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Rheumatoid arthritis

**The management of rheumatoid arthritis
in adults**

NICE clinical guideline 79
Rheumatoid arthritis: The management of rheumatoid arthritis in adults

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- The NICE guideline (this document) – all the recommendations.
- A quick reference guide – a summary of the recommendations for healthcare professionals.
- ‘Understanding NICE guidance’ – a summary for patients and carers.
- The full guideline – all the recommendations, details of how they were developed, and reviews of the evidence they were based on.

For printed copies of the quick reference guide or ‘Understanding NICE guidance’, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk and quote:

- N1790 (quick reference guide)
- N1791 (‘Understanding NICE guidance’).

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions in the NHS in England and Wales.

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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Introduction

Rheumatoid arthritis (RA) is an inflammatory disease. It largely affects synovial joints, which are lined with a specialised tissue called synovium. RA typically affects the small joints of the hands and the feet, and usually both sides equally and symmetrically, although any synovial joint can be affected. It is a systemic disease and so can affect the whole body, including the heart, lungs and eyes.

There are approximately 400,000 people with RA in the UK. The incidence of the condition is low, with around 1.5 men and 3.6 women developing RA per 10,000 people per year. This translates into approximately 12,000 people developing RA per year in the UK. The overall occurrence of RA is two to four times greater in women than men. The peak age of incidence in the UK for both genders is the 70s, but people of all ages can develop the disease.

Drug management aims to relieve symptoms, as pain relief is the priority for people with RA, and to modify the disease process. Disease modification slows or stops radiological progression. Radiological progression is closely correlated with progressive functional impairment.

RA can result in a wide range of complications for people with the disease, their carers, the NHS and society in general. The economic impact of this disease includes:

- direct costs to the NHS and associated healthcare support services
- indirect costs to the economy, including the effects of early mortality and lost productivity
- the personal impact of RA and subsequent complications for people with RA and their families.

Approximately one third of people stop work because of the disease within 2 years of onset, and this prevalence increases thereafter. The total costs of RA in the UK, including indirect costs and work-related disability, have been estimated at between £3.8 and £4.75 billion per year. Clearly this disease is costly to the UK economy and to individuals.

NICE has published five technology appraisals relevant to RA. Two of these are updated in this guideline ('Anakinra for rheumatoid arthritis', NICE technology appraisal guidance 72; see section 1.4.3; and 'Guidance on the use of cyclo-oxygenase (Cox) II selective inhibitors, celecoxib, rofecoxib, meloxicam and etodolac for osteoarthritis and rheumatoid arthritis', NICE technology appraisal guidance 27; see section 1.4.4). Recommendations from the other appraisals are incorporated into section 2.

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform their decisions for individual patients.

Person-centred care

This guideline offers best practice advice on the care of adults with RA.

Treatment and care should take into account peoples' needs and preferences. People with RA should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If people do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – 'Reference guide to consent for examination or treatment' (2001) (available from www.dh.gov.uk). Healthcare professionals should also follow the code of practice that accompanies the Mental Capacity Act (summary available from www.publicguardian.gov.uk).

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the person's needs. Treatment and care, and the information people are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the person agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.

Key priorities for implementation

Referral for specialist treatment

- Refer for specialist opinion any person with suspected persistent synovitis of undetermined cause. Refer urgently if any of the following apply:
 - the small joints of the hands or feet are affected
 - more than one joint is affected
 - there has been a delay of 3 months or longer between onset of symptoms and seeking medical advice.

Disease-modifying and biological drugs

- In people with newly diagnosed active RA, offer a combination of disease-modifying anti-rheumatic drugs (DMARDs) (including methotrexate and at least one other DMARD, plus short-term glucocorticoids) as first-line treatment as soon as possible, ideally within 3 months of the onset of persistent symptoms.
- In people with newly diagnosed RA for whom combination DMARD therapy is not appropriate¹, start DMARD monotherapy, placing greater emphasis on fast escalation to a clinically effective dose rather than on the choice of DMARD.
- In people with recent-onset RA receiving combination DMARD therapy and in whom sustained and satisfactory levels of disease control have been achieved, cautiously try to reduce drug doses to levels that still maintain disease control.

Monitoring disease

- In people with recent-onset active RA, measure C-reactive protein (CRP) and key components of disease activity (using a composite score such as DAS28) monthly until treatment has controlled the disease to a level previously agreed with the person with RA.

¹ For example, because of comorbidities or pregnancy, during which certain drugs would be contraindicated.

The multidisciplinary team

- People with RA should have access to a named member of the multidisciplinary team (for example, the specialist nurse) who is responsible for coordinating their care.

1 Guidance

The following guidance is based on the best available evidence. The full guideline (www.nice.org.uk/CG79fullguideline) gives details of the methods and the evidence used to develop the guidance.

The Guideline Development Group (GDG) accepted a clinical diagnosis of RA as being more important than the 1987 American Rheumatism Association classification criteria² for RA. This is because an early persistent synovitis in which other pathologies have been ruled out needs to be treated as if it is RA to try to prevent damage to joints. International committees are addressing the diagnostic criteria for early RA.

The GDG categorised RA into two categories: 'recent onset' (disease duration of up to 2 years) and 'established' (disease duration of longer than 2 years). Within recent-onset RA, categories of suspected persistent synovitis or suspected RA refer to patients in whom a diagnosis is not yet clear, but in whom referral to specialist care or further investigation is required.

1.1 *Referral, diagnosis and investigations*

1.1.1 Referral for specialist treatment

1.1.1.1 Refer for specialist opinion any person with suspected persistent synovitis of undetermined cause. Refer urgently if any of the following apply:

- the small joints of the hands or feet are affected
- more than one joint is affected
- there has been a delay of 3 months or longer between onset of symptoms and seeking medical advice.

² Arnett FC, Edworthy SM, Bloch DA et al. (1988) The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis & Rheumatism* 31(3): 315–24.

- 1.1.1.2 Do not avoid referring urgently any person with suspected persistent synovitis of undetermined cause whose blood tests show a normal acute-phase response or negative rheumatoid factor.

1.1.2 Investigations

- 1.1.2.1 Offer to carry out a blood test for rheumatoid factor in people with suspected RA who are found to have synovitis on clinical examination.
- 1.1.2.2 Consider measuring anti-cyclic citrullinated peptide (CCP) antibodies in people with suspected RA if:
- they are negative for rheumatoid factor, and
 - there is a need to inform decision-making about starting combination therapy (see 1.4.1.1).
- 1.1.2.3 X-ray the hands and feet early in the course of the disease in people with persistent synovitis in these joints.

1.2 Communication and education

- 1.2.1.1 Explain the risks and benefits of treatment options to people with RA in ways that can be easily understood. Throughout the course of their disease, offer them the opportunity to talk about and agree all aspects of their care, and respect the decisions they make.
- 1.2.1.2 Offer verbal and written information to people with RA to:
- improve their understanding of the condition and its management, and
 - counter any misconceptions they may have.
- 1.2.1.3 People with RA who wish to know more about their disease and its management should be offered the opportunity to take part in existing educational activities, including self-management programmes.

1.3 *The multidisciplinary team*

- 1.3.1.1 People with RA should have ongoing access to a multidisciplinary team. This should provide the opportunity for periodic assessments (see 1.5.1.3 and 1.5.1.4) of the effect of the disease on their lives (such as pain, fatigue, everyday activities, mobility, ability to work or take part in social or leisure activities, quality of life, mood, impact on sexual relationships) and help to manage the condition.
- 1.3.1.2 People with RA should have access to a named member of the multidisciplinary team (for example, the specialist nurse) who is responsible for coordinating their care.
- 1.3.1.3 People with RA should have access to specialist physiotherapy, with periodic review (see 1.5.1.3 and 1.5.1.4), to:
- improve general fitness and encourage regular exercise
 - learn exercises for enhancing joint flexibility, muscle strength and managing other functional impairments
 - learn about the short-term pain relief provided by methods such as transcutaneous electrical nerve stimulators [TENS] and wax baths.
- 1.3.1.4 People with RA should have access to specialist occupational therapy, with periodic review (see 1.5.1.3 and 1.5.1.4), if they have:
- difficulties with any of their everyday activities, or
 - problems with hand function.
- 1.3.1.5 Offer psychological interventions (for example, relaxation, stress management and cognitive coping skills³) to help people with RA adjust to living with their condition.
- 1.3.1.6 All people with RA and foot problems should have access to a podiatrist for assessment and periodic review of their foot health needs (see 1.5.1.3 and 1.5.1.4).

³ Such as managing negative thinking.

- 1.3.1.7 Functional insoles and therapeutic footwear should be available for all people with RA if indicated.

1.4 *Pharmacological management*

1.4.1 DMARDs

Introducing and withdrawing DMARDs

- 1.4.1.1 In people with newly diagnosed active RA, offer a combination of DMARDs (including methotrexate and at least one other DMARD, plus short-term glucocorticoids) as first-line treatment as soon as possible, ideally within 3 months of the onset of persistent symptoms.
- 1.4.1.2 Consider offering short-term treatment with glucocorticoids (oral, intramuscular or intra-articular) to rapidly improve symptoms in people with newly diagnosed RA if they are not already receiving glucocorticoids as part of DMARD combination therapy.
- 1.4.1.3 In people with recent-onset RA receiving combination DMARD therapy and in whom sustained and satisfactory levels of disease control have been achieved, cautiously try to reduce drug doses to levels that still maintain disease control.
- 1.4.1.4 In people with newly diagnosed RA for whom combination DMARD therapy is not appropriate⁴, start DMARD monotherapy, placing greater emphasis on fast escalation to a clinically effective dose rather than on the choice of DMARD.
- 1.4.1.5 In people with established RA whose disease is stable, cautiously reduce dosages of disease-modifying or biological drugs. Return promptly to disease-controlling dosages at the first sign of a flare.
- 1.4.1.6 When introducing new drugs to improve disease control into the treatment regimen of a person with established RA, consider

⁴ For example, because of comorbidities or pregnancy, during which certain drugs would be contraindicated.

decreasing or stopping their pre-existing rheumatological drugs once the disease is controlled.

- 1.4.1.7 In any person with established rheumatoid arthritis in whom disease-modifying or biological drug doses are being decreased or stopped, arrangements should be in place for prompt review.

1.4.2 Glucocorticoids

- 1.4.2.1 Offer short-term treatment with glucocorticoids for managing flares in people with recent-onset or established disease to rapidly decrease inflammation.

- 1.4.2.2 In people with established RA, only continue long-term treatment with glucocorticoids when:
- the long-term complications of glucocorticoid therapy have been fully discussed, and
 - all other treatment options (including biological drugs) have been offered.

1.4.3 Biological drugs

Please see section 2 for other NICE technology appraisal guidance on biological drugs for RA.

- 1.4.3.1 On the balance of its clinical benefits and cost effectiveness, anakinra is not recommended for the treatment of RA, except in the context of a controlled, long-term clinical study⁵.
- 1.4.3.2 Patients currently receiving anakinra for RA may suffer loss of wellbeing if their treatment were discontinued at a time they did not anticipate. Therefore, patients should continue therapy with anakinra until they and their consultant consider it is appropriate to stop⁵.

⁵ These recommendations are from 'Anakinra for rheumatoid arthritis', NICE technology appraisal guidance 72. The GDG reviewed the evidence on anakinra but made no changes to the recommendations.

- 1.4.3.3 Do not offer the combination of tumour necrosis factor- α (TNF- α) inhibitor therapy and anakinra for RA.

1.4.4 Symptom control

Recommendations 1.4.4.2–1.4.4.5 in this section replace the rheumatoid arthritis aspects only of ‘Guidance on the use of cyclo-oxygenase (Cox) II selective inhibitors, celecoxib, rofecoxib, meloxicam and etodolac for osteoarthritis and rheumatoid arthritis’ (NICE technology appraisal guidance 27). They are adapted from ‘Osteoarthritis: the care and management of osteoarthritis in adults’ (NICE clinical guideline 59).

- 1.4.4.1 Offer analgesics (for example, paracetamol, codeine or compound analgesics) to people with RA whose pain control is not adequate, to potentially reduce their need for long-term treatment with non-steroidal anti-inflammatory drugs (NSAIDs) or cyclo-oxygenase-2 (COX-2) inhibitors.
- 1.4.4.2 Oral NSAIDs/COX-2 inhibitors should be used at the lowest effective dose for the shortest possible period of time.
- 1.4.4.3 When offering treatment with an oral NSAID/COX-2 inhibitor, the first choice should be either a standard NSAID or a COX-2 inhibitor. In either case, these should be co-prescribed with a proton pump inhibitor (PPI), choosing the one with the lowest acquisition cost.
- 1.4.4.4 All oral NSAIDs/COX-2 inhibitors have analgesic effects of a similar magnitude but vary in their potential gastrointestinal, liver and cardio-renal toxicity; therefore, when choosing the agent and dose, healthcare professionals should take into account individual patient risk factors, including age. When prescribing these drugs, consideration should be given to appropriate assessment and/or ongoing monitoring of these risk factors.
- 1.4.4.5 If a person with RA needs to take low-dose aspirin, healthcare professionals should consider other analgesics before substituting

or adding an NSAID or COX-2 inhibitor (with a PPI) if pain relief is ineffective or insufficient.

- 1.4.4.6 If NSAIDs or COX-2 inhibitors are not providing satisfactory symptom control, review the disease-modifying or biological drug regimen.

1.5 *Monitoring rheumatoid arthritis*

- 1.5.1.1 Measure CRP and key components of disease activity (using a composite score such as DAS28) regularly in people with RA to inform decision-making about:
- increasing treatment to control disease
 - cautiously decreasing treatment when disease is controlled.
- 1.5.1.2 In people with recent-onset active RA, measure CRP and key components of disease activity (using a composite score such as DAS28) monthly until treatment has controlled the disease to a level previously agreed with the person with RA.
- 1.5.1.3 Offer people with satisfactorily controlled established RA review appointments at a frequency and location suitable to their needs. In addition, make sure they:
- have access to additional visits for disease flares,
 - know when and how to get rapid access to specialist care, and
 - have ongoing drug monitoring.

- 1.5.1.4 Offer people with RA an annual review to:
- assess disease activity and damage, and measure functional ability (using, for example, the Health Assessment Questionnaire [HAQ])
 - check for the development of comorbidities, such as hypertension, ischaemic heart disease, osteoporosis and depression
 - assess symptoms that suggest complications, such as vasculitis and disease of the cervical spine, lung or eyes
 - organise appropriate cross referral within the multidisciplinary team
 - assess the need for referral for surgery (see section 1.6)
 - assess the effect the disease is having on a person's life.

1.6 *Timing and referral for surgery*

- 1.6.1.1 Offer to refer people with RA for an early specialist surgical opinion if any of the following do not respond to optimal non-surgical management:
- persistent pain due to joint damage or other identifiable soft tissue cause
 - worsening joint function
 - progressive deformity
 - persistent localised synovitis.
- 1.6.1.2 Offer to refer people with any of the following complications for a specialist surgical opinion before damage or deformity becomes irreversible:
- imminent or actual tendon rupture
 - nerve compression (for example, carpal tunnel syndrome)
 - stress fracture.

- 1.6.1.3 When surgery is offered to people with RA, explain that the main⁶ expected benefits are:
- pain relief,
 - improvement, or prevention of further deterioration, of joint function, and
 - prevention of deformity.
- 1.6.1.4 Offer urgent combined medical and surgical management to people with RA who have suspected or proven septic arthritis (especially in a prosthetic joint).
- 1.6.1.5 If a person with RA develops any symptoms or signs that suggest cervical myelopathy⁷:
- request an urgent MRI scan, and
 - refer for a specialist surgical opinion.
- 1.6.1.6 Do not let concerns about the long-term durability of prosthetic joints influence decisions to offer joint replacements to younger people with RA.

1.7 *Diet and complementary therapies*

- 1.7.1.1 Inform people with RA who wish to experiment with their diet that there is no strong evidence that their arthritis will benefit. However, they could be encouraged to follow the principles of a Mediterranean diet (more bread, fruit, vegetables and fish; less meat; and replace butter and cheese with products based on vegetable and plant oils).
- 1.7.1.2 Inform people with RA who wish to try complementary therapies that although some may provide short-term symptomatic benefit, there is little or no evidence for their long-term efficacy.

⁶ Cosmetic improvements should not be the dominant concern.

⁷ For example, paraesthesiae, weakness, unsteadiness, reduced power, extensor plantars.

1.7.1.3 If a person with RA decides to try complementary therapies, advise them:

- these approaches should not replace conventional treatment
- this should not prejudice the attitudes of members of the multidisciplinary team, or affect the care offered.

2 Related NICE technology appraisal guidance

The recommendations in this section are existing NICE technology appraisal guidance. They were formulated as part of the technology appraisals and not by the guideline developers. They have been incorporated into this guideline in line with NICE procedures for developing clinical guidelines, and the evidence to support the recommendations can be found with the individual appraisals.

NICE technology appraisal guidance 126 and 141 have been replaced by NICE technology appraisal guidance 195, 'Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor' published in August 2010 (available at www.nice.org.uk/guidance/TA195). The recommendations from the replaced appraisals are crossed out below.

~~2.1 Rituximab for the treatment of rheumatoid arthritis (NICE technology appraisal guidance 126)~~

Available at www.nice.org.uk/TA126

- ~~2.1.1.1 Rituximab in combination with methotrexate is recommended as an option for the treatment of adults with severe active rheumatoid arthritis who have had an inadequate response to or intolerance of other disease-modifying anti-rheumatic drugs (DMARDs), including treatment with at least one tumour necrosis factor α (TNF- α) inhibitor therapy.~~
- ~~2.1.1.2 Treatment with rituximab plus methotrexate should be continued only if there is an adequate response following initiation of therapy. An adequate response is defined as an improvement in disease activity score (DAS28) of 1.2 points or more. Repeat courses of treatment with rituximab plus methotrexate should be given no more frequently than every 6 months.~~

- 2.1.1.3 ~~Treatment with rituximab plus methotrexate should be initiated, supervised and treatment response assessed by specialist physicians experienced in the diagnosis and treatment of rheumatoid arthritis.~~

2.2 *Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis (NICE technology appraisal guidance 130)*

Available at www.nice.org.uk/TA130

- 2.2.1.1 The tumour necrosis factor alpha (TNF- α) inhibitors adalimumab, etanercept and infliximab are recommended as options for the treatment of adults who have both of the following characteristics.
- Active rheumatoid arthritis as measured by disease activity score (DAS28) greater than 5.1 confirmed on at least two occasions, 1 month apart.
 - Have undergone trials of two disease-modifying anti-rheumatic drugs (DMARDs), including methotrexate (unless contraindicated). A trial of a DMARD is defined as being normally of 6 months, with 2 months at standard dose, unless significant toxicity has limited the dose or duration of treatment.
- 2.2.1.2 TNF- α inhibitors should normally be used in combination with methotrexate. Where a patient is intolerant of methotrexate or where methotrexate treatment is considered to be inappropriate, adalimumab and etanercept may be given as monotherapy.
- 2.2.1.3 Treatment with TNF- α inhibitors should be continued only if there is an adequate response at 6 months following initiation of therapy. An adequate response is defined as an improvement in DAS28 of 1.2 points or more.
- 2.2.1.4 After initial response, treatment should be monitored no less frequently than 6-monthly intervals with assessment of DAS28.

Treatment should be withdrawn if an adequate response (as defined in 2.2.1.3) is not maintained.

- 2.2.1.5 An alternative TNF- α inhibitor may be considered for patients in whom treatment is withdrawn due to an adverse event before the initial 6-month assessment of efficacy, provided the risks and benefits have been fully discussed with the patient and documented.
- 2.2.1.6 Escalation of dose of the TNF- α inhibitors above their licensed starting dose is not recommended.
- 2.2.1.7 Treatment should normally be initiated with the least expensive drug (taking into account administration costs, required dose and product price per dose). This may need to be varied in individual cases due to differences in the mode of administration and treatment schedules.
- 2.2.1.8 Use of the TNF- α inhibitors for the treatment of severe, active and progressive rheumatoid arthritis in adults not previously treated with methotrexate or other DMARDs is not recommended.
- 2.2.1.9 Initiation of TNF- α inhibitors and follow-up of treatment response and adverse events should be undertaken only by a specialist rheumatological team with experience in the use of these agents.

~~2.3 Abatacept for the treatment of rheumatoid arthritis (NICE technology appraisal guidance 141)~~

~~Available at www.nice.org.uk/TA141~~

- ~~2.3.1.1 Abatacept is not recommended (within its marketing authorisation) for the treatment of people with rheumatoid arthritis.~~
- ~~2.3.1.2 Patients currently receiving abatacept for the treatment of rheumatoid arthritis should have the option to continue therapy until they and their clinicians consider it appropriate to stop.~~

3 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The scope of this guideline is available from www.nice.org.uk/guidance/index.jsp?action=download&o=37807

Groups that will be covered:

- Adults with RA.

Groups that will not be covered:

- Patients with other chronic inflammatory polyarthritis.

How this guideline was developed

NICE commissioned the National Collaborating Centre for Chronic Conditions to develop this guideline. The Centre established a Guideline Development Group (see appendix A), which reviewed the evidence and developed the recommendations. An independent Guideline Review Panel oversaw the development of the guideline (see appendix B).

There is more information in the booklet: 'The guideline development process: an overview for stakeholders, the public and the NHS' (third edition, published April 2007), which is available www.nice.org.uk/guidelinesprocess or from NICE publications (phone 0845 003 7783 or email publications@nice.org.uk and quote reference N1233).

4 Implementation

The Healthcare Commission assesses how well NHS organisations meet core and developmental standards set by the Department of Health in ‘Standards for better health’ (available from www.dh.gov.uk). Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that NHS organisations should take into account national agreed guidance when planning and delivering care.

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/CG79).

- Slides highlighting key messages for local discussion.
- Costing tools:
 - costing report to estimate the national savings and costs associated with implementation
 - costing template to estimate the local costs and savings involved.
- Audit support for monitoring local practice.

5 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the full guideline (see section 6).

5.1 *Diagnosis and investigations*

How cost effective are MRI and ultrasound in establishing the diagnosis and prognosis of small joint synovitis?

How cost effective is the use of anti-CCP in establishing the diagnosis and prognosis of early inflammatory arthritis?

Why these are important

The sooner persistent synovitis is recognised and treated with DMARDs, the better the long-term outcome. In an aggressive acute-onset polyarthritis, the physical signs enable diagnosis. However, in other types of RA, the signs are not always obvious. Rheumatoid factor can be helpful both diagnostically and prognostically, but it is not as specific as anti-CCP antibodies. However, MRI and ultrasound are significantly more expensive than conventional radiology, particularly if new equipment needs to be purchased to provide this service. Testing for anti-CCP costs more than double testing for rheumatoid factor. It is important to determine the role of imaging and anti-CCP antibodies in early diagnosis and management decisions, and whether the added cost of these investigations is justified by better disease outcome, making these tests cost effective.

5.2 *Pharmacological management of mild rheumatoid arthritis*

The role of DMARDs in the treatment of mild RA should be assessed.

Why this is important

All trials of DMARDs have had active disease as an inclusion criterion. There has been no research on how to manage people with milder and less-active

disease. Studies need to determine whether it would be safe/effective for people with mild disease to be observed over time without DMARD therapy, or with monotherapy, unless their disease becomes more aggressive. It may be that combination therapies are not appropriate for all people with mild RA.

5.3 *Biological drugs in early rheumatoid arthritis*

The cost effectiveness of early management with biological drugs (prior to the failure of two conventional DMARDs) should be assessed.

Why this is important

There is some evidence to suggest that if infliximab is introduced early in the course of the disease, a significant proportion of people can go into early and sustained remission, which can be maintained by conventional DMARDs alone. There is a need to determine whether this approach could be applied to other anti-TNF- α inhibitors, and if this approach is cost effective.

5.4 *Symptom duration and patient outcomes*

What is the effect of symptom duration on patient outcomes?

Why this is important

There is some evidence from the Finnish Rheumatoid Arthritis Combination Therapy (FinRACo) trial and other studies that suggests that symptom duration is a key determinant of outcomes in RA. However, this evidence is limited. This is very important in early RA management, so studies should look at the length of the 'window of opportunity' to intervene in RA, beyond which DMARDs are less likely to improve long-term outcomes.

5.5 *Therapy after the failure of anti-TNF- α inhibitors*

What is the most appropriate treatment strategy when the first TNF- α inhibitor fails?

Why this is important

If the first TNF- α inhibitor fails because of lack of or reduced efficacy, at the moment people with RA can only try rituximab or go back to conventional DMARDs. There is good evidence to suggest that biological drugs, including a second TNF- α inhibitor, are effective under these circumstances. Studies need to address whether other biological drugs should be considered in preference to rituximab for all people with RA, or certain subgroups, on the grounds of clinical and cost effectiveness.

6 Other versions of this guideline

6.1 *Full guideline*

The full guideline, 'Rheumatoid arthritis: the management of rheumatoid arthritis in adults' contains details of the methods and evidence used to develop the guideline. It is published by the National Collaborating Centre for Chronic Conditions and is available from www.rcplondon.ac.uk/college/NCC-CC, our website (www.nice.org.uk/CG79fullguideline) and the National Library for Health (www.nlh.nhs.uk).

6.2 *Quick reference guide*

A quick reference guide for healthcare professionals is available from www.nice.org.uk/CG79quickrefguide

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N1790).

6.3 *‘Understanding NICE guidance’*

Information for patients and carers (‘Understanding NICE guidance’) is available from www.nice.org.uk/CG79publicinfo

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N1791).

We encourage NHS and voluntary sector organisations to use text from this booklet in their own information about rheumatoid arthritis.

7 Related NICE guidance

Published

- Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women. NICE technology appraisal guidance 160 (2008). Available from www.nice.org.uk/TA160
- Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women. NICE technology appraisal guidance 161 (2008). Available from www.nice.org.uk/TA161
- Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. NICE clinical guideline 67 (2008). Available from www.nice.org.uk/CG67
- Abatacept for the treatment of rheumatoid arthritis. NICE technology appraisal guidance 141 (2008). Available from www.nice.org.uk/TA141
- Osteoarthritis: the care and management of osteoarthritis in adults. NICE clinical guideline 59 (2008). Available from www.nice.org.uk/CG59
- Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis. NICE technology appraisal guidance 130 (2007). Available from www.nice.org.uk/TA130
- Rituximab for the treatment of rheumatoid arthritis. NICE technology appraisal guidance 126 (2007). Available from www.nice.org.uk/TA126
- Hypertension: management of hypertension in adults in primary care (this is a partial update of NICE clinical guideline 18). NICE clinical guideline 34 (2006). Available from www.nice.org.uk/CG34

Under development

NICE is developing the following guidance (details available from www.nice.org.uk):

- Tocilizumab for the treatment of rheumatoid arthritis. NICE technology appraisal guidance (publication expected October 2009).
- Certolizumab pegol for the treatment of rheumatoid arthritis. NICE technology appraisal guidance (publication expected February 2010).

8 Updating the guideline

NICE clinical guidelines are updated so that recommendations take into account important new information. New evidence is checked 3 years after publication, and healthcare professionals and patients are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.

Appendix A: The Guideline Development Group

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Dr Chris Deighton

NCC-CC Clinical Advisor/Consultant Rheumatologist, Derby Hospitals NHS Foundation Trust

Mrs Ailsa Bosworth

Patient and Carer Representative, Maidenhead

Dr Jane Hall

Senior Clinical Research Physiotherapist and Hon. Sen. Lecturer
RACE/Physiotherapy Royal National Hospital for Rheumatic Diseases and University of Bath

Dr Alison Hammond

Reader in Rheumatology Rehabilitation, University of Salford

Ms Sheena Hennell

Consultant Nurse, Wirral University Teaching Hospital

Dr Patrick Kiely

Consultant Rheumatologist, St George's NHS Healthcare Trust, London.

Dr Raashid Luqmani

Consultant Rheumatologist, Nuffield Orthopaedic Centre and University of Oxford

Dr David Morgan

General Practitioner (non RA specialist), Birmingham

Dr Rachel O' Mahony

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Mrs Enid Quest

Patient and Carer Representative, Bristol

Mrs Isabel Raiman

Community based nurse, Brighton and Hove City Teaching PCT

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Professor David L Scott

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Ms Jaim Sutton

NCC-CC Project Manager – until March 2008

Mr Jonathan Tosh

SCHARR Health Economist, University of Sheffield

Ms Claire Turner

NCC-CC Senior Project Manager – from April 2008

Dr Louise Warburton

General Practitioner (specialist in RA), Shrewsbury

The following individuals acted as either deputies for GDG members or were invited experts:

Ms Zara Bingham

Patient and carer representative (acted as a deputy for Ailsa Bosworth at one GDG meeting), Manchester

Dr Paul D’Orso

General Practitioner (non RA specialist), Birmingham (acted as a deputy for Dr Morgan at one GDG meeting)

Mr Colin Howie

Consultant Orthopaedic and Trauma Surgeon, Edinburgh New Royal Infirmary (invited expert, attended one GDG meeting)

Dr Anthony Redmond

Podiatrist & Senior Lecturer, University of Leeds (invited expert, attended two GDG meetings)

Mr Andrew Robinson

Consultant Foot and Ankle Surgeon, Cambridge University Hospital NHS Trust (invited expert, attended one GDG meeting)

Dr Joanna Sheldon

Immunologist, St George's Hospital, London (invited expert, attended one GDG meeting)

Appendix B: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

Dr John Hyslop (Chair)

Consultant Radiologist, Royal Cornwall Hospital NHS Trust

Dr Ash Paul

Medical Director, Bedfordshire Primary Care Trust

Professor Liam Smeeth

Professor of Clinical Epidemiology, London School of Hygiene and Tropical Medicine

Mr Peter Gosling

Lay member

Mr Johnathan Hopper

Medical Director (Northern Europe), ConvaTec Ltd

Appendix C: The algorithm

The algorithm is provided as a separate file.