NICE National Institute for Health and Care Excellence

NICE guideline

Spondyloarthritis in over 16s: diagnosis and management

NICE guideline
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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

This guideline is the basis of QS170.

This guideline should be read in conjunction with QS155 and NG193.

Overview

This guideline covers diagnosing and managing suspected or confirmed spondyloarthritis in people 16 years or older. It aims to raise awareness of the features of spondyloarthritis and provide clear advice on what action to take when people with signs and symptoms first present in healthcare settings. It also provides advice on the range of treatments available.

NICE has also produced guidelines on psoriasis and low back pain and sciatica in over 16s.

Who is it for?

- Healthcare professionals
- Commissioners and providers
- People with spondyloarthritis and their families and carers

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

Spondyloarthritis is a group of inflammatory conditions that have a range of manifestations. Spondyloarthritis may be predominantly:

- axial:
  - ankylosing spondylitis (radiographic axial spondyloarthritis)
  - non-radiographic axial spondyloarthritis **or**
- peripheral:
  - psoriatic arthritis
  - reactive arthritis
  - enteropathic spondyloarthritis.

People with predominantly axial spondyloarthritis may have additional peripheral symptoms, and vice versa.

Axial presentations of spondyloarthritis are often misdiagnosed as mechanical low back pain, leading to delays in access to effective treatments. Peripheral presentations are often seen as unrelated joint or tendon problems, and can be misdiagnosed because problems can move around between joints.

1.1 Recognition and referral in non-specialist care

settings

1.1.1 Do not rule out the possibility that a person has spondyloarthritis solely on the presence or absence of any individual sign, symptom or test result. **[2017]**

Suspecting spondyloarthritis

1.1.2 Recognise that spondyloarthritis can have diverse symptoms and be difficult to identify, which can lead to delayed or missed diagnoses. Signs and symptoms may be musculoskeletal (for example, inflammatory back pain, enthesitis and dactylitis) or extra-articular (for example, uveitis and psoriasis [including psoriatic nail symptoms]). Risk factors include recent genitourinary infection and a family history of spondyloarthritis or psoriasis. **[2017]**

1.1.3 Be aware that axial and peripheral spondyloarthritis may be missed, even if the onset is associated with established comorbidities (for example, uveitis, psoriasis, inflammatory bowel disease [Crohn's disease or ulcerative colitis], or a gastrointestinal or genitourinary infection). **[2017]**

1.1.4 Be aware that axial spondyloarthritis:

- affects a similar number of women as men
- can occur in people who are human leukocyte antigen B27 (HLA-B27) negative
- may be present despite no evidence of sacroiliitis on a plain film X-ray. **[2017]**

Referral for suspected axial spondyloarthritis

1.1.5 If a person has low back pain that started before the age of 45 years and has lasted for longer than 3 months, refer the person to a rheumatologist for a spondyloarthritis assessment if **4 or more** of the following additional criteria are also present:

- low back pain that started before the age of 35 years (this further increases

the likelihood that back pain is due to spondyloarthritis compared with low back pain that started between 35 and 44 years)

- waking during the second half of the night because of symptoms
- buttock pain
- improvement with movement
- improvement within 48 hours of taking non-steroidal anti-inflammatory drugs (NSAIDs)
- a first-degree relative with spondyloarthritis
- current or past arthritis
- current or past enthesitis
- current or past psoriasis.

If exactly **3** of the additional criteria are present, perform an HLA-B27 test. If the test is positive, refer the person to a rheumatologist for a spondyloarthritis assessment. **[2017]**

1.1.6 If the person does not meet the criteria in recommendation 1.1.5 but clinical suspicion of axial spondyloarthritis remains, advise the person to seek repeat assessment if new signs, symptoms or risk factors listed in recommendation 1.1.5 develop. This may be especially appropriate if the person has current or past inflammatory bowel disease (Crohn's disease or ulcerative colitis), psoriasis or uveitis (see recommendation 1.1.12 for guidance on referral for immediate [same-day] ophthalmological assessment for people with acute anterior uveitis). **[2017]**

Referral for suspected psoriatic arthritis and other peripheral spondyloarthritides

1.1.7 For guidance on identifying spondyloarthritis in people with an existing diagnosis of psoriasis, see assessment and referral for psoriatic arthritis in the NICE

guideline on psoriasis. **[2017]**

1.1.8 Urgently refer people with suspected new-onset inflammatory arthritis to a rheumatologist for a spondyloarthritis assessment, unless rheumatoid arthritis, gout or acute calcium pyrophosphate (CPP) arthritis ('pseudogout') is suspected. If rheumatoid arthritis is suspected, see referral for specialist treatment in the NICE guideline on rheumatoid arthritis in adults. **[2017]**

1.1.9 Refer people with dactylitis to a rheumatologist for a spondyloarthritis assessment. **[2017]**

1.1.10 Refer people with enthesitis without apparent mechanical cause to a rheumatologist for a spondyloarthritis assessment if:

- it is persistent **or**
- it is in multiple sites **or**
- any of the following are also present:
  - back pain without apparent mechanical cause
  - current or past uveitis (see recommendation 1.1.12 for guidance on immediate [same-day] ophthalmological assessment for people with acute anterior uveitis)
  - current or past psoriasis
  - gastrointestinal or genitourinary infection
  - inflammatory bowel disease (Crohn's disease or ulcerative colitis)
  - a first-degree relative with spondyloarthritis or psoriasis. **[2017]**

Recognising psoriasis

1.1.11 If a person with suspected spondyloarthritis has signs or symptoms of undiagnosed psoriasis, follow the recommendations in the NICE guideline on psoriasis. **[2017]**

Referral for suspected acute anterior uveitis

1.1.12 Refer people for an immediate (same-day) ophthalmological assessment if they have symptoms of acute anterior uveitis (for example, eye pain, eye redness, sensitivity to light or blurred vision). **[2017]**

Case-finding in people with acute anterior uveitis

1.1.13 Ophthalmologists should ask people with acute anterior uveitis whether they have:

- consulted their GP about joint pains **or**
- experienced low back pain that started before the age of 45 years and has lasted for longer than 3 months. **[2017]**

1.1.14 If the person meets either of the criteria in recommendation 1.1.13, establish whether they have psoriasis or skin complaints that appear psoriatic on physical examination.

- If they do, refer the person to a rheumatologist for a spondyloarthritis assessment.
- If they do not, perform an HLA-B27 test. If the test is positive, refer the person to a rheumatologist for a spondyloarthritis assessment. **[2017]**

1.2 Diagnosing spondyloarthritis in specialist care settings

Diagnostic criteria for suspected spondyloarthritis

1.2.1 In specialist care settings, consider using validated spondyloarthritis criteria to guide clinical judgement when diagnosing spondyloarthritis. Examples include:

- general spondyloarthritis criteria:

  - Amor
  - European Spondyloarthropathy Study Group (ESSG)
- axial spondyloarthritis criteria:
  - Assessment of Spondyloarthritis International Society (ASAS; axial)
  - Berlin
  - Rome
  - modified New York
- peripheral spondyloarthritis criteria:
  - ASAS (peripheral)
  - Classification of Psoriatic Arthritis (CASPAR)
  - French Society of Rheumatology (reactive arthritis). **[2017]**

1.2.2 Do not rule out a diagnosis of spondyloarthritis solely on the basis of a negative HLA-B27 result. **[2017]**

1.2.3 Do not rule out a diagnosis of spondyloarthritis if a person's C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are normal. **[2017]**

Imaging for suspected axial spondyloarthritis

Initial investigation using X-ray

1.2.4 Offer plain film X-ray of the sacroiliac joints for people with suspected axial spondyloarthritis, unless the person is likely to have an immature skeleton. **[2017]**

1.2.5 Diagnose ankylosing spondylitis if the plain film X-ray shows sacroiliitis meeting the modified New York criteria (bilateral grade 2 to 4 or unilateral grade 3 to 4 sacroiliitis). **[2017]**

1.2.6 If the plain film X-ray does not show sacroiliitis meeting modified New York criteria (bilateral grade 2 to 4 or unilateral grade 3 to 4 sacroiliitis), or an X-ray is not appropriate because the person's skeleton is not fully mature, request unenhanced MRI using an inflammatory back pain protocol. **[2017]**

Subsequent investigation using MRI

1.2.7 Radiologists receiving a request for an inflammatory back pain MRI should perform short T1 inversion recovery (STIR) and T1 weighted sequences of the whole spine (sagittal view), and sacroiliac joints (coronal oblique view). **[2017]**

1.2.8 Use the ASAS/Outcome Measures in Rheumatology (OMERACT) MRI criteria to interpret the MRI as follows:

- If the MRI meets the ASAS/OMERACT MRI criteria:
  - diagnose non-radiographic axial spondyloarthritis.
- If the MRI does not meet the ASAS/OMERACT MRI criteria:
  - do not exclude the possibility of axial spondyloarthritis
  - consider specialist musculoskeletal radiology review if there is disparity between the clinical suspicion and imaging findings, particularly in people with an immature skeleton
  - offer an HLA-B27 test if it has not already been done. If positive, base the diagnosis of non-radiographic axial spondyloarthritis on clinical features, for example, using the clinical 'arm' of the ASAS axial classification criteria. **[2017]**

1.2.9 If a diagnosis of axial spondyloarthritis cannot be confirmed and clinical suspicion remains high, consider a follow-up MRI. **[2017]**

Other types of imaging for diagnosing axial spondyloarthritis

1.2.10 Do not offer scintigraphy for people with suspected axial spondyloarthritis.

[2017]

Imaging for suspected psoriatic arthritis and other peripheral spondyloarthritides

1.2.11 Offer plain film X-ray of symptomatic hands and feet for people with suspected peripheral spondyloarthritis in these areas. **[2017]**

1.2.12 If a diagnosis cannot be made from the plain film X-ray, consider ultrasound of:

- the hands and feet to assess for joint involvement
- suspected enthesitis sites. **[2017]**

1.2.13 Consider plain film X-rays, ultrasound and/or MRI of other peripheral and axial symptomatic sites. **[2017]**

1.2.14 Interpret a positive HLA-B27 result as increasing the likelihood of peripheral spondyloarthritis. **[2017]**

1.2.15 If a diagnosis of peripheral spondyloarthritis is confirmed, offer plain film X-ray of the sacroiliac joints to assess for axial involvement, even if the person does not have any symptoms. **[2017]**

Antibody testing for suspected reactive arthritis

1.2.16 Do not routinely test for infective antibody status to diagnose reactive arthritis in people with a history of gastrointestinal infection. **[2017]**

1.3 Information and support

Information about spondyloarthritis

1.3.1 Provide people with spondyloarthritis, and their family members or carers (as appropriate), with information that is:

- available on an ongoing basis
- relevant to the stage of the person's condition
- tailored to the person's needs.

  For more guidance on providing information to people and discussing their preferences with them, see the NICE guideline on patient experience in adult NHS services. **[2017]**

1.3.2 Provide explanations and information about spondyloarthritis, for example:

- what spondyloarthritis is
- diagnosis and prognosis
- treatment options (pharmacological and non-pharmacological), including possible side effects
- likely symptoms and how they can be managed
- flare episodes and extra-articular symptoms
- self-help options
- opportunities for people with spondyloarthritis to be involved in research
- which healthcare professionals will be involved with the person's care and how to get in touch with them
- information about employment rights and ability to work
- local support groups, online forums and national charities, and how to get in touch with them. **[2017]**

Information about disease flares

1.3.3 Advise people with spondyloarthritis about the possibility of experiencing flare episodes and extra-articular symptoms. **[2017]**

1.3.4 Consider developing a flare management plan that is tailored to the person's individual needs, preferences and circumstances. **[2017]**

1.3.5 When discussing any flare management plan, provide information on:

- access to care during flares (including details of a named person to contact [for example, a specialist rheumatology nurse])
- self-care (for example, exercises, stretching and joint protection)
- pain and fatigue management
- potential changes to medicines
- managing the impact on daily life and ability to work. **[2017]**

1.4 Pharmacological management of spondyloarthritis

See the MHRA's safety advice on Janus kinase (JAK) inhibitors (April 2023). See terms used in this guideline for a description and examples of JAK inhibitors.

1.4.1 If people with spondyloarthritis and their clinicians consider there to be a range of suitable medicines, after discussing the advantages and disadvantages of all the options, the least expensive should be used. Administration costs, dosages, price per dose and commercial arrangements should all be taken into account. **[2025]**

Axial spondyloarthritis

Initial pharmacological treatment

1.4.2 Offer an NSAID at the lowest effective dose to people with pain associated with axial spondyloarthritis, and think about appropriate clinical assessment, ongoing monitoring of risk factors, and the use of gastroprotective treatment. **[2017]**

1.4.3 If an NSAID taken at the maximum tolerated dose for 2 to 4 weeks does not provide adequate pain relief, consider switching to another NSAID. **[2017]**

Further pharmacological treatment for active ankylosing spondylitis

1.4.4 For medicines recommended as options in NICE technology appraisal guidance for treating active ankylosing spondylitis in adults, if the condition has a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of 4 units or more and a spinal visual analogue scale (VAS) of 4 cm or more, and NSAIDs have not controlled the condition well enough or are not tolerated, see the guidance on:

- secukinumab (TA407, September 2016)
- adalimumab (TA383, February 2016)
- certolizumab pegol (TA383, February 2016)
- etanercept (TA383, February 2016)
- golimumab (TA383, February 2016)
- infliximab (TA383, February 2016).

1.4.5 For medicines recommended as options in NICE technology appraisal guidance for treating active ankylosing spondylitis in adults, if the condition has a BASDAI score of 4 units or more and a spinal VAS of 4 cm or more, and TNF-alpha inhibitors are not suitable or have not controlled the condition well enough, see the guidance on:

- tofacitinib (TA920, October 2023)

- bimekizumab (TA918, October 2023)
- upadacitinib (TA829, September 2022)
- ixekizumab (TA718, July 2021)
- secukinumab (TA407, September 2016).

Also, follow recommendation 1.4.18 on reviewing treatment.

Further pharmacological treatment for non-radiographic axial spondyloarthritis

1.4.6 For medicines recommended as options in NICE technology appraisal guidance for treating non-radiographic axial spondyloarthritis in adults, if the condition has a BASDAI score of 4 units or more and a spinal VAS of 4 cm or more, and NSAIDs have not controlled the condition well enough or are not tolerated, see the guidance on:

- golimumab (TA497, January 2018)
- adalimumab (TA383, February 2016)
- certolizumab pegol (TA383, February 2016)
- etanercept (TA383, February 2016).

1.4.7 For medicines recommended as options in NICE technology appraisal guidance for treating active non-radiographic axial spondyloarthritis with objective signs of inflammation (shown by elevated C-reactive protein or MRI) in adults, if the condition has a BASDAI score of 4 units or more and a spinal VAS of 4 cm or more, and TNF-alpha inhibitors are not suitable or have not controlled the condition well enough, see the guidance on:

- bimekizumab (TA918, October 2023)
- upadacitinib (TA861, February 2023)
- secukinumab (TA719, July 2021)

- ixekizumab (TA718, July 2021).

Also, follow recommendation 1.4.18 on reviewing treatment.

Psoriatic arthritis and other peripheral spondyloarthritides

Initial pharmacological treatment

1.4.8 Consider local corticosteroid injections as monotherapy for non-progressive monoarthritis. **[2017]**

1.4.9 Offer standard disease-modifying anti-rheumatic drugs (DMARDs) to people with:

- peripheral polyarthritis
- oligoarthritis
- persistent or progressive monoarthritis associated with peripheral spondyloarthritis. **[2017]**

1.4.10 When deciding which standard DMARD to offer, take into account:

- the person's needs, preferences and circumstances (such as pregnancy planning and alcohol consumption)
- comorbidities such as uveitis, psoriasis and inflammatory bowel disease
- disease characteristics
- potential side effects. **[2017]**

1.4.11 If a standard DMARD taken at the maximum tolerated dose for at least 3 months does not provide adequate relief from symptoms, consider switching to or adding another standard DMARD. **[2017]**

1.4.12 Consider NSAIDs as an adjunct to DMARDs or to manage symptoms. Use oral NSAIDs at the lowest effective dose for the shortest possible period of time, and think about appropriate clinical assessment, ongoing monitoring of risk factors, and the use of gastroprotective treatment. **[2017]**

1.4.13 If NSAIDs do not provide adequate relief from symptoms, consider corticosteroid injections (local or intramuscular) or short-term oral steroid therapy as an adjunct to DMARDs to manage symptoms. **[2017]**

1.4.14 If extra-articular disease is adequately controlled by an existing standard DMARD but peripheral spondyloarthritis is not, consider adding another standard DMARD. **[2017]**

Further pharmacological treatment for active psoriatic arthritis

1.4.15 For medicines recommended as options in NICE technology appraisal guidance for treating active psoriatic arthritis in adults when the condition has not responded to adequate trials of at least 2 standard DMARDs, either individually or in combination, see the guidance on:

- tofacitinib (TA543, October 2018)
- ixekizumab (TA537, August 2018)
- certolizumab pegol (TA445, May 2017)
- secukinumab (TA445, May 2017)
- apremilast (TA433, February 2017)
- golimumab (TA220, April 2011)
- adalimumab (TA199, August 2010)
- etanercept (TA199, August 2010)
- infliximab (TA199, August 2010)

or, if a TNF-alpha inhibitor is contraindicated, see the guidance on:

- bimekizumab (TA916, October 2023)
- guselkumab (TA815, August 2022)
- upadacitinib (TA768, February 2022)

- ustekinumab (TA340, March 2017).

1.4.16 For medicines recommended as options in NICE technology appraisal guidance for treating active psoriatic arthritis in adults when at least 1 biological DMARD has not controlled the condition well enough or is not tolerated, see the guidance on:

- bimekizumab (TA916, October 2023)
- guselkumab (TA815, August 2022)
- risankizumab (TA803, July 2022), only if the person has moderate to severe psoriasis
- upadacitinib (TA768, February 2022)
- tofacitinib (TA543, October 2018)
- ixekizumab (TA537, August 2018)
- certolizumab pegol (TA445, May 2017)
- secukinumab (TA445, May 2017)
- ustekinumab (TA340, March 2017).

  For tofacitinib, ixekizumab, certolizumab pegol, secukinumab and ustekinumab, previous biological DMARD treatment should include a TNF-alpha inhibitor.

Also, follow recommendation 1.4.18 on reviewing treatment.

Reactive arthritis

1.4.17 After treating the initial infection, do not offer long-term (4 weeks or longer) treatment with antibiotics solely to manage reactive arthritis caused by a gastrointestinal or genitourinary infection. **[2017]**

Reviewing treatment

1.4.18 For adults with spondyloarthritis who are receiving a biological or targeted synthetic DMARD (listed in recommendations 1.4.4 to 1.4.7, 1.4.15 and 1.4.16), continue treatment only if there is clear evidence of response (see definitions of response and timeframes in the relevant NICE technology appraisal guidance). **[2025]**

1.5 Non-pharmacological management of spondyloarthritis

1.5.1 Refer people with axial spondyloarthritis to a specialist physiotherapist to start an individualised, structured exercise programme, which should include:

- stretching, strengthening and postural exercises
- deep breathing
- spinal extension
- range of motion exercises for the lumbar, thoracic and cervical sections of the spine
- aerobic exercise. **[2017]**

1.5.2 Consider hydrotherapy as an adjunctive therapy to manage pain and maintain or improve function for people with axial spondyloarthritis. **[2017]**

1.5.3 Consider a referral to a specialist therapist (such as a physiotherapist, occupational therapist, hand therapist, orthotist or podiatrist) for people with spondyloarthritis who have difficulties with any of their everyday activities. The specialist therapist should:

- assess people's needs
- provide advice about physical aids
- arrange periodic reviews to assess people's changing needs. **[2017]**

1.6 Surgery for spondyloarthritis

1.6.1 Do not refer people with axial spondyloarthritis to a complex spinal surgery service to be assessed for spinal deformity correction unless the spinal deformity is:

- significantly affecting their quality of life **and**
- severe or progressing despite optimal non-surgical management (including physiotherapy). **[2017]**

1.6.2 If a person with axial spondyloarthritis presents with a suspected spinal fracture, refer them to a specialist to confirm the spinal fracture and carry out a stability assessment. After the stability assessment, the specialist should refer people with a potentially unstable spinal fracture to a spinal surgeon. **[2017]**

1.7 Managing flares

1.7.1 Manage flares in either specialist care or primary care depending on the person's needs. **[2017]**

1.7.2 When managing flares in primary care, seek advice from specialist care as needed, particularly for people who:

- have recurrent or persistent flares
- are taking biological or targeted synthetic DMARDs
- have comorbidities that may affect treatment or management of flares. **[2017]**

1.7.3 Be aware that uveitis can occur during flare episodes. See recommendation 1.1.12 for guidance on immediate (same-day) ophthalmological assessment for people with acute anterior uveitis. **[2017]**

1.8 Long-term complications

1.8.1 For guidance on monitoring long-term pharmacological treatments, see the NICE guideline on medicines optimisation. **[2017]**

1.8.2 Take into account the adverse effects associated with NSAIDs and DMARDs when monitoring spondyloarthritis in primary care. **[2017]**

1.8.3 Advise people that there may be a greater risk of skin cancer in people treated with TNF\u2011\alpha inhibitors. **[2017]**

1.8.4 Discuss risk factors for cardiovascular comorbidities with all people with spondyloarthritis. **[2017]**

1.8.5 Consider regular osteoporosis assessments (every 2 years) for people with axial spondyloarthritis. Be aware that bone mineral density measures may be elevated on spinal dual-energy X-ray absorptiometry (DEXA) due to the presence of syndesmophytes and ligamentous calcification, whereas hip measurements may be more reliable. **[2017]**

1.8.6 Advise people with axial spondyloarthritis that they may be prone to fractures, and should consult a healthcare professional following falls or physical trauma, particularly in the event of increased musculoskeletal pain. **[2017]**

1.9 Organisation of care

Coordinating care across settings

1.9.1 Commissioners should ensure that local arrangements are in place to coordinate care for people across primary and secondary (specialist) care. These should cover:

- prescribing NSAIDs and DMARDs
- monitoring NSAIDs and DMARDs

- managing flares
- ensuring prompt access to specialist rheumatology care when needed
- ensuring prompt access to other specialist services to manage comorbidities and extra-articular symptoms. **[2017]**

1.9.2 Ensure that people with spondyloarthritis have access to specialist care in primary or secondary care settings throughout the disease course to ensure optimal long-term spondyloarthritis management (see section 1.7 for arrangements for managing flares). **[2017]**

1.9.3 Ensure that there is effective communication and coordination between all healthcare professionals involved in the person's care, particularly if the person has comorbidities or extra-articular symptoms. **[2017]**

1.9.4 Ensure that there is communication and coordination between rheumatology and other relevant specialities (such as dermatology, gastroenterology and ophthalmology). This is particularly important for people who:

- are already receiving DMARDs for another condition
- need to start taking DMARDs for another condition. **[2017]**

1.9.5 For guidance on managing the transition of young people with juvenile idiopathic arthritis to adult services, see the NICE guideline on transition from children's to adults' services for young people using health or social care services. **[2017]**

Terms used in this guideline

This section defines terms that have been used in a particular way for this guideline.

Active psoriatic arthritis

Peripheral arthritis with 3 or more tender joints and 3 or more swollen joints.

Biological DMARD

A biological disease-modifying anti-rheumatic drug (DMARD) is any DMARD made by or derived from a biological (natural) source, for example, an animal cell or microorganism. This includes the anti-lymphocyte monoclonal antibodies, interleukin inhibitors and TNF-alpha inhibitors. Examples include bimekizumab and secukinumab (interleukin inhibitors), and adalimumab, golimumab and infliximab (TNF-alpha inhibitors).

Janus kinase (JAK) inhibitor

A targeted synthetic DMARD that inhibits the inflammatory activity of the Janus kinase enzymes. They are given orally. Examples include upadacitinib and tofacitinib.

Tumour necrosis factor (TNF)-alpha inhibitor

A biological DMARD that inhibits an inflammatory protein, tumour necrosis factor-alpha. They are given by injection or infusion. Examples include adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab.

Recommendations for research

The guideline committee has made the following recommendations for research. The committee's full set of research recommendations is detailed in the full guideline.

1 Referral criteria for people with suspected axial spondyloarthritis

What are the optimal referral criteria for people with suspected axial spondyloarthritis?

Why this is important

The Dutch CaFaSpA study (van Hoeven et al. 2014, 2015) should be repeated in a UK population. This would involve examining GP databases to identify a cohort of people who have a diagnosis of non-specific back pain who first consulted their GP for back symptoms under the age of 45. These people would be invited for a full rheumatological assessment (including identifying signs and symptoms relevant to axial spondyloarthritis, X-ray, MRI and HLA-B27 test). All participants would be given a reference-standard diagnosis of axial spondyloarthritis or not (ideally using expert clinician opinion, or if this is not possible, using the ASAS [Assessment of Spondyloarthritis International Society] classification criteria). The cohort would be split into a development and validation set, to derive and validate optimal rules for case-finding from the available data, with each candidate strategy judged according to expected cost per quality-adjusted life year (QALY) gained (the NICE economic model developed for this guideline could easily be used to estimate these).

As a result of the large number of permutations of possible referral strategies, it is impractical to run separate validation studies for all referral criteria that are developed. Therefore, a single large, representative cohort study would, provided it measured the predictor variables for all reasonable referral strategies, provide the ability to develop and validate any number of possible referral strategies. The study would need to be large enough that sufficient data are available to derive new referral rules and to validate those rules in a separate, independent subset of the data. A UK-specific dataset would provide more relevant data to do this than is currently available from the Dutch CaFaSpA study. For example, that study found an HLA-B27 prevalence of 20% in people with axial

spondyloarthritis and 2% in people without; much lower than the estimates found elsewhere (75% and 20% respectively). This lowers the validity of extrapolating any results found to the UK, and reinforces the need for UK-specific data to address this question.

2 Long-term complications of spondyloarthritis

What is the incidence of long-term complications, in particular osteoporosis, cardiovascular disease (CVD) and metabolic syndrome, in people with spondyloarthritis, and how does this compare with the general population? Are any specific spondyloarthritis features or risk factors associated with the incidence and outcomes of these complications?

Why this is important

Spondyloarthritides are a group of systemic inflammatory conditions, and as such it is thought that people with these conditions may have an elevated risk of CVD, particularly if their disease is not adequately controlled. This may have direct vascular effects as well as precluding maintenance of a good level of cardiovascular fitness.

There is also clinical uncertainty around the long-term use of non-steroidal anti-inflammatory drugs (NSAIDs): whether the long-term CVD risks associated with this class of drugs are observed in this population, or whether the suppression of inflammation with these drugs mitigates some of the CVD risks associated with these conditions. In addition, risks of osteoporosis and fracture are known to be higher in people with axial spondyloarthritis than the general population, and the prevalence of axial manifestations in people diagnosed with peripheral disease implies the risks may also be high in peripheral spondyloarthritis.

The longer-term complication rates in the spondyloarthritides need to be established, as well as whether standard biological disease-modifying anti-rheumatic drug (DMARD) therapies and biological DMARDs influence these outcomes. Research that evaluates incidence of osteoporosis, CVD and metabolic syndrome in people with either axial or peripheral spondyloarthritis compared with the general population would therefore be of value. This research should take into account disease stage, personal activity levels and medicine use, and look to address how frequently it is appropriate to monitor people with spondyloarthritis for long-term complications.

3 Educational intervention to improve healthcare professionals' awareness of spondyloarthritis

What is the effectiveness and cost effectiveness of educational interventions for healthcare professionals in order to increase the number of prompt diagnoses of spondyloarthritis?

Why this is important

One of the major reasons for the delays in diagnosing spondyloarthritis is a lack of awareness of the condition by healthcare professionals. This can take many forms, such as a lack of awareness of different spondyloarthritis subtypes, lack of knowledge about associated clinical features (for example, the differences between inflammatory and mechanical back pain) or characteristics of the patient populations (for example, that spondyloarthritis affects similar numbers of men and women, or that a substantial proportion of people with spondyloarthritis are HLA-B27 negative). Educational interventions to improve the level of awareness may therefore lead to reductions in diagnosis delays, but there is a lack of evidence as to the efficacy of these interventions. Randomised controlled trials of structured educational interventions are therefore needed to assess both whether they reduce the length of time it takes for people to be correctly diagnosed, and whether they represent a cost-effective use of NHS resources.

4 Pharmacological management of peripheral spondyloarthritis

What is the comparative effectiveness and cost effectiveness of standard DMARDs for managing peripheral spondyloarthritis, and is this effectiveness affected by differences in dose escalation protocols?

Why this is important

The committee noted that, although there are a number of randomised controlled trials comparing standard DMARDs with placebo for managing peripheral spondyloarthritis, there is a lack of evidence comparing individual standard DMARDs to other standard DMARDs. This lack of evidence makes it difficult to optimise initial therapy, either by specifying specific drugs within the class or optimising dose, administration and

monitoring protocols. There is therefore the need for randomised controlled trials looking at alternative drug, dosing and administration route alternatives for the administration of standard DMARDs for managing peripheral spondyloarthritis. These trials should ensure NSAIDs and steroids are available to participants as needed, and should include (as outcome measures) both health-related quality of life (measured using the EQ-5D) and health service resource use, to enable the results to be used to assess the cost effectiveness of the interventions.

5 Biological therapies for peripheral spondyloarthritis

What is the effectiveness and cost effectiveness of biological DMARDs in people with persistent peripheral spondyloarthritis (excluding psoriatic arthritis) or undifferentiated spondyloarthritis?

Why this is important

Although there have been trials conducted of biological therapies for psoriatic arthritis, which have led to positive recommendations in NICE technology appraisals, no such good-quality evidence exists in enteropathic arthritis, reactive arthritis or undifferentiated spondyloarthritis. The substantial side effects possible with biological therapies, and their significant cost, means it is difficult to justify offering them to these groups without good evidence of efficacy. There is therefore the need for randomised controlled trials, with a sufficient sample size to identify possible benefits, in these 3 populations. If trials were to recruit participants from multiple spondyloarthritis subpopulations, results should be clearly stratified by diagnosis to enable any differences in benefits or harms between the groups to be identified. These trials should include (as outcome measures) both health-related quality of life (measured using the EQ-5D) and health service resource use, to enable the results to be used to assess the cost effectiveness of the interventions.

Context

Spondyloarthritis encompasses a group of inflammatory conditions with some shared features, including extra-articular manifestations. Both peripheral and axial joints can be affected. The spondyloarthritides are distinct from rheumatoid arthritis but are as important to recognise and manage early in their presentation to improve health outcomes.

Most people with these conditions have either psoriatic arthritis or axial spondyloarthritis, which includes ankylosing spondylitis. Ankylosing spondylitis and non-radiographic axial spondyloarthritis primarily affect the spine, in particular the sacroiliac joint. Both conditions present in similar ways; the primary classification difference is whether sacroiliitis is detectable on X-ray.

Psoriatic arthritis may manifest in a number of different patterns. These include predominant involvement of small joints in the hands and feet, predominant large joint involvement, particularly in the knees, or combinations of these. Psoriatic arthritis may also involve the axial joints, and inflammation of the entheses and/or finger and toe joints. Skin and nail involvement may not be present at diagnosis and in its absence, a family history of psoriasis is required to meet the diagnostic criteria.

Less common subgroups are enteropathic spondyloarthritis, which is associated with inflammatory bowel disease (Crohn's disease and ulcerative colitis), and reactive arthritis, which can occur in people after gastrointestinal or genitourinary infections.

The final subgroup is people who have undifferentiated spondyloarthritis. These people generally have an asymmetrical oligoarticular (fewer than 5 involved joints) arthritis, often involving the knees. They do not meet the diagnostic criteria of the other subgroups at presentation but their disease may evolve to do so at a later stage.

This guideline also includes people who are 16 years or older with axial or peripheral symptoms who have previously been diagnosed with juvenile idiopathic arthritis.

Healthcare professionals in non-specialist settings do not always recognise the signs and symptoms of spondyloarthritis, particularly spinal symptoms, which may be mistakenly attributed to other causes of low back pain. This can lead to substantial delays in diagnosis and treatment with consequent disease progression and disability. This

guideline seeks to raise awareness of the features of spondyloarthritis and provide clear advice on what action to take when people with signs and symptoms first present in healthcare settings.

This guideline also provides advice on the interventions available to people with spondyloarthritis. These include pharmacological and non-pharmacological treatments, and surgery. The guidance also provides advice on how care for people with spondyloarthritis should be organised across healthcare settings, and what information and support should be provided.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the NICE topic pages on musculoskeletal conditions and psoriasis.

For full details of the evidence and the guideline committee's discussions, see the full guideline. You can also find information about how the guideline was developed, including details of the committee.

NICE has produced tools and resources to help you put this guideline into practice. For general help and advice on putting our guidelines into practice, see resources to help you put NICE guidance into practice.

Update information

May 2017: Recommendation 1.2.7 was amended to clarify the advice on what imaging should be done.

Minor changes since publication

March 2025: We added links to relevant technology appraisal guidance in the section on pharmacological management of spondyloarthritis. Recommendations marked **[2025]** clarify how to use medicines recommended in NICE technology appraisal guidance.

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