Management of rheumatoid arthritis: summary of NICE guidance

Chris Deighton consultant rheumatologist ¹, Rachel O’Mahony senior research fellow ², Jonathan Tosh health economist ³, Claire Turner project manager ², Michael Rudolf consultant physician ⁴, on behalf of the Guideline Development Group

¹Department of Rheumatology, Derbyshire Royal Infirmary, Derby DE1 2QY; ²National Collaborating Centre for Chronic Conditions, Royal College of Physicians of London NW1 4LE; ³Health Economics and Decision Science, ScHARR, University of Sheffield, Sheffield S10 2TN; ⁴Department of Respiratory Medicine, Ealing Hospital, Ealing UB1 3HW

This is one of a series of BMJ summaries of new guidelines, which are based on the best available evidence; they highlight important recommendations for clinical practice, especially where uncertainty or controversy exists.

Why read this summary?

Rheumatoid arthritis is a chronic, progressive autoimmune disease associated with inflammation principally in synovial joints and affecting over 400 000 people in the United Kingdom. In recent years it has become clear that pain and disability can be avoided if the disease is recognised early and treated promptly and appropriately. It is therefore crucial that all health professionals have knowledge of the recognition, management, and appropriate referral of patients with rheumatoid arthritis. This article summarises the recommendations in the guideline from the National Institute for Health and Clinical Excellence (NICE) on the management of rheumatoid arthritis, from early identification to managing chronic and severe disease.

Recommendations

NICE recommendations are based on systematic reviews of best available evidence. When minimal evidence is available, recommendations are based on the opinion of the Guideline Development Group (GDG) of what constitutes good practice. Evidence levels for the recommendations are given in italic in square brackets.

Referral, diagnosis, and investigations

- Refer for specialist opinion anyone with suspected persistent synovitis of undetermined cause. Refer urgently even if blood tests show a normal acute-phase response or negative rheumatoid factor and if:
  - The small joints of the hands or feet are affected
  - More than one joint is affected, or
  - There has been a delay of three months or longer between symptom onset and seeking medical advice.

[X Based on high and moderate quality observational studies of early prognosis and identification or diagnosis]

- Offer to test for rheumatoid factor in people with suspected rheumatoid arthritis who have synovitis. [X Based on high and moderate quality early identification observational studies]

- Consider measuring anticyclic citrullinated peptide antibodies in people with suspected rheumatoid arthritis if:
  - They are negative for rheumatoid factor, and
  - Combination therapy is being considered (see section on disease modifying antirheumatic drugs).

[X Based on data from case series]

- X ray the hands and feet early in people with persistent synovitis in these joints. [X Based on high and moderate quality early identification studies]

Communication and education

- Offer verbal and written information to people with rheumatoid arthritis to:
  - Improve their understanding of the condition and its management, and
  - Counter any misconceptions they may have.

- For those wishing to know more, offer participation in existing educational activities, including self management programmes.

Correspondence to: C Deighton chris.deighton@derbyhospitals.nhs.uk
Both recommendations are based on high and moderate quality meta-analyses, randomised controlled trials, and the GDG’s opinion]

**The multidisciplinary team**

- Ensure ongoing access to a multidisciplinary team with opportunity for periodic assessments and help to manage the condition. [Based on moderate quality randomised controlled trials, case series, and the GDG’s opinion]
- Ensure people with rheumatoid arthritis have access to a named member of the multidisciplinary team (for example, the specialist nurse), who is responsible for coordinating their care. [Based on moderate quality randomised controlled trials, case series, and the GDG’s opinion]
- Ensure access, with periodic review, to:
  - Specialist physiotherapy to enhance general fitness, joint flexibility, and muscle strength; to improve function; and to learn about short term pain relief provided by methods such as transcutaneous electrical nerve stimulators (TENS) and wax baths.
  - Specialist occupational therapy if they have problems with everyday activities or hand function.
  - A podiatrist if they have foot problems, and make sure functional insoles and therapeutic footwear are available if indicated. [Based on high quality meta-analyses and high and moderate quality randomised controlled trials, and the GDG’s opinion]
- Offer psychological interventions (for example, relaxation, stress management, and cognitive coping skills) to help adjust to living with the condition. [Based on high quality meta-analyses and high and moderate quality randomised controlled trials]

**Management of symptoms: analgesics and NSAIDs**

**Analgesics**

- Offer analgesics (for example, paracetamol, codeine, or compound analgesics) if pain control is inadequate, to potentially reduce their need for long term treatment with non-steroidal anti-inflammatory drugs (NSAIDs) or cyclo-oxygenase-2 (COX 2) inhibitors. [Based on moderate quality randomised controlled trials, case series, and the GDG’s opinion]

**Non-steroidal anti-inflammatory drugs**

- When offering an oral NSAID or COX 2 inhibitor, the first choice should be either a standard NSAID or a COX 2 inhibitor (other than etoricoxib 60 mg) at the lowest effective dose for the shortest possible time. In either case, coprescribe a proton pump inhibitor with the lowest acquisition cost.
- All oral NSAIDs and COX 2 inhibitors have analgesic effects of a similar magnitude but vary in their potential gastrointestinal, liver, and cardioenal toxicity; therefore, when choosing the agent and dose, consider the individual’s risk factors, including age. When prescribing these drugs, consider appropriate assessment and/or monitoring of these risk factors.
- If a person with rheumatoid arthritis needs to take low dose aspirin, consider other analgesics before substituting or adding an NSAID or COX 2 inhibitor (with a proton pump inhibitor) if pain relief is ineffective or insufficient.

[The above four NSAID recommendations are based on randomised controlled trials (mostly moderate quality), case series, and the GDG’s opinion]

**Management of symptoms: disease modifying antirheumatic drugs**

**For people with newly diagnosed active disease**

- Offer a combination of disease modifying antirheumatic drugs as first line treatment as soon as possible, ideally within three months of the onset of persistent symptoms. This should include methotrexate and at least one other, plus short term glucocorticoids. [Based on high and moderate quality meta-analyses and randomised controlled trials, moderate quality cohort studies, health economic modelling, and the GDG’s opinion]
- If combination therapy with disease modifying drugs is not appropriate (for example, owing to comorbidities or pregnancy), start monotherapy, focusing on fast escalation to a clinically effective dose rather than choice of drug. [Based on high and moderate quality meta-analyses and randomised controlled trials, moderate quality cohort studies, health economic modelling, and the GDG’s opinion]
- Offer short term oral, intramuscular, or intra-articular glucocorticoids to rapidly improve symptoms (if the individual is not already receiving glucocorticoids as part of the combination therapy). [Based on high and moderate quality randomised controlled trials and the GDG’s opinion]

**For people with recent onset disease (within past two years)**

- If they have achieved sustained and satisfactory levels of disease control with a combination of disease modifying antirheumatic drugs, cautiously try to reduce doses to levels that still maintain disease control. [Based on high and moderate quality meta-analyses and randomised controlled trials, moderate quality cohort studies, and the GDG’s opinion]

**For people with established disease (longer than two years)**

- If disease is stable, cautiously reduce dosages of disease modifying or biological drugs; return promptly to disease controlling doses at the first sign of a flare-up.
- When introducing new drugs to improve disease control, consider decreasing or stopping an individual’s pre-existing rheumatological drugs once the disease is controlled.
- If doses of disease modifying or biological drugs are being decreased, or the drugs are being stopped, arrange for prompt review. [The above three recommendations are based on high and moderate quality randomised controlled trials, case series, and the GDG’s opinion]
Management of symptoms: glucocorticoids

For people with recent onset or established disease

- Offer short term glucocorticoid treatment for managing flare-ups. [Based on high and moderate quality randomised controlled trials and on the GDG’s opinion]

In people with established disease

- Continue long term treatment with glucocorticoids only after fully discussing with the individual the long term complications of the treatment and after offering all other treatment options (including biological drugs). [Based on high and moderate quality randomised controlled trials and the GDG’s opinion]

Monitoring rheumatoid arthritis

- Regularly measure C reactive protein and key components of disease activity (using a composite score such as the DAS28—a disease activity score that includes assessment of 28 joints) to inform decision making about increasing treatment to control disease or cautiously decreasing treatment when disease is controlled. If the disease is of recent onset and active, measure these variables monthly until control reaches a level previously agreed with the individual. [Based on high and moderate quality randomised controlled trials, case series, and the GDG’s opinion]

- For people with satisfactorily controlled established disease offer review appointments at a suitable frequency and location, ensuring that they know when and how to get rapid access to specialist care, have access to additional visits for disease flare-ups, and have ongoing drug monitoring. [Based on high and moderate quality randomised controlled trials and the GDG’s opinion]

- Offer annual review to:
  - Assess disease activity, damage, and overall impact and to measure functional ability (using, for example, the health assessment questionnaire’)
  - Check for 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. [Based on the GDG’s opinion]

Timing and referral for surgery

- Offer referral for an early specialist surgical opinion if any of the following do not respond to optimal non-surgical management:
  - Persistent pain as a result of joint damage or other identifiable damage to soft tissue
  - Worsening joint function
  - Progressive deformity
  - Persistent localised synovitis. [Based on the GDG’s opinion]

- For people with the following complications offer referral 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. [Based on the GDG’s opinion]

Diet and complementary therapies

- Inform people who wish to experiment with their diet that no strong evidence exists that their arthritis will benefit. However, encourage them 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). [Based on high quality meta-analyses, high and moderate quality randomised controlled trials, and the GDG’s opinion]

Inform those wishing to try complementary therapies that little or no evidence exists for their long term efficacy and that although some may provide short term symptomatic benefit, complementary therapies should not replace conventional treatment. Advise them that use of such therapies will not preclude the offer of conventional care. [Based on meta-analyses, randomised controlled trials, case series, and the GDG’s opinion]

Overcoming barriers

Effective implementation of these recommendations depends on early recognition of persistent synovitis in primary care with rapid referral to specialist care; aggressive use of disease modifying antirheumatic drugs in active disease; close monitoring of disease activity and intervention when control is unsatisfactory; and multidisciplinary care for both recent onset and established rheumatoid arthritis. General practitioners need to be taught how to recognise early synovitis and not to simply treat the symptoms if the synovitis is persistent. Resources are needed for specialist teams to see patients with recent onset rheumatoid arthritis promptly and to follow them up regularly with objective measures. However, this should not be at the expense of treating those with established disease. Annual review and ongoing access to the multidisciplinary team should be available to address the physical and psychosocial impact of rheumatoid arthritis, ensure appropriate medication, and equip
the patient with the knowledge, skills, and resources to minimise the effects of the disease.

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Further information on the guidance

A wealth of guidance is now available on the diagnosis, investigations, and treatment of rheumatoid arthritis. Treatment aims to control pain and inflammation and to reduce joint damage, disability, and loss of function, thereby improving quality of life. This latest NICE guideline includes a combination of pharmacological and non-pharmacological interventions but also highlights the importance of early diagnosis and intervention. It draws on the most up-to-date evidence and pulls together areas covered in existing guidance9-13 and in the NICE technology appraisals.14 Its aim is to improve the quality of life of patients and reduce variation in practice, such as drug sequencing, choice and combination of disease modifying antirheumatic drugs, and access to, and interventions provided by, the multidisciplinary team.

Methods

The guideline was developed using current NICE guideline methodology,14 which involved systematic literature searches and critical appraisal and summarising of evidence. A Guideline Development Group (GDG) discussed the evidence and formulated the clinical recommendations. The GDG comprised people with rheumatoid arthritis as well as healthcare professionals representing a typical multidisciplinary team, both in primary and secondary care, and invited experts when additional expertise was required. The supporting technical team included those with specific expertise in literature search techniques, systematic evidence review, health economics, and project management.

The GDG accepted a clinical diagnosis of rheumatoid arthritis as being more important than the 1987 American Rheumatism Association’s classification criteria for rheumatoid arthritis.15 This is because an early persistent synovitis in which other disease has been ruled out needs to be treated as if it is rheumatoid arthritis to try to prevent damage to joints. International committees are currently examining the diagnostic criteria for early rheumatoid arthritis.

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

The recommendations on NSAIDs replace the rheumatoid arthritis aspects only of NICE’s 2001 technology appraisal on cyclo-oxygenase-2 (COX-2) selective inhibitors.16 All the recommendations (except the last one) in the latest guideline on rheumatoid arthritis are taken from NICE’s 2008 osteoarthritis guideline,17 which updated the guidance on COX-2 selective inhibitors and NSAIDs. This was done because the GDG believed that the results of the extensive cost effectiveness modelling for the osteoarthritis guideline were unlikely to differ for rheumatoid arthritis.

Health economic evidence was reviewed to evaluate whether guideline recommendations would be a cost effective use of healthcare resources.

The evidence comprised published economic analyses, which compare costs and benefits (in terms of quality adjusted life years) between two or more interventions. Where health economic evidence was limited, the guideline process allowed the health economist from the GDG to develop a new economic evaluation—for example, in evaluating the use of combinations of disease modifying antirheumatic drugs and steroids in patients with early disease. The model is described in detail in the full NICE guideline.6

The guideline was subject to a web based, external consultation from stakeholders. This drew 415 submitted comments, each of which was considered by the GDG for its validity and usefulness, and where deemed appropriate the guideline was modified in the light of these.

NICE has produced four different versions of the guideline: a full version; a quick reference guide; a version known as the “NICE guideline” that summarises the recommendations; and a version for patients and carers. All these versions are available from the NICE website (www.nice.org.uk/CG79).

Additional recommendations: biological drugs

It was part of the remit of the GDG to re-evaluate the information outlined in NICE’s technical appraisal on anakinra18 and incorporate updated information in the new guideline, but after reviewing the evidence on anakinra, the GDG made no changes to the recommendations. The GDG also had a remit to incorporate the information on other biological drugs outlined in the NICE technical appraisals.9-13

- On the balance of its clinical benefits and cost effectiveness, anakinra is not recommended as a treatment for rheumatoid arthritis, except in the context of a controlled, long term clinical study. If patients are already receiving anakinra, continue this until they and their consultant consider it is appropriate to stop. [Based on a NICE technical appraisal13]

- Do not offer the combination of tumour necrosis factor-alpha inhibitor therapy and anakinra. [Based on high and moderate quality meta-analyses and randomised controlled trials]

Future research

The exercise of developing guidelines on managing rheumatoid arthritis drew attention to enormous gaps in the knowledge of the GDG. Several areas not covered by the literature remain to be evaluated. Recognising early synovitis is not always straightforward, and clinical skills alone are not always reliable. Thus the cost effectiveness of more objective tests such as magnetic resonance imaging, ultrasonography, and testing for anticyclic citrullinated peptide antibodies needs to be examined in establishing the diagnosis and prognosis of small joint synovitis. Although the treatment of early active disease has to be aggressive, the role of disease modifying antirheumatic drugs (and the effect of symptom duration on patient outcomes) in the treatment of mild rheumatoid arthritis should be assessed. The cost effectiveness of early management with biological drugs (before the failure of two conventional disease modifying antirheumatic drugs) should be assessed to determine if this could be a cost effective strategy in subgroups of patients with rheumatoid arthritis. As more patients are exposed to biological therapies, research needs to determine the most appropriate treatment strategy if a first tumour necrosis factor-alpha inhibitor fails.