Landewé R, van der Heijde D. Ann Rheum Dis. 2018;77:1539–40.

Longer-term follow-up of patients with axial SpA

In addition to routine monitoring of disease activity, other follow-up considerations include:

Monitor **renal function** in patients taking regular NSAIDs (and other medicine-specific adverse effects)

- There is also an increased risk of gastrointestinal adverse effects and kidney stones (though still rare)

Look for symptoms/signs of **cardiovascular disease** as the risk is slightly elevated in people with inflammatory conditions

Educate patients on the **increased risk of infection** if they are taking biologics

The risk of osteoporosis is low – unlike for other inflammatory arthropathies, the routine use of bisphosphonates or bone scans is not necessary as corticosteroids are rarely used

Pregnancy/fertility is usually unaffected by axial SpA – however, patients with severe disease involving sacroiliac joint fusion have higher rates of caesarean section

- Pregnancy is not a contra-indication to biologic treatment but avoid giving infants live vaccines for at least six months after birth if they are exposed in utero

Axial SpA, axial spondyloarthritis.1. Ward MM, Deodhar A, Gensler LS, *et al*. Arthritis Care Res. 2019;71:1285–99; 2. Mokbel A, Lawson DO, Farrokhyar. Clin Rheumatol. 2021; doi: 10.1007/s10067-021-05588-9. Published online ahead of print.