NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SCOPE

1 Guideline title

Seronegative arthropathies: the diagnosis and management of seronegative arthropathies.[1]

1.1 Short title

Seronegative arthropathies.[1]

2 The remit

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

3 Need for the guideline

3.1 Epidemiology

a) 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.

[1] It is proposed to change this title to Spondyloarthritis: the diagnosis and management of spondyloarthritis

b) 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 urinary tract. 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.

c) 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’.

d) 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.

e) Spondyloarthritis has a reported prevalence of in Western Europe 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

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.

3.2 Current practice

a) 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 make a diagnosis of spondyloarthritis. Diagnosis can be slow (it can take several years to diagnose ankylosing spondylitis). In particular, women with axial symptoms are thought to be underdiagnosed.

b) 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.

c) People generally present with joint symptoms, related comorbidities, or a combination of both.

d) Investigations will depend on clinical presentation and can include:

- blood tests (erythrocyte sedimentation rate, antinuclear antibodies and C-reactive protein)
- imaging (joint ultrasound, X-ray, MRI and positron emission tomography [PET]).

e) Spondyloarthritis is managed based on the presenting symptom site (axial or peripheral) rather than the specific condition. It includes:

- physiotherapy
- analgesics
- non-steroidal anti-inflammatory drugs
- corticosteroids (oral or injections)

- standard disease-modifying anti-rheumatic drugs
- biological disease-modifying anti-rheumatic drugs (such as tumour necrosis factor inhibitors)
- surgery (including joint replacement and spinal straightening).

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.

4.1 Population

4.1.1 Groups that will be covered

a) 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
- psoriatic arthritis
- undifferentiated spondyloarthritis

and also:

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

b) The following patient subgroups have been identified as needing specific consideration

- women with non-radiographic 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.

4.1.2 Groups that will not be covered

a) People whose signs or symptoms are caused by rheumatoid arthritis, osteoarthritis or gout.

b) People with reactive arthritis not related to *salmonella*, *shigella*, *yersinia*, *campylobacter* or *chlamydia*.

c) Children and young people under the age of 16 years.

4.2 Setting

a) All settings in which NHS-funded care is received.

4.3 Management

4.3.1 Key issues that will be covered

a) Initial assessment (including early recognition, opportunistic case-finding, risk factors, signs and symptoms, blood tests and imaging).

b) Educating healthcare professionals to recognise the condition early.

c) Information for patients and carers.

d) Non-pharmacological interventions (for example, hydrotherapy, structured exercise, physiotherapy, acupuncture, and physical aids such as braces).

e) Pharmacological interventions (for example, 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.

f) Switching and sequencing of pharmacological interventions.

g) Referral for surgical intervention (including joint replacement and spinal straightening).

h) Management of flare episodes.

i) Ongoing management and review, including managing the risk of long-term complications.

j) Organisation of care, including involving other healthcare professionals, in multidisciplinary and multi-professional teams and transition of care to adult services.

4.3.2 Issues that will not be covered

a) Signs, symptoms and referral for those with a diagnosis of psoriasis.

b) Management of the non-articular complications of spondyloarthritis.

c) Management of comorbidities related to HLA B27 (although the need for special consideration for management in this group is recognised).

d) The effectiveness of commonly-used analgesics such as aspirin or paracetamol.

e) The effectiveness of herbal remedies.

f) The effectiveness of biological disease-modifying anti-rheumatic drugs for ankylosing spondylitis and non-radiographic axial spondyloarthritis.

g) The effectiveness of biological disease-modifying anti-rheumatic drugs for psoriatic arthritis.

4.4 Main outcomes

a) Functional capacity (such as the Health Assessment Questionnaire) and participation. Ability to work may be used as a measure of functional capacity. However, NICE guidance does prioritise treatments most likely to benefit people of working age at the expense of other groups).

b) Health-related quality of life (using a generic quality-of-life scale such as EQ-5D).

c) Disease-specific quality of life.

d) Fatigue.

e) Pain.

f) Mental health.

g) 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 [BASDA]).

h) Radiological assessment of disease progression or remission.

i) Adverse events.

j) Tolerance of treatments.

4.5 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.

4.5.1 Initial assessment in young people (16 and older) and adults

1. What are the signs and symptoms of spondyloarthritis?
2. What are the risk factors for spondyloarthritis?
3. What is the diagnostic utility of a HLA B27 test for investigating suspected spondyloarthritis?
4. What is the diagnostic utility of an erythrocyte sedimentation rate test for investigating suspected spondyloarthritis?
5. What is the diagnostic utility of a C-reactive protein test for investigating suspected spondyloarthritis?
6. What is the diagnostic utility of an ultrasound for investigating suspected spondyloarthritis?
7. What is the diagnostic utility of an X-ray for investigating suspected spondyloarthritis?
8. What is the diagnostic utility of an MRI scan for investigating suspected spondyloarthritis
9. What is the diagnostic utility of a PET scan for investigating suspected spondyloarthritis?

4.5.2 Referral to secondary care and specialist advice

10. What information do healthcare professionals in non-specialist settings need to help them make a timely diagnosis of spondyloarthritis?

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

4.5.3 Transition to adult services

12. How should transition to adult services be managed for young people between the ages of 16 and 18?

4.5.4 Non-pharmacological interventions

13. What is the effectiveness of physiotherapy compared with standard care for managing spondyloarthritis?

14. What is the effectiveness of structured exercise compared with standard care for managing spondyloarthritis?

15. What is the effectiveness of hydrotherapy compared with standard care for managing spondyloarthritis?

16. What is the effectiveness of acupuncture compared with sham acupuncture for managing spondyloarthritis?

17. What is the effectiveness of physical aids (for example, braces) compared with standard care for managing spondyloarthritis?

4.5.5 Pharmacological interventions

18. What is the effectiveness of corticosteroids compared with placebo for first-line pharmacological management of spondyloarthritis?

19. What is the effectiveness of non-steroidal anti-inflammatory drug therapy compared with placebo for the first-line pharmacological management of spondyloarthritis?

20. What is the effectiveness of combinations of pharmacological interventions for the first-line management of spondyloarthritis?

21. When first-line therapy has failed, what is the effectiveness of the following for managing spondyloarthritis:

- switching to a different pharmacological intervention?
- augmenting with a second first-line pharmacological intervention?

22. How often should people receiving pharmacological interventions for managing spondyloarthritis be monitored?

23. What are the indications for starting treatment with standard disease-modifying anti-rheumatic drugs to manage spondyloarthritis?

24. What is the effectiveness of standard disease-modifying anti-rheumatic drugs compared with standard care for managing axial symptoms in spondyloarthritis?

25. What is the comparative effectiveness of different standard disease-modifying anti-rheumatic drugs compared with standard care for managing peripheral symptoms in spondyloarthritis?

26. When a standard disease-modifying anti-rheumatic drug has failed, what is the effectiveness of the following for managing spondyloarthritis:

- switching to a different standard disease-modifying anti-rheumatic drug?
- augmenting with a second standard disease-modifying anti-rheumatic drug?

27. What is the effectiveness of biological disease-modifying anti-rheumatic drugs for managing symptoms of enteropathic arthritis

that have not responded to 2 different standard disease-modifying anti-rheumatic drugs?

28. What is the effectiveness of biological disease-modifying anti-rheumatic drugs for managing symptoms of reactive arthritis related to HLA B27 that have not responded to 2 different standard disease-modifying anti-rheumatic drugs?

29. What is the effectiveness of biological disease-modifying anti-rheumatic drugs for managing symptoms of undifferentiated spondyloarthritis, other than non-radiographic axial spondyloarthritis that have not responded to 2 different standard disease-modifying anti-rheumatic drugs?

30. What is the effectiveness of biological disease-modifying anti-rheumatic drugs for managing the symptoms of young people and adults who have previously been diagnosed with enthesitis or psoriatic-related juvenile idiopathic arthritis that have not responded to 2 different standard disease-modifying anti-rheumatic drugs?

4.5.6 Information

31. What information do young people and adults with spondyloarthritis find useful?

4.5.7 Ongoing management

32. What is the effectiveness of information and education in the management of flare episodes?

33. What are the long-term complications associated with spondyloarthritis?

4.5.8 Referral for surgical interventions

34. What factors predict clinical improvement after spinal straightening surgery?

35. What factors predict clinical improvement after joint replacement surgery?

4.6 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 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.

4.7 Status

4.7.1 Scope

This is the consultation draft of the scope. The consultation dates are 20 May to 18 June 2014.

4.7.2 Timing

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

5 Related NICE guidance

5.1 Published guidance

5.1.1 NICE guidance to be updated

None.

5.1.2 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).

5.1.3 NICE guidance to be cross-referred to

- Psoriasis. NICE clinical guideline 153 (2012).
- 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.
- Ustekinumab for treating active psoriatic arthritis. NICE technology appraisal guidance. Publication expected May 2014

5.1.4 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).
- 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).
- Low back pain. NICE clinical guideline 88 (2009).
- Rheumatoid arthritis. NICE clinical guideline 79 (2009).
- Adalimumab, etanercept and infliximab for ankylosing spondylitis. NICE technology appraisal guidance 143 (2008).

6 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.