Appendix B: Guideline scope

B.1 Guideline title

Spondyloarthritis: the diagnosis and management of spondyloarthritis.

B.1.1 Short title

Spondyloarthritis

B.2 The remit

The Department of Health has asked NICE: 'to produce a guideline on the diagnosis and management of seronegative arthropathies'.

B.3 Need for the guideline

B.3.1 Epidemiology

1. Spondyloarthritis refers to a group of inflammatory seronegative arthropathies with common characteristics, frequently including axial skeleton and peripheral asymmetric joint involvement, enthesitis (inflammation of the areas where tendons or ligaments insert into bone), extra articular features, an absence of rheumatoid factor in the blood and an association with HLA B27 antigen. 'Seronegative' used to refer to the absence of rheumatoid factor, but this terminology is no longer considered useful in clinical practice.
2. Spondyloarthritis includes psoriatic arthritis, ankylosing spondylitis, reactive arthritis, enteropathic arthritis, and undifferentiated spondyloarthritis.
    - Psoriatic arthritis is a chronic, relapsing condition affecting the joints and is associated with psoriasis of the skin or nails.
    - Ankylosing spondylitis is a chronic progressive systemic disease that primarily affects the sacroiliac joints and spine, causing chronic back pain.
    - Reactive arthritis is associated with HLA B27. It often affects the lower limb joints and is associated with inflammation of the eyes and urethra. It is an immune reaction to infections such as *salmonella*, *shigella*, *yersinia*, *campylobacter* and *chlamydia*.
    - Enteropathic arthritis is associated with chronic inflammatory bowel disease, including ulcerative colitis and Crohn's disease, and can be progressive.
    - Undifferentiated spondyloarthritis is spondyloarthritis that does not match the diagnostic criteria for the conditions above. This includes non-radiographic axial spondyloarthritis.
3. Spodyloarthritis also includes adults with axial or peripheral symptoms who had previous been diagnosed with juvenile idiopathic arthritis.
4. In the rest of this document 'spondyloarthritis' covers the conditions listed above. These conditions mainly affect either the axial or peripheral joints. The axial conditions are sometimes classified based on how they were diagnosed, as 'X-ray confirmed', 'MRI confirmed' or 'clinically diagnosed without radiological confirmation'.
5. If spondyloarthritis is suspected, patients are referred to a rheumatologist for investigation, diagnosis and management. Management is usually based on which joints (axial or peripheral) are most affected.
6. Spondyloarthritis has a reported prevalence in Western Europe of between 0.8% in Lithuania and 1.7% in Germany, and is more common than rheumatoid arthritis. The age of onset varies. Ankylosing spondylitis most commonly starts in the teens or early

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twenties. As well as joint and spine symptoms, the other co-morbidities and complications related to HLA B27 can impact negatively on quality of life.

B.3.2 Current practice

7. Diagnosis of spondyloarthritis can be challenging. Some of the clinical features are common in the general population, and there are no single clinical features or laboratory tests that can be used to diagnose spondyloarthritis. Some forms of spondyloarthritis are estimated to take 8 to 10 years to diagnose. In particular, women with axial symptoms are thought to be underdiagnosed, as ankylosing spondylitis has historically been seen as a predominantly male disease and there is no change on X-ray.
8. Early diagnosis is important, as there may be effective treatments for spondyloarthritis. The Assessment of Spondyloarthritis International Society (ASAS) criteria have recently been developed to help with classifying and diagnosing individual patients. Other criteria such as Classification for Psoriatic Arthritis (CASPAR) and the New York criteria are also widely used in the UK.
9. People generally present with joint symptoms, related comorbidities, or a combination of both.
10. Investigations will depend on clinical presentation and can include:
11. blood tests (erythrocyte sedimentation rate, HLA B27, antinuclear antibodies and C-reactive protein)
12. Imaging (joint ultrasound, X-ray, CT, MRI and positron emission tomography [PET]).
13. Spondyloarthritis is managed based on the presenting symptom site (axial or peripheral) rather than the specific condition. Management includes:
14. Physiotherapy and other manual therapies
15. Analgesics
16. Non-steroidal anti-inflammatory drugs
17. Corticosteroids (oral or injections)
18. Standard disease-modifying anti-rheumatic drugs
19. Biological disease-modifying anti-rheumatic drugs (such as tumour necrosis factor inhibitors)
20. Surgery (including joint replacement and spinal surgery such as osteotomy or fusion).

B.4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, ‘Further information’).

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

B.4.1 Population

B.4.1.1 Groups that will be covered

1. Young people aged 16 years and older and adults with suspected or confirmed spondyloarthritis. This includes people with:
   - ankylosing spondylitis
   - non-radiographic axial spondyloarthritis
   - enteropathic arthritis
   - reactive arthritis related to HLA B27

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- psoriatic arthritis
- undifferentiated spondyloarthritis

and also:

- young people and adults with spondyloarthritis whose symptoms developed in childhood, including people who have previously been diagnosed with enthesitis-related and psoriatic-related juvenile idiopathic arthritis.

2. The following patient subgroups have been identified as needing specific consideration
   - women with axial spondyloarthritis
   - people with comorbidities related to HLA B27 (such as inflammatory bowel disease and psoriasis) that may influence the choice of therapeutic agents and the ongoing management plan.

B.4.2 Groups that will not be covered

1. People whose signs or symptoms are caused by rheumatoid arthritis, osteoarthritis or gout.
2. People with reactive arthritis confirmed as unrelated to *salmonella*, *shigella*, *yersinia*, *campylobacter* or *chlamydia*.
3. Children and young people under the age of 16 years.7

B.5 Setting

1. All settings in which NHS-funded care is received.

B.6 Management

B.6.1 Key issues that will be covered

1. Early recognition (signs and symptoms, risk factors).
2. Early diagnosis (factors that make early diagnosis harder, strategies to improve early diagnosis, and risk assessment scores).
3. Initial assessment (including case-finding in people with a comorbid condition, risk factors, signs and symptoms, blood tests and imaging).
4. Information for patients and carers.
5. Non-pharmacological interventions (for example, hydrotherapy, structured exercise, physiotherapy and other manual therapies, acupuncture, and physical aids such as braces).
6. Pharmacological interventions for articular symptoms (for example, antibiotics for reactive arthritis, non-steroidal anti-inflammatory drugs, corticosteroids, standard disease-modifying anti-rheumatic drugs, and biological disease-modifying anti-rheumatic drugs). Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication ('off-label use') may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.
7. Switching and sequencing of pharmacological interventions.
8. Referral for surgical intervention (including joint replacement and spinal surgery such as osteotomy or fusion).
9. Management of flare episodes.
10. Ongoing management and review, including managing the risk of the long-term complications of both the condition and the treatments used.

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11. Organisation of care, including involving other healthcare professionals, multidisciplinary and multi-professional teams, and transition of care from specialist paediatric services to specialist adult rheumatology services.

B.6.2 Issues that will not be covered

1. Signs, symptoms and referral for people with an existing diagnosis of psoriasis (the guideline will cross refer to Psoriasis [NICE clinical guideline 153]).
2. Management of non-articular symptoms that are associated with spondyloarthritis, including:
3. Infections that cause HLA B27 reactive arthritis (unless management is altered to treat articular symptoms)
4. Comorbidities related to HLA B27 (although the implications for the cross-specialty organisation of care in this group is recognised).
5. The effectiveness of commonly used analgesics such as aspirin or paracetamol.
6. The effectiveness of herbal remedies.
7. The effectiveness of biological disease-modifying anti-rheumatic drugs for ankylosing spondylitis and non-radiographic axial spondyloarthritis.
8. The effectiveness of biological disease-modifying anti-rheumatic drugs for psoriatic arthritis.

B.7 Main outcomes

1. Functional capacity (such as the Health Assessment Questionnaire or the Bath Ankylosing Spondylitis Functional Index [BASFI]) and participation. Ability to work may be used as a measure of functional capacity. However, NICE guidance does not prioritise treatments most likely to benefit people of working age at the expense of other groups.
2. Health-related quality of life (using a generic quality-of-life scale such as EQ-5D).
3. Disease-specific quality of life.
4. Fatigue.
5. Pain.
6. Mental health.
7. Disease activity and measures of treatment response (such as the psoriatic arthritis response criteria [PsARC], the American College of Rheumatology Criteria [ACR20/50/70], and the Bath Ankylosing Spondylitis Disease Activity Index [BASDAI]).
8. Radiological assessment of disease progression or remission.
9. Adverse events.
10. Tolerance of treatments
11. Mobility
12. Long-term sequelae of treatments.

B.8 Review questions

Review questions guide a systematic review of the literature. They address only the key issues covered in the scope, and usually relate to interventions, diagnosis, prognosis, service delivery or patient experience. Please note that these review questions are draft versions and will be finalised with the Guideline Development Group.

B.8.1 Recognition of spondyloarthritis

1. What signs and symptoms should prompt a healthcare professional to think of spondyloarthritis?

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2. What risk factors should increase suspicion of spondyloarthritis?
3. What are the obstacles to a prompt diagnosis of spondyloarthitis?
4. What is the diagnostic utility of a risk assessment score for identifying spondyloarthritis?
5. What is the effectiveness of information gathering (for example family history, self-report questionnaires, and screening criteria) in improving early diagnosis of spondyloarthritis?
6. What is the comparative effectiveness of different referral strategies in diagnosing spondyloarthritis?

B.8.2 Initial assessment in young people (16 and older) and adults

7. What is the diagnostic utility of a HLA B27 test for investigating suspected spondyloarthritis?
8. What is the diagnostic utility of an erythrocyte sedimentation rate test for investigating suspected spondyloarthritis?
9. What is the diagnostic utility of a C-reactive protein test for investigating suspected spondyloarthritis?
10. What is the diagnostic utility of imaging (alone or in sequence) for investigating suspected spondyloarthritis?
11. What is the diagnostic utility of testing for infection such as *salmonella*, *shigella*, *yersinia*, *campylobacter* and *chlamydia* in cases of suspected reactive arthritis?

B.8.3 Referral to secondary care and specialist advice

12. What are the indications (signs, risk factors, test or scan findings) for referral for specialist advice at initial diagnosis?

B.8.4 Transition to adult services

13. How should transition from specialist paediatric services to specialist adult rheumatology services be managed for young people between the ages of 16 and 18?

B.8.5 Non-pharmacological interventions

14. What is the effectiveness of physiotherapy and other manual therapies (such as osteopathy and chiropractory) compared with standard care for managing spondyloarthritis?
15. What is the effectiveness of structured exercise compared with standard care for managing spondyloarthritis?
16. What is the effectiveness of hydrotherapy compared with standard care for managing spondyloarthritis?
17. What is the effectiveness of acupuncture compared with sham acupuncture for managing spondyloarthritis?
18. What is the effectiveness of physical aids (for example, braces) compared with standard care for managing spondyloarthritis?

B.8.6 Pharmacological interventions

19. What is the effectiveness of long-term (3 months or longer) treatment with antibiotics for first-line management of reactive arthritis compared with standard treatment?
20. What is the comparative effectiveness of the following pharmacological interventions for management of axial spondyloarthritis:
    - corticosteroids
    - non-steroidal anti-inflammatory drugs
    - standard disease-modifying anti-rheumatic drugs.

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21. What is the comparative effectiveness of the following pharmacological interventions for management of peripheral spondyloarthritis:
    - corticosteroids
    - non-steroidal anti-inflammatory drugs
    - standard disease-modifying anti-rheumatic drugs.
22. How often should people receiving pharmacological interventions for managing spondyloarthritis be monitored?
23. When a first-line treatment has failed, what is the effectiveness of the following for managing spondyloarthritis:
    - switching to a different pharmacological intervention?
    - augmenting with a second pharmacological intervention?
24. What is the effectiveness of systemic biological disease-modifying anti-rheumatic drugs for managing symptoms of enteropathic arthritis?
25. What is the effectiveness of systemic biological disease-modifying anti-rheumatic drugs for managing symptoms of reactive arthritis?
26. What is the effectiveness of systemic biological disease-modifying anti-rheumatic drugs for managing symptoms of undifferentiated spondyloarthritis, excluding non-radiographic ankylosing spondylitis?

B.8.7 Information

27. What information on treatment, long-term complications and self-management do young people and adults with spondyloarthritis find useful?
28. What is the effectiveness of information and education in the management of flare episodes?

B.8.8 Ongoing management

29. What is the effectiveness of direct access to specialist care, compared with initial primary care access followed by specialist care, in the management of flare episodes?
30. What is the effectiveness of specialist-led long-term management of spondyloarthritis compared with primary-care-led long-term management
31. How should the cross-speciality care for people with spondyloarthritis be organised?
32. What are the long-term complications associated with spondyloarthritis?
33. What are the long-term complications associated with the treatments for spondyloarthritis?

B.8.9 Referral for surgical interventions

34. What factors predict clinical improvement after spinal surgery (including osteotomy and fusion) in people with axial inflammation?
35. What factors predict clinical improvement after joint replacement surgery?

B.9 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. In line with the reference case for economic evaluation detailed in 'The guidelines manual', productivity costs will not be included in health economic analyses. However, it is possible that the ability to work may be considered as a surrogate measure of broader functional

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capacity and this may, in turn, contribute to estimates of health-related quality of life. Further detail on the methods can be found in The guidelines manual.

B.10 Status

B.10.1 Scope

This is the final scope.

B.10.2 Timing

The development of the guideline recommendations will begin in September 2014.

B.11 Related NICE guidance

B.11.1 Published guidance

B.11.1.1 NICE guidance to be updated

None.

B.11.1.2 NICE guidance to be incorporated

- Golimumab for the treatment of psoriatic arthritis. NICE technology appraisal guidance 220 (2011).
- Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis. NICE technology appraisal guidance 199 (2010).

B.11.1.3 NICE guidance to be cross-referred to

- Guidance on the use of etanercept for the treatment of juvenile idiopathic arthritis. NICE technology appraisal guidance 35 (2002).
- Tocilizumab for the treatment of systemic juvenile idiopathic arthritis. NICE technology appraisal 238 (2011).
- Abatacept for treating rheumatoid arthritis after the failure of conventional disease-modifying anti-rheumatic drugs (rapid review of technology appraisal guidance 234). NICE technology appraisal 280 (2013).
- Abatacept for treating rheumatoid arthritis after the failure of conventional disease-modifying anti-rheumatic drugs (rapid review of technology appraisal guidance 234). NICE technology appraisal 280 (2013).
- Ustekinumab for treating active psoriatic arthritis. NICE technology appraisal guidance 344 (2014).
- Psoriasis. NICE clinical guideline 153 (2012).

B.11.1.4 Other related NICE guidance

- Total hip replacement and resurfacing arthroplasty for end-stage arthritis of the hip (review of technology appraisal guidance 2 and 44). NICE technology appraisal 304 (2014).
- Osteoarthritis. NICE clinical guideline 177 (2014).
- Ulcerative colitis. NICE clinical guideline 166 (2013).
- Crohn's disease. NICE clinical guideline 152 (2012).
- Patient experience in adult NHS services. NICE clinical guidance 138 (2012).

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- Golimumab for the treatment of ankylosing spondylitis. NICE technology appraisal guidance 233 (2011).
- Depression with a chronic physical health problem. NICE clinical guideline 91 (2009).
- Rheumatoid arthritis. NICE clinical guideline 79 (2009).
- Adalimumab, etanercept and infliximab for ankylosing spondylitis. NICE technology appraisal guidance 143 (2008).
- Guidance under development
- NICE is currently developing the following related guidance (details available from the NICE website)
- Transition from children's to adult services. NICE social care guidance. Publication expected February 2016.
- TNF-alpha inhibitors for ankylosing spondylitis and axial spondyloarthritis without radiographic evidence of ankylosing spondylitis (including a review of technology appraisal 143 and technology appraisal 233). NICE technology appraisal guidance. Publication expected January 2015.
- Low back pain. NICE clinical guideline 88 (2009; update in progress).

B.12 Further information

Information on the guideline development process is provided in the following documents, available from the NICE website:

- How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS: 5th edition
- The guidelines manual.

Information on the progress of the guideline will also be available from the NICE website.

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