NICE National Institute for Health and Care Excellence

NICE guideline

Rheumatoid arthritis in adults: management

Clinical guideline

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Your responsibility

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

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

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

Contents

This guideline replaces TA72.

This guideline partially replaces TA27.

This guideline is the basis of QS33.

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.

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. [2009]

1.1.1.2 Refer urgently any person with suspected persistent synovitis of undetermined cause, even if their blood tests show a normal acute-phase response or negative rheumatoid factor. [2009]

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. [2009]

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). [2009]

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. [2009]

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. [2009]

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. [2009]

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. [2009]

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. [2009]

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. [2009]

Physiotherapy

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. **[2009]**

Occupational therapy

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. **[2009]**

Psychological interventions

1.3.1.5 Offer psychological interventions (for example, relaxation, stress management and cognitive coping skills[1]) to help people with RA adjust to living with their condition. **[2009]**

Podiatry

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). **[2009]**

1.3.1.7 Functional insoles and therapeutic footwear should be available for all people with RA if indicated. **[2009]**

Hand exercise programmes

1.3.1.8 Consider a tailored strengthening and stretching hand exercise programme for people with RA with pain and dysfunction of the hands or wrists if:

- they are not on a drug regimen for RA, or
- they have been on a stable drug regimen for RA for at least 3 months. **[new 2015]**

1.3.1.9 The tailored hand exercise programme for people with RA should be delivered by a practitioner with training and skills in this area. **[new 2015]**

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. **[2009]**

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. **[2009]**

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. **[2009]**

1.4.1.4 In people with newly diagnosed RA for whom combination DMARD therapy is not appropriate[2], start DMARD monotherapy, placing greater emphasis on fast escalation to a clinically effective dose rather than on the choice of DMARD. **[2009]**

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. **[2009]**

1.4.1.6 When introducing new drugs to improve disease control into the treatment regimen of a person with established RA, consider decreasing or stopping their pre-existing rheumatological drugs once the disease is controlled. [2009]

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. [2009]

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. [2009]

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. [2009]

1.4.3 Biological drugs

Please see our web page on arthritis 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 study[3]. [2009]

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 stop[3]. [2009]

1.4.3.3 Do not offer the combination of tumour necrosis factor-α (TNF-α) inhibitor therapy and anakinra for RA. [2009]

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 the NICE guideline on osteoarthritis: the care and management of osteoarthritis in adults (CG59).

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. [2009]

1.4.4.2 Oral NSAIDs/COX-2 inhibitors should be used at the lowest effective dose for the shortest possible period of time. [2009]

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. [2009]

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. [2009]

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. [2009]

1.4.4.6 If NSAIDs or COX-2 inhibitors are not providing satisfactory symptom control, review the disease-modifying or biological drug regimen. [2009]

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. **[2009]**

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. **[2009]**

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. **[2009]**

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. **[2009]**

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. **[2009]**

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. **[2009]**

1.6.1.3 When surgery is offered to people with RA, explain that the main[4] expected benefits are:

- pain relief,
- improvement, or prevention of further deterioration, of joint function, and
- prevention of deformity. **[2009]**

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). **[2009]**

1.6.1.5 If a person with RA develops any symptoms or signs that suggest cervical myelopathy[5]:

- request an urgent MRI scan, and
- refer for a specialist surgical opinion. **[2009]**

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. [2009]

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). [2009]

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. [2009]

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. [2009]

1.8 Terms used in this guideline

Rheumatoid arthritis

The Guideline Development Group (GDG) accepted a clinical diagnosis of rheumatoid arthritis (RA) as being more important than the 1987 American Rheumatism Association classification criteria[6] 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).

Recent onset rheumatoid arthritis

Rheumatoid arthritis with a duration of up to 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.

Established rheumatoid arthritis

Rheumatoid arthritis with a duration of longer than 2 years.

To find out what NICE has said on topics related to this guideline, see our web page on arthritis.

[1] Such as managing negative thinking.

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

[3] 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.

[4] Cosmetic improvements should not be the dominant concern.

[5] For example, paraesthesiae, weakness, unsteadiness, reduced power, extensor plantars.

[6] 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.

Context

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.

In 2015 we reviewed the evidence on hand exercise programmes and added 2 new recommendations.

Recommendations for research

In 2009, the Guideline Development Group (GDG) made the following recommendations for research. The GDG's full set of research recommendations is detailed in the full guideline.

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.

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.

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.

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 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.

Update information

Recommendations have been added on hand exercise programmes for people (adults) with rheumatoid arthritis.

These are marked as **[new 2015].**

Where recommendations end **[2009]**, the evidence has not been reviewed since the original guideline.

Changes since publication

August 2013: A clarification was made to recommendation 1.1.1.2 about urgent referral for people with suspected persistent synovitis of undetermined cause.

August 2010: NICE published 'Rheumatoid arthritis – drugs for treatment after failure of a TNF inhibitor', NICE technology appraisal guidance 195. This replaces NICE technology appraisal guidance 126 'Rheumatoid arthritis (refractory) – rituximab' and NICE technology appraisal guidance 141 'Rheumatoid arthritis (refractory) – abatacept'. Please see NICE technology appraisal guidance 195 Rheumatoid arthritis – drugs for treatment after failure of a TNF inhibitor for the updated recommendations.

April 2009: A correction was made to the guideline. Recommendation 1.4.4.3 has been amended to remove text that stated an incorrect dose of etoricoxib for people with rheumatoid arthritis. The recommendation now reads: 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.

Note that recommendations 1.4.4.2–1.4.4.5 are adapted from the NICE guideline on osteoarthritis (CG59). These recommendations form part of the rheumatoid arthritis clinical guideline update of the rheumatoid arthritis aspects of TA27 Osteoarthritis and rheumatoid arthritis – cox II inhibitors.

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