Spondyloarthritis in over 16s: diagnosis and management

NICE guideline: short version

Draft for consultation, September 2016

This guideline covers diagnosing and managing spondyloarthritis that is suspected or confirmed in adults who are 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.

Who is it for?

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

This version of the guideline contains the draft recommendations, context and recommendations for research. Information about how the guideline was developed is on the guideline's page on the NICE website. This includes the guideline committee's discussion and the evidence reviews (in the full guideline), the scope, and details of the committee and any declarations of interest.

Contents

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in 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 and non-radiographic axial spondyloarthritis) or predominantly peripheral (psoriatic arthritis, reactive arthritis and enteropathic spondyloarthritis). Axial presentations of spondyloarthritis are often misdiagnosed as mechanical low back pain, leading to delays in access to effective treatments.

1.1 Recognition and referral in non-specialist 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.

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, dactylitis) or extra-articular (for example, uveitis, psoriasis [including psoriatic nail symptoms]), and risk factors include recent genitourinary infection and a family history of spondyloarthritis or psoriasis.

1.1.3 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.

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

Referral for suspected axial spondyloarthritis

1.1.5 Refer people with low back pain, that started at under 45 years and has lasted for longer than 3 months, to a rheumatologist for a spondyloarthritis assessment when at least **4** of the following are present:

- onset of back pain at under 35 years (this further increases the likelihood that back pain is due to spondyloarthritis compared with onset of back pain at 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 NSAIDs
- a first-degree relative with spondyloarthritis
- current or past arthritis
- current or past enthesitis
- current or past psoriasis.

If 3 criteria are present, perform an HLA-B27 test and refer to a rheumatologist for a spondyloarthritis assessment if this test is positive.

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 assessments 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 1.1.11 for

guidance on referral for immediate [same-day] ophthalmological assessment for people with acute anterior uveitis).

Referral for suspected peripheral spondyloarthritis

1.1.7 For guidance on identifying spondyloarthritis in people with an existing diagnosis of psoriasis, see the NICE guideline on psoriasis.

1.1.8 Urgently refer people with suspected new-onset inflammatory polyarthritis 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.

1.1.9 Refer people with dactylitis to a rheumatologist for a spondyloarthritis assessment.

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 1.1.11 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.

Referral for suspected acute anterior uveitis

1.1.11 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).

Case-finding in people with acute anterior uveitis

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

- consulted their GP about joint pains **or**
- experienced chronic low back pain that started at under 45 years and has lasted for longer than 3 months.

1.1.13 If the person meets either of the criteria in recommendation 1.1.12, 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 and refer the person to a rheumatologist for a spondyloarthritis assessment if this test is positive.

1.2 Diagnosing spondyloarthritis in specialist care

1.2.1 In specialist settings, consider using validated spondyloarthritis criteria to diagnose spondyloarthritis. Examples of criteria include:

- Amor criteria
- ASAS axial or peripheral criteria
- Berlin criteria
- European Spondyloarthropathy Study Group (ESSG) criteria
- French Society of Rheumatology reactive arthritis criteria
- Rome criteria
- modified New York criteria.

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

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

Suspected axial spondyloarthritis

1.2.4 Offer plain film X-ray of the sacroiliac joints for people with suspected axial spondyloarthritis.

1.2.5 Diagnose axial spondyloarthritis if the plain film X-ray shows sacroiliitis meeting the modified New York criteria (bilateral grade 2–4 or unilateral grade 3–4 sacroiliitis).

1.2.6 If the plain film X-ray does not show sacroiliitis meeting modified New York criteria (bilateral grade 2–4 or unilateral grade 3–4 sacroiliitis), request unenhanced MRI using an inflammatory back pain protocol.

1.2.7 Radiologists receiving a request for an inflammatory back pain MRI should perform short T1 inversion recovery (STIR), T1 (both views), cervical, thoracic and lumbar (whole spine, sagittal view), and sacroiliac joints (coronal view).

1.2.8 Use the ASAS/OMERACT MRI criteria to interpret the MRI.

1.2.9 Diagnose axial spondyloarthritis if the MRI meets the ASAS/OMERACT MRI criteria.

1.2.10 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.

1.2.11 If interpretation of MRI findings remains negative, offer an HLA-B27 test if it has not already been done.

1.2.12 If the HLA-B27 test is positive, base the diagnosis on clinical features, for example, using the clinical ‘arm’ of the ASAS axial classification criteria.

1.2.13 If a diagnosis of spondyloarthritis cannot be made and clinical suspicion remains high, consider a follow-up MRI.

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

Suspected peripheral spondyloarthritis

1.2.15 Offer plain film X-ray of symptomatic hands and feet for people with suspected peripheral spondyloarthritis in these areas.

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

- of the hands and feet to assess for joint involvement
- of suspected enthesitis sites.

1.2.17 Consider plain film X-rays, ultrasound and/or MRI of other peripheral symptomatic sites.

1.2.18 If a diagnosis of peripheral spondyloarthritis is confirmed:

- offer plain film X-ray of the sacroiliac joint to assess for axial involvement, even if the person does not have any symptoms
- only consider MRI of the sacroiliac joint if the result is likely to change management.

1.2.19 Interpret a positive HLA-B27 result as increasing the likelihood of peripheral spondyloarthritis.

1.2.20 Do not routinely test for infective antibody status to diagnose reactive arthritis in people with a history of gastrointestinal infection.

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.

1.3.2 Provide explanations and information about spondyloarthritis. Information should be oral and written, and may include:

- what spondyloarthritis is
- diagnosis and prognosis
- treatment options (pharmacological and non-pharmacological)
- likely symptoms and how they can be managed
- flares and extra-articular symptoms
- self-help options
- research and medicines
- which healthcare professionals will be involved with the person's care and how to get in touch with them
- local support groups, online forums and national charities, and how to get in touch with them.

Information about disease flares

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

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

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

- access to care during flares
- self-care (for example, exercises, stretching and joint protection)
- pain and fatigue management
- medicines
- managing the impact on daily life and ability to work.

1.4 Pharmacological management of spondyloarthritis

Axial spondyloarthritis

NSAIDs

1.4.1 Offer NSAIDs to people with pain associated with axial spondyloarthritis.

1.4.2 If an NSAID taken at the maximum tolerated dose for 2–4 weeks does not provide adequate pain relief, consider switching to another NSAID.

Biological DMARDs

1.4.3 For guidance on treating axial spondyloarthritis with biological disease-modifying anti-rheumatic drugs (DMARDs), see NICE's technology appraisal guidance on TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis[1].

Peripheral spondyloarthritis

Non-biological therapies

1.4.4 Consider local corticosteroid injections as monotherapy for non-progressive monoarthritis.

1.4.5 Offer standard DMARDs to people with:

- peripheral polyarthritis
- oligoarthritis

[1] NICE guidance on secukinumab for treating ankylosing spondylitis is in development and is due to be published in October 2016.

- persistent or progressive monoarthritis associated with peripheral spondyloarthritis.

1.4.6 When deciding which DMARD to offer, take into account:

- the person's needs, preferences and circumstances (such as pregnancy planning and alcohol consumption)
- comorbidities
- disease characteristics.

1.4.7 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.

1.4.8 Consider NSAIDs as an adjunct to standard DMARDs or biological DMARDs to manage symptoms.

1.4.9 If NSAIDs do not provide adequate relief from symptoms, consider steroid injections (local or intramuscular) or short-term oral steroid therapy as an adjunct to DMARDs or biological DMARDs to manage symptoms.

1.4.10 If extra-articular disease is adequately controlled by an existing standard DMARD but spondyloarthritis is not, consider adding another standard DMARD.

Reactive arthritis

Antibiotics

1.4.11 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.

Psoriatic arthritis

Biological DMARDs – etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis

1.4.12 Etanercept, infliximab and adalimumab are recommended for the treatment of adults with active and progressive psoriatic arthritis when the following criteria are met:

- The person has peripheral arthritis with 3 or more tender joints and 3 or more swollen joints, **and**
- The psoriatic arthritis has not responded to adequate trials of at least 2 standard DMARDs, administered either individually or in combination. [This recommendation is from NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis.]

1.4.13 Treatment as described in 1.4.12 should normally be started with the least expensive drug (taking into account drug administration costs, required dose and product price per dose). This may need to be varied for individual patients because of differences in the method of administration and treatment schedules. [This recommendation is from NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis.]

1.4.14 Etanercept, adalimumab or infliximab treatment should be discontinued in people whose psoriatic arthritis has not shown an adequate response using the Psoriatic Arthritis Response Criteria (PsARC) at 12 weeks. An adequate response is defined as an improvement in at least 2 of the 4 PsARC criteria, (1 of which has to be joint tenderness or swelling score) with no worsening in any of the 4 criteria. People whose disease has a Psoriasis Area and Severity Index (PASI) 75 response at 12 weeks but whose PsARC response does not justify continuation of treatment should be assessed by a dermatologist to determine whether continuing treatment is appropriate on the basis of skin response (see Etanercept and efalizumab for the treatment of adults with psoriasis [NICE technology

appraisal guidance 103],Infliximab for the treatment of adults with psoriasis [NICE technology appraisal guidance 134] and Adalimumab for the treatment of adults with psoriasis [NICE technology appraisal guidance 146] for guidance on the use of tumour necrosis factor [TNF] inhibitors in psoriasis). [This recommendation is from NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis.]

1.4.15 When using the PsARC healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate. [This recommendation is from NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis.]

Biological DMARDs – golimumab

1.4.16 Golimumab is recommended as an option for the treatment of active and progressive psoriatic arthritis in adults only if:

- it is used as described for other tumour necrosis factor (TNF) inhibitor treatments in etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (NICE technology appraisal guidance 199; see recommendations 1.4.12–1.4.15 in this guideline),
  and
- the manufacturer provides the 100 mg dose of golimumab at the same cost as the 50 mg dose. [This recommendation is from NICE's technology appraisal guidance on golimumab for the treatment of psoriatic arthritis.]

1.4.17 When using the Psoriatic Arthritis Response Criteria (PsARC; as set out in NICE technology appraisal guidance 199; see recommendations 1.4.12–1.4.15 in this guideline), healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate. [This recommendation

is from NICE's technology appraisal guidance on golimumab for the treatment of psoriatic arthritis.]

Biological DMARDs – ustekinumab

1.4.18 For guidance on treating psoriatic arthritis with ustekinumab, see NICE's technology appraisal guidance on ustekinumab for treating active psoriatic arthritis.

Biological DMARDs – apremilast

1.4.19 For guidance on treating psoriatic arthritis with apremilast, see NICE's technology appraisal guidance on apremilast for treating active psoriatic arthritis.

1.5 Non-pharmacological management of spondyloarthritis

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

- stretching
- deep breathing
- spinal extension
- range of motion exercises for the lumbar, thoracic and cervical sections of the spine
- aerobic exercise.

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

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

- assess their needs
- provide advice about physical aids
- arrange periodic reviews to assess the person's changing needs.

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).

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.

1.7 Managing flares

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

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 DMARDs
- have comorbidities that may affect treatment or management of flares.

1.7.3 Be aware that uveitis can occur during flare episodes. See recommendation 1.1.11 for guidance on immediate (same-day) ophthalmological assessment for people with acute anterior uveitis.

1.8 Long-term complications

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

1.8.2 Take into account the adverse effects associated with NSAIDs, standard DMARDs and biological DMARDs when monitoring spondyloarthritis in primary care.

1.8.3 Be aware there may be a greater risk of skin cancer in people treated with TNF-alpha inhibitors.

1.8.4 Discuss risk factors for cardiovascular comorbidities with all people with spondyloarthritis.

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 DEXA due to the presence of syndesmophytes and ligamentous calcification, whereas hip measurements may be more reliable.

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.

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 care. These should cover:

- prescribing NSAIDs and standard DMARDs
- monitoring NSAIDs, standard DMARDs and biological 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.

1.9.2 Ensure that people with spondyloarthritis have access to specialist care in primary or secondary settings throughout the disease course to ensure optimal long-term spondyloarthritis management.

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.

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 standard DMARDs or biological DMARDs for another condition
- need to start taking standard DMARDs or biological DMARDs for another condition.

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.

Putting this guideline into practice

[This section will be completed after consultation]

NICE has produced tools and resources [link to tools and resources tab] to help you put this guideline into practice.

[Optional paragraph if issues raised] Some issues were highlighted that might need specific thought when implementing the recommendations. These were raised during the development of this guideline. They are:

- [add any issues specific to guideline here]
- [Use 'Bullet left 1 last' style for the final item in this list.]

Putting recommendations into practice can take time. How long may vary from guideline to guideline, and depends on how much change in practice or services is needed. Implementing change is most effective when aligned with local priorities.

[Clinical topics only] Changes recommended for clinical practice that can be done quickly – like changes in prescribing practice – should be shared quickly. This is because healthcare professionals should use guidelines to guide their work – as is required by professional regulating bodies such as the General Medical and Nursing and Midwifery Councils.

Changes should be implemented as soon as possible, unless there is a good reason for not doing so (for example, if it would be better value for money if a package of recommendations were all implemented at once).

Different organisations may need different approaches to implementation, depending on their size and function. Sometimes individual practitioners may be able to respond to recommendations to improve their practice more quickly than large organisations.

Here are some pointers to help organisations put NICE guidelines into practice:

1. **Raise awareness** through routine communication channels, such as email or newsletters, regular meetings, internal staff briefings and other communications with all relevant partner organisations. Identify things staff can include in their own practice straight away.

2. **Identify a lead** with an interest in the topic to champion the guideline and motivate others to support its use and make service changes, and to find out any significant issues locally.

3. **Carry out a baseline assessment** against the recommendations to find out whether there are gaps in current service provision.

4. **Think about what data you need to measure improvement** and plan how you will collect it. You may want to work with other health and social care organisations and specialist groups to compare current practice with the recommendations. This may also help identify local issues that will slow or prevent implementation.

5. **Develop an action plan**, with the steps needed to put the guideline into practice, and make sure it is ready as soon as possible. Big, complex changes may take longer to implement, but some may be quick and easy to do. An action plan will help in both cases.

6. **For very big changes** include milestones and a business case, which will set out additional costs, savings and possible areas for disinvestment. A small project group could develop the action plan. The group might include the guideline champion, a senior organisational sponsor, staff involved in the associated services, finance and information professionals.

7. **Implement the action plan** with oversight from the lead and the project group. Big projects may also need project management support.

8. **Review and monitor** how well the guideline is being implemented through the project group. Share progress with those involved in making improvements, as well as relevant boards and local partners.

NICE provides a comprehensive programme of support and resources to maximise uptake and use of evidence and guidance. See our into practice pages for more information.

Also see Leng G, Moore V, Abraham S, editors (2014) Achieving high quality care – practical experience from NICE. Chichester: Wiley.

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.

The majority of 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 manifest 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 following 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.

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 spondyloarthritis

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

Repeat the CaFaSpA study (van Hoeven et al. 2014, 2015) in a UK population. This would involve examination of 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 full rheumatological work-up (including: identification of signs and symptoms relevant to axial spondyloarthritis, X-ray, MRI, HLA-B27 test). All participants would be given a reference-standard diagnosis of axial spondyloarthritis or not (ideally using expert clinician opinion; if not feasible, use ASAS 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 QALY gained (NICE model could be used to estimate these).

Why this is important

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 Referral criteria for people with suspected spondyloarthritis

At what stage and using what criteria should people with inflammatory bowel disease be referred to a rheumatologist for a spondyloarthritis assessment?

Why this is important

The guideline committee noted that people with inflammatory bowel disease (Crohn's disease or ulcerative colitis) are more likely to have or develop spondyloarthritis than those without. During the development of this guideline specific, validated referral rules were identified for people with inflammatory back pain or acute anterior uveitis, but not for people with inflammatory bowel disease. An inflammatory bowel disease-specific referral rule would provide additional value as the diagnostic importance of other spondyloarthritis associated features may be different in the presence of inflammatory bowel disease, something which is not possible to judge from the currently available data. There is therefore a need for the development of inflammatory bowel disease-specific referral rules, which would need to be prospectively validated in a cohort of people with confirmed inflammatory bowel disease and suspected spondyloarthritis. This study would need to follow up both those people who were and were not referred until a definitive diagnosis has been made (ideally using expert clinician opinion; if this is not feasible, using the ASAS classification criteria).

3 Educational intervention to improve healthcare professional 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 identified during this guideline for the delays in diagnosis of 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 corticosteroids, NSAIDs and standard DMARDs for the management of peripheral spondyloarthritis, and is this effectiveness affected by differences in dose escalation protocols, frequency of monitoring or route of drug administration?

Why this is important

The committee noted that, whilst there are a number of randomised controlled trials comparing standard DMARDs with placebo for the management of peripheral spondyloarthritis, there is a lack of evidence comparing individual standard DMARDs to either NSAIDs or 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 pharmacological management of peripheral spondyloarthritis. These trials should include as outcomes 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 outcomes 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.

ISBN: