Clinical guideline for the diagnosis and management of early rheumatoid arthritis

August 2009

Approved by NHMRC
on 12 June 2009

Australian Government
National Health and Medical Research Council
N H M R C

The Royal Australian College of General Practitioners

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The National Health and Medical Research Council (NHMRC) is Australia's leading funding body for health and medical research. The NHMRC also provides the government, health professionals and the community with expert and independent advice on a range of issues that directly affect the health and wellbeing of all Australians.

The NHMRC provided support to this project through the Guidelines Assessment Register (GAR) process. The GAR consultant on this project was Karen Grimmer-Somers.

The guidelines were approved by the Chief Executive Officer of the NHMRC on 12 June 2009 under section 14A of the *National Health and Medical Research Council Act* 1992. Approval for the guidelines by NHMRC is granted for a period not exceeding 5 years, at which date the approval expires. The NHMRC expects that all guidelines will be reviewed no less than once every 5 years.

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INTRODUCTION

Chronic disease is a major public health burden on Australian society. An increasing proportion of the population has risk factors for, or at least one, chronic disease, leading to increasing public health costs. Health service policy and delivery must address not only acute conditions, but also effectively respond to the wide range of health and public services required by people with chronic illness.[1,2] Strong primary health care policy is an important foundation for a successful national health delivery system and long term management of public health. It is also linked to practical outcomes, including lower mortality, decreased hospitalisation and improved health outcomes.[1] National strategic health policy has recently given increased recognition to the importance of chronic disease management, with federal government endorsement of a number of initiatives for the prevention or delay in onset, early detection, and evidence based management of chronic diseases, including rheumatoid arthritis (RA).[1,3]

Chronic musculoskeletal conditions, including arthritis, account for over 4% of the national disease burden in terms of disability adjusted life years. In 2007, the total cost of arthritis to the Australian economy was estimated to be $23.9 billion, an increase of more than $4 billion on the cost calculated in 2004.[4] Access Economics estimated that, in 2007, the allocated health system expenditure associated with arthritis was $4.2 billion or $1100 per person with arthritis. Expenditure allocated to RA was more than $400 million.[4] Rheumatoid arthritis exerts a significant burden on the individual and community due to its impact on patients' quality of life as a result of the chronic, painful and disabling character of the condition;[5] the diminished employment capacity of many affected individuals; and increased health care costs. For further details refer to the *Evidence to support the National Plan for Osteoarthritis, Rheumatoid Arthritis and Osteoporosis: opportunities to improve health related quality of life and reduce the burden of disease and disability.*[6]

As such, Australian Government health policy has identified arthritis as a National Health Priority Area and adopted a number of initiatives aimed at: decreasing the burden of chronic disease and disability, raising awareness of preventive disease factors, providing access to evidence based knowledge, and improving the overall management of arthritis within the community.[7] In 2002, all Australian health ministers designated arthritis and musculoskeletal conditions as Australia's seventh National Health Priority Area. In response, a National Action Plan was developed in 2004 by the National Arthritis and Musculoskeletal Conditions Advisory Group (NAMSCAG).[6] The aim of this document was to provide a blueprint for national initiatives to improve the health related quality of life of people living with osteoarthritis, RA and osteoporosis; reduce the cost and prevalence of these conditions; and to reduce the impact on individuals, their carers and communities within Australia. The National Action Plan was developed to complement both the National Chronic Disease Strategy (which is broader) and the National Service Improvement Framework for Osteoarthritis, Rheumatoid Arthritis and Osteoporosis, and other national and state/territory structures. As part of the Australian Government's Better Arthritis and Osteoporosis Care (BAOC) 2006–2007 budget initiative,[7] guidelines for the management of osteoarthritis, RA, and juvenile idiopathic arthritis have been developed to inform evidence based primary care of chronic disease in general practice.

Expiry date for the recommendations

This guideline presents a comprehensive review of pharmacological and non-pharmacological management of early RA within the Australian health care context, based on the best available evidence available up to December 2006. Evidence published after this date has not been reviewed for the guideline.

The guideline was approved by the CEO of the National Health and Medical Research Council (NHMRC) on 12 June 2009, under section 14A of the *National Health and Medical Research Council Act* 1992. Approval for the guideline by the NHMRC is granted for a period not exceeding 5 years. It is expected that the guideline will be reviewed, and revised if necessary, no less than once every 5 years. Review should be more frequent in areas where clinical practice or research is known to be changing rapidly. Readers should check with The Royal Australian College of General Practitioners (RACGP) for any reviews or updates of this guideline.

The guideline has been endorsed by the NHMRC.

The role of general practitioners

General practice plays an important role within the Australian health care system in the prevention, early detection and management of chronic disease. The nature of general practice provides the opportunity for early screening for chronic disease and enables preventable risk factors to be addressed. General practitioners play an important role in monitoring disease progression and response to treatment, as well as managing comorbidities, in conjunction with the treating rheumatologist and other members of the multidisciplinary team. General practitioners are well placed to assess and treat RA patients in relation to cardiovascular risk factors such as smoking, obesity, physical inactivity, hypercholesterolaemia, hypertension and diabetes. Because of the relatively low prevalence of RA in the general population, GPs often have minimal experience with the diagnosis or management of RA. The *Clinical guideline for the diagnosis and management of early rheumatoid arthritis* is designed to fill this gap.

This guideline presents recommendations to assist GPs in managing patients with RA. It focuses on diagnosis, early management, and coordination of multidisciplinary care needs. The purpose of this guideline is to support clinical judgment, not replace it. This means:

- taking into consideration any contraindications in deciding whether or not to administer any treatment recommended by this guideline, and
- considering the appropriateness of any recommended treatment for a particular patient in terms of the patient's relevant clinical and non-clinical characteristics.

This project was supported by the RACGP and the Australian Department of Health and Ageing (DoHA).
The following experts were involved in the development of the guideline as part of the RACGP Rheumatoid Arthritis Working Group:

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NOTE: All website references were current at the time of publication.

Commonly used abbreviations

ANA	antinuclear antibody
anti-CCP	anti-cyclic citrullinated peptide (antibody)
BMI	body mass index
BSR	British Society of Rheumatology
CI	confidence interval
COX-2	cyclo-oxygenase-2 selective inhibitors
CRP	C-reactive protein
DMARD	disease modifying antirheumatic drug
EORA	elderly onset rheumatoid arthritis
EPC	Enhanced Primary Care
ESR	erythrocyte sedimentation rate
EULAR	European League Against Rheumatism
FBC	full blood count
GIT	gastrointestinal tract
GLA	gamma linolenic acid
GP	general practitioner
HR	hazard ratio
LFT	liver function tests
MA	meta-analysis
MTX	methotrexate
NNH	number needed to harm
NNT	number needed to treat
NHMRC	National Health and Medical Research Council
NSAIDs	non-steroidal anti-inflammatory drugs
OR	odds ratio
OT	occupational therapy
PMR	polymyalgia rheumatica
RA	rheumatoid arthritis
RACGP	[The] Royal Australian College of General Practitioners
RCT	randomised controlled trial
RhF	rheumatoid factor
SMD	standardised mean difference
SIGN	Scottish Intercollegiate Guidelines Network
SR	systematic review
TENS	transcutaneous electrical nerve stimulation
TNF	tumour necrosis factor
WMD	weighted mean difference

BACKGROUND

Early inflammatory arthritis can be a self limiting disease, develop into RA, or differentiate into another form of chronic arthritis. As is the case for other forms of arthritis, RA is thought to result from the combination of genetic susceptibility and exposure to an appropriate environmental trigger. It is the second most common form of arthritis and the most common autoimmune disease in Australia.[7] It is a chronic, inflammatory joint disease of unknown cause affecting approximately 2.5% of the Australian population, and is associated with substantial disability and economic losses.[2,9] It is more commonly diagnosed in women (57% in Australia).

Rheumatoid arthritis is characterised by persistent joint synovial tissue inflammation.[4,10] Joint damage in RA begins with the proliferation of synovial macrophages and fibroblasts after a triggering incident, possibly autoimmune or infectious.[11] Over time, bone erosion and irreversible joint damage can occur, leading to permanent disability.[12] Although most readily recognised by its articular manifestations, multiple organ systems may be affected and may result in shortened life expectancy, with increased deaths due to cardiovascular disease, infection, and cancer.[11] Systemic features may be associated with a poor prognosis, especially vasculitis, amyloidosis and pulmonary fibrosis.[13]

There is some evidence that the inheritability of RA appears to be high, with the genetic contribution to susceptibility estimated to be around 60%.[14] However, the genetic link is not a straightforward one, as no single gene is identifiable as the cause of RA. Although genetic factors may play an important part in developing RA, they are insufficient for development of the disease. Environmental factors appear to play an important but uncertain role. Some studies have shown that the risk of developing RA is higher among smokers,[15] with a 2006 study in the USA finding that smokers had six times the odds of developing RA compared to non-smokers.[16]

The presentation and disease course are distinct for each patient, making diagnosis and management a complex and dynamic process. There is significant morbidity and mortality (over half of patients will either need to significantly reduce or stop work 10 years after onset of the disease).[4] Chronic systemic inflammation also contributes significantly to excess cardiovascular disease.

The typical case of RA begins insidiously, with the slow development of signs and symptoms over weeks to months. Stiffness, usually accompanied by pain on movement and by tenderness in the joint, is usually the first symptom. Several joints are usually affected at the onset, typically in a symmetrical fashion. However, RA usually becomes polyarticular, involving five or more joints. Rheumatoid arthritis is an additive polyarthritis, with the sequential addition of involved joints, in contrast to systemic lupus erythematosus (SLE) or gout. Occasionally, patients experience an explosive polyarticular onset occurring over 24–48 hours.[17]

Rheumatoid arthritis is a chronic disease and may last a lifetime. Patients often experience periods of remission when the disease subsides. Remissions can last for short periods of time or for several years. Some patients, especially in the older age group, will have a positive blood test without having RA.

Early diagnosis and management of RA presents an important opportunity to alter the course of this progressive disease. There is a window of opportunity within the first few months of disease onset to provide treatment that effectively limits structural damage and improves health outcomes.[18] Such treatment involves:

- the early introduction of disease modifying drug therapy
- education to assist individuals in the day-to-day management of their condition
- rehabilitation to restore function
- comprehensive multidisciplinary approach to the provision of care, and
- support to manage the physical, social, emotional and occupational impact of the disease.

Current treatment options

Current treatment of patients with undifferentiated inflammatory arthritis consists primarily of non-steroidal anti-inflammatory drugs (NSAIDs) and cyclo-oxygenase-2 selective (COX-2) inhibitors. These medications have both analgesic and anti-inflammatory effects in RA; however, there is no evidence that they prevent joint damage.[9,19,20]

There is increasing evidence that a critical period may exist during which an intervention may reverse the RA disease process. This has produced a shift to earlier treatment rather than the previous practice of treatment with disease modifying antirheumatic drugs (DMARDs) when the disease has progressed further.

In some studies, methotrexate (MTX) treatment has resulted in postponing the diagnosis of RA and retarding radiographic joint damage in undifferentiated inflammatory arthritis patients.[21] It is now well accepted that patients who are most likely to develop disabling arthritis should start DMARD therapy as soon as possible.[22] When patients start DMARD therapy early, they experience reduced radiographic joint damage and greater maintenance of function compared with patients whose treatment is delayed.[21,23,24]

The diagnosis and management of RA is a fast evolving field and it is important to keep up-to-date with the latest information. Articles such as *Efficacy of MTX treatment in patients with probable RA*[21] and *What determines the evolution of early undifferentiated arthritis and rheumatoid arthritis?*[22] are good sources of information.

Principles of management of RA

Successful treatment to limit joint damage and functional loss requires early diagnosis, timely initiation of disease modifying agents, and provision of multidisciplinary support to manage the physical, social, emotional and occupational impact. The ultimate aim in treating RA is to induce complete remission. If remission is unable to be achieved, treatment aims to control disease activity and slow the rate of joint damage.[25] Other treatment goals include alleviation of pain, maintenance of function for essential activities of daily living (ADL) and work, and maximisation of quality of life.

Aim of the guideline

This guideline seeks to provide recommendations to assist primary care professionals to:

- prevent and minimise joint damage
- minimise functional loss
- alleviate or minimise pain
- improve quality of life.

Scope and target populations

The guideline is mainly intended for use in the primary care setting by both GPs and their patients. The guideline is also relevant to other health care professionals working within a multidisciplinary team. These include, but are not limited to, physiotherapists, nurses, occupational therapists, sports medicine personnel, podiatrists, dieticians, psychologists, pharmacists and community health workers. The guideline is applicable to primary care settings in metropolitan, regional, rural, and remote areas of Australia.

The guideline focuses on the diagnosis and management of adults with early stage RA. The early stage of RA is defined as 'disease duration of less than 2 years'. The guideline seeks to support primary care professionals in providing optimal, evidence based care for adult patients **over 16 years of age** presenting with symptoms indicative of RA. It does not address treatment of extra-articular disease or surgical interventions.

Except where guidance is provided within the recommendation itself, advice on pharmacological treatment should be sought from a specialist rheumatologist, or the most recent information provided by the National Prescribing Service (NPS) (www.nps.org.au) or the Rheumatology Therapeutic Guidelines (www.tg.com.au).

Focus of the guideline

The guideline focus is early RA. The guideline does not cover children under the age of 16 years or persons who have been affected with the condition for more than 2 years from the onset of symptoms. The guideline does not cover treatment of extra-articular disease or surgical interventions. *Figure 1* identifies the stages in chronic disease management (CDM) and the focus of the guideline.

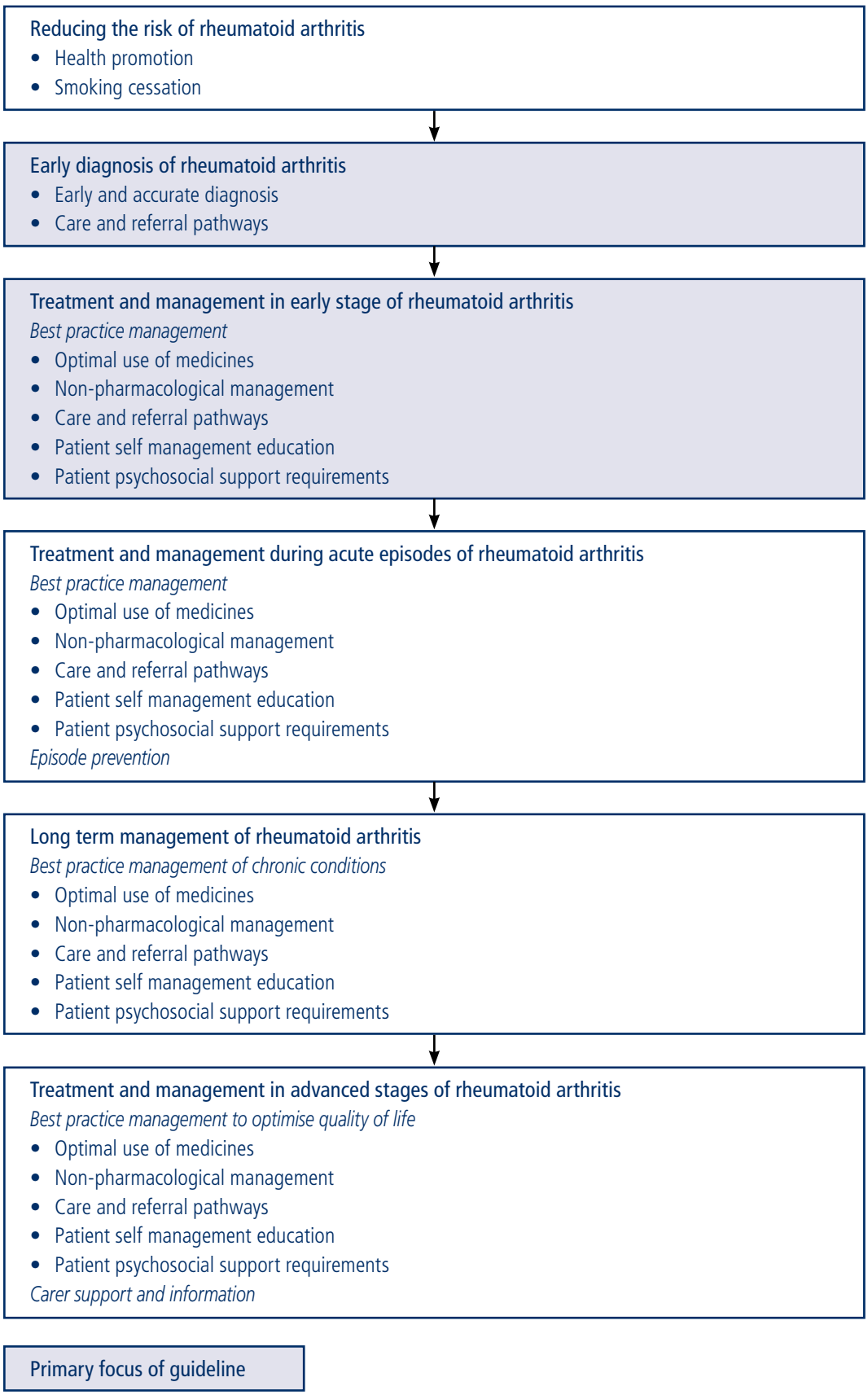


Figure 1. Stages in chronic disease management and the focus of the guideline

Methods

The process used to develop the guideline is outlined in full in the Process Report (*Appendix A*). This guideline is based on an evidence based literature review to NHMRC requirements. Where evidence is not available, the guideline is supported by expert opinion. The RACGP Working Group that has overseen the development of the guideline and companion documents, comprised 12 experts. The membership of the Working Group included rheumatologists, GPs, consumer representatives, arthritis organisation representatives and an NHMRC advisor.

The evidence for the RA guideline is based on:

1. A review of the literature through a systematic search for Level I evidence published from January 2000 to December 2006 (post-publication of the four primary guidelines)
2. Four existing international guidelines[9,10,19,20] that were identified from seven guidelines as being the most appropriate, recently published, high quality guidelines to use as primary references. The guidelines were assessed using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument[26]
3. Additional manual literature searches
4. The Working Group's expert opinion.

Literature review

The method used to conduct the evidence based literature review is outlined in full in *Appendix A* and in *Early rheumatoid arthritis: a literature review of recent evidence* (www.racgp.org.au/guidelines/rheumatoidarthritis/literaturereview). The literature review comprised a systematic search of MEDLINE, EMBASE, CINAHL and the Cochrane Library for English language publications. An additional manual search was used to identify evidence for interventions not represented in the initial search or not covered by the primary guidelines. Articles were also identified through review of reference lists of retrieved papers and research known to Working Group members. Papers were initially selected for inclusion based on reading the title and/or the abstract. Included literature relating to diagnosis of RA was limited to Level I–III evidence and graded according to the *NHMRC additional levels of evidence and grades for recommendations for developers of guidelines.*[27] Included literature relating to the management of RA was limited to Level I evidence. Papers that met the inclusion criteria were critically appraised using checklists developed by the Scottish Intercollegiate Guidelines Network (SIGN)[28] and given an overall quality grade of high, moderate or low. Findings from the literature were reported descriptively and in a tabulated format. The full methods and findings are presented in *Early rheumatoid arthritis: a literature review of recent evidence* (www.racgp.org.au/guidelines/rheumatoidarthritis/literaturereview).

Recommendations

Grading of recommendations in the primary reference guidelines

Four existing guidelines[9,10,19,20] were used as primary references for this guideline. Different grading systems were used for the grading of the recommendations in the primary reference guidelines. Three primary guidelines[9,19,20] used similar methods for classifying evidence and designating strength or grade for a recommendation. All three guidelines required high quality meta-analyses of randomised controlled trials (RCTs), systematic reviews (SRs), and/or RCTs to support grade A. While both SIGN[9] and the European League Against Rheumatism (EULAR)[19] attach grade D to expert opinion and clinical experience of respected authorities, the British Society of Rheumatology (BSR)[20] uses grade C; there is no grade D in BSR. All three primary guidelines[9,19,20] link the strength of evidence directly to the recommendation grade. The fourth guideline,[10] used largely as a primary reference for pharmacological management, based information on SRs and RCTs but did not grade recommendations based on levels of evidence.

Grading of recommendations for this clinical guideline

The method used to develop and grade recommendations is outlined in full in *Appendix A*. Recommendations were on based the literature review and primary reference guidelines. The Working Group developed evidence statements from which each recommendation was developed. These evidence statements are available in *Recommendations for the diagnosis and management of early rheumatoid arthritis* (www.racgp.org.au/guidelines/rheumatoidarthritis/recommendations). Each recommendation statement is supported by a grading that reflects the strength of the recommendation and its implementability in terms of trust or confidence practitioners can have in the recommendation when applied in a clinical situation. The recommendation gradings used throughout the guideline are based on the *NHMRC additional levels of evidence and grades for recommendations for developers of guidelines*,[27] which are presented in *Table 1*.

Table 1. Recommendation grades[27]

A	Excellent evidence – body of evidence can be trusted to guide practice
B	Good evidence – body of evidence can be trusted to guide practice in most situations
C	Some evidence – body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Weak evidence – body of evidence is weak and recommendation must be applied with caution

The overall grade of each recommendation is based on a summation of an appraisal of individual components of the body of evidence on which the recommendation is based, including volume and consistency of the evidence. *Table 2* shows the body of evidence assessment matrix. It also lists all the components that were considered when assessing the body of evidence, together with the grades used.[27] One of the five components, volume of evidence, classifies evidence the same way as three of the primary reference guidelines.[9,19,20]

Table 2. Body of evidence assessment matrix[14]

Component	A	B	C	D
	Excellent	**Good**	**Satisfactory**	**Poor**
Volume of evidence	Several Level I or Level II studies with low risk of bias	One or two Level II studies with low risk of bias or a SR of multiple Level III studies with low risk of bias	Level III studies with low risk of bias or Level II studies with moderate risk of bias	Level IV studies or Level I–III studies with high risk of bias
Consistency	All studies consistent	Most studies consistent and inconsistencies may be explained	Some inconsistency reflecting genuine uncertainty around clinical question	Evidence is inconsistent
Clinical impact	Very large	Substantial	Moderate	Slight or restricted
Generalisability	Population(s) studied in body of evidence are the same as the target population for the guideline	Population(s) studied in the body of evidence are similar to the target population for the guideline	Population(s) studied in the body of evidence different to the target population for the guideline but it is clinically sensible to apply this evidence to the target population (eg. results in adults that are clinically sensible to apply to children)	Population(s) studied in the body of evidence different to the target population for the guideline and hard to judge whether it is sensible to generalise to the target population
Applicability	Directly applicable to Australian health care context	Applicable to Australian health care context with few caveats	Probably applicable to Australian health care context with some caveats	Not applicable to Australian health care context

The guideline

The RA guideline has been designed to provide clear information to assist clinical decision making and support optimal patient care. It is based on the best evidence available up to December 2006. Where appropriate, the evidence has been interpreted with regard to the Australian context in which the guideline will be implemented. It is intended that the guideline be considered according to the limitations outlined in section 7 and used in conjunction with clinical judgment and patient preference. The guideline contains the following information.

Algorithms (flow charts)

The three algorithms summarise the main recommendations of the guideline and provide an accessible desktop reference. The first two algorithms are detailed flow charts for the diagnosis and the management of RA. The third algorithm is a 'simplified' version that highlights the entire process.

Recommendations

The 30 recommendations contained in this guideline are limited to the first 2 years of onset of RA in adults. They do not cover the management of other forms of arthritis, complex or unusual conditions, or give detailed guidance on pharmacological therapy in RA. The recommendations have been developed on the basis of the best evidence available up to December 2006.

Each recommendation has been graded (A to D) according to the *NHMRC additional levels of evidence and grades for recommendations for developers of guidelines*.[27] The grade reflects the degree of 'trust' that the clinician can place on the clinical application of the recommendation. Each recommendation is supported by a summary of the evidence. The RACGP Working Group supports all 30 recommendations and intends they be used in conjunction with clinical judgment and patient preferences. The full grading and evidence base for each recommendation is available in *Recommendations for the diagnosis and management early rheumatoid arthritis* (www.racgp.org.au/guidelines/rheumatoidarthritis/recommendations).

Good practice points

Where appropriate, recommendations are followed by good practice points. The good practice points are essential tips on how to effectively implement the recommendations. Unless otherwise referenced, the source of information presented in the good practice points is the Working Group. These points are followed by a summary of the evidence for each recommendation.

Resources

Useful references and supporting information are provided throughout the guideline. *Appendix B* contains additional resources, as well as contact details for organisations providing services and support to people with RA. This includes the chronic disease management flow chart.

The RACGP Working Group recommends consulting the Therapeutic Guidelines (www.tg.com.au) and the National Prescribing Service (www.nps.org.au) for detailed prescribing information, including adverse effects.

Limitations of the guideline

Medication information

The literature search was not designed to retrieve safety trials for pharmacological interventions. The guideline does not seek to provide full safety and usage information on pharmacological interventions. The pharmacological interventions outlined in the guideline should not be applied without consideration to the patient's clinical profile and personal preferences. The RACGP Working Group recommends consulting the Therapeutic Guidelines (www.tg.com.au) and the National Prescribing Service (www.nps.org.au) for detailed prescribing information including:

- indications
- drug dosage
- method and route of administration
- contraindications
- supervision and monitoring
- product characteristics.

Search date

The guideline is based on the best evidence available up to December 2006. Evidence published after this date has not been reviewed for the guideline.

Interventions included

The search strategy was limited to include only papers graded as Level I to Level III evidence for diagnosis of RA, and Level I evidence for management of RA. Other interventions, eg. 'dietician referral' and 'complex multifaceted interventions' that may have been investigated using different study designs are not represented in the guideline. The guideline is not intended to confirm or refute the effectiveness, nor provide guidance on the use of interventions that have not been included, as the evidence has not been reviewed.

Lack of evidence

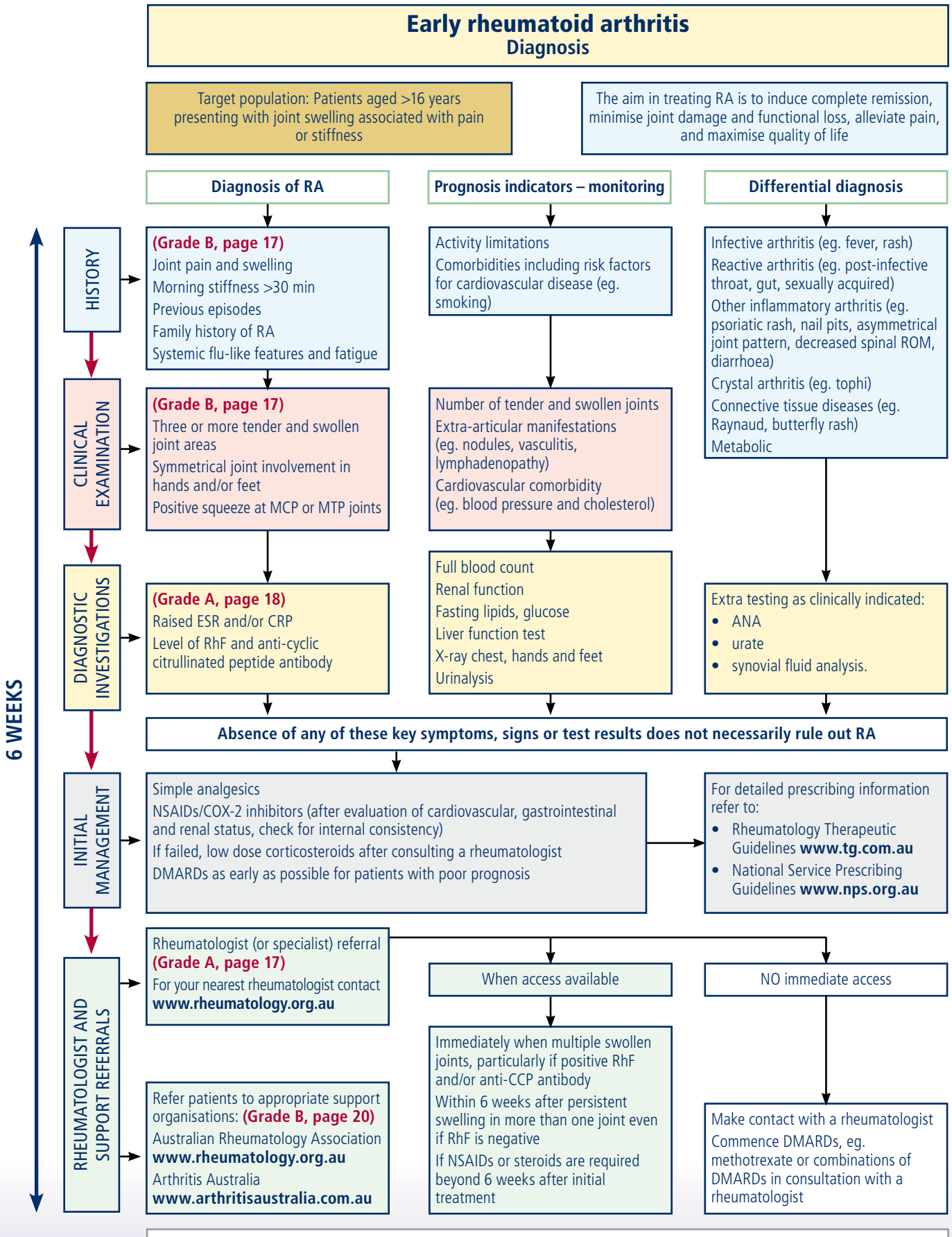
For some interventions included in the recommendations there was limited evidence from which to draw conclusions on the intervention's effectiveness. The Working Group acknowledges that lack of evidence is not evidence of lack of effect, and has attempted to reflect this in the strength of the grading given to recommendations on interventions that are not supported. In addition, some interventions were not supported in the recommendations due to lack of evidence of effect. The Working Group acknowledges that this refers to lack of evidence of effect over placebo; that is, patients may receive some beneficial outcomes from the intervention but these do not exceed the beneficial effects that can be expected from a placebo therapy.

Cost effectiveness

As part of the brief, the evidence for this guideline does not include the cost effectiveness of the recommended practice versus current/established practice. It also does not cover the economic feasibility of the recommendations.

ALGORITHMS

Early RA diagnosis



GO TO EARLY RHEUMATOID ARTHRITIS MANAGEMENT (PAGE 14)

Early RA management

Early rheumatoid arthritis
Management

0–6 WEEKS

DIAGNOSIS
(see page 11)

→ Early referral and treatment with DMARDs can reduce the increased morbidity and mortality seen with active RA **(Grade A, page 17)**

MANAGEMENT

→
- Every RA patient should be assessed for individual needs and should have access to a range of health professionals including but not limited to: rheumatologist, physiotherapist, occupational therapist, orthopaedic surgeon, dietician, podiatrist, pharmacist, social worker and others **(Grade B, page 19)**
- All patients should have a care plan **(Grade B, page 19)**

6–12 WEEKS

PHARMACOLOGICAL INTERVENTIONS →

BASIC THERAPY

Simple analgesics (eg. paracetamol) **(Grade B, page 22)**

Omega-3 supplements **(Grade A, page 22)**

GLA supplements **(Grade C, page 22)**

NSAIDs/COX-2 inhibitors **(Grade A, page 23)**

DMARDs: **(Grade A, page 25)**
- investigations before DMARD therapy: chest X-ray, FBC, ESR, CRP, hepatitis B and C, renal and liver function tests
- commence DMARDs within 12 weeks of onset in consultation with a rheumatologist
- once weekly methotrexate is first choice as single or combination therapy unless contraindicated
- DMARDs require at least 2–3 months for effect
- cease smoking and limit alcohol if on methotrexate or leflunomide

Corticosteroids: **(oral: Grade A, page 26 intra-articular: Grade B, page 26)**
- intra-articular for individual joints to suppress synovitis
- oral, intramuscular, or intravenous for general flare while waiting for DMARD action
- low dose oral corticosteroids (7.5 mg/day) may have DMARD action but long term use is not recommended
- ongoing monitoring for medication safety and comorbidities is an important shared GP role
- discuss medication interactions (including over-the-counter preparations and complementary medicines)

NON-PHARMACOLOGICAL INTERVENTIONS

Weight control **(Grade B, page 28)**
Patient education and self management programs **(Grade B, page 19)**
Occupational therapy **(Grade B, page 29)**
Exercise (eg. dynamic, aerobic, tai chi) **(Grade C, page 28)**
Psychosocial support **(Grade C, page 20)**
Sleep promotion **(Grade B, page 21)**
Appropriate foot care **(Grade C, page 30)**
Thermotherapy (eg. heat and/or ice packs) **(Grade D, page 30)**

For detailed prescribing information refer to:
- Rheumatology Therapeutic Guidelines **www.tg.com.au**
- National Service Prescribing Guidelines **www.nps.org.au**

ADVANCED THERAPY
Initial prescription by a rheumatologist (eg. eflunomide, cyclosporin, biological agents, etanercept, adalimumab, infliximab, anakinra, rituximab)

WARNING: DO NOT recommend Chinese herb *Tripterygium wilfordii* due to risk of serious adverse effects **(Grade B, page 27)**

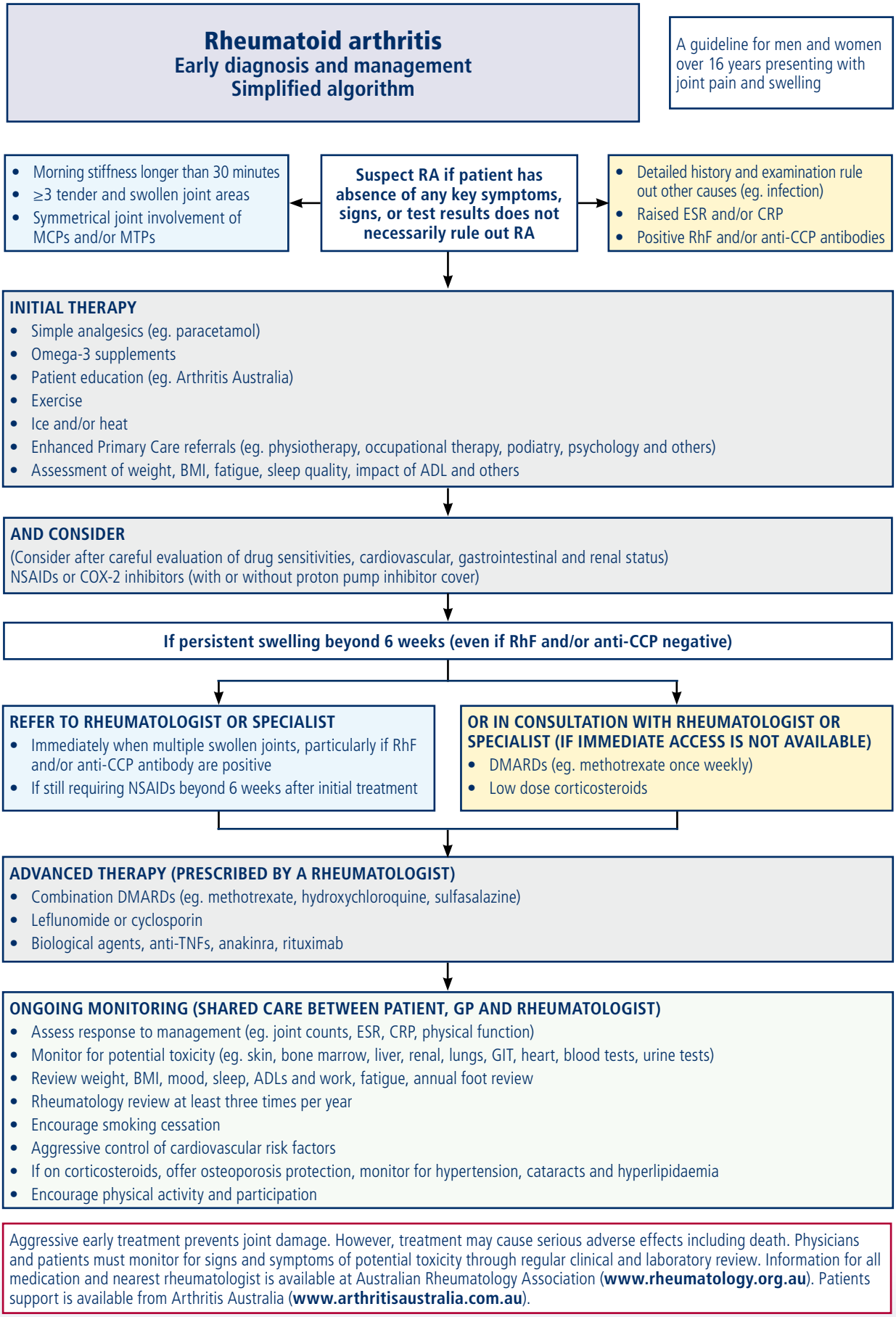
12 WEEKS – 2 YEARS

ONGOING MONITORING (Grade B, page 31) →
- Monitor for potential toxicity (eg. skin, lungs, GIT, heart, blood and/or urine tests)
- Assess response to management (eg. joint counts, ESR/CRP, physical function)
- Aggressive control of cardiovascular risk factors (eg. smoking cessation)
- If on corticosteroids offer osteoporosis prevention and monitor for hypertension, cataracts and hyperlipidaemia
- Review weight, BMI, mood, sleep, ADLs/work, fatigue, annual foot review
- Ensure rheumatology review at least three times per year

MANAGEMENT OF ACUTE EPISODES →
- Readjust/recommence analgesics/NSAIDs/COX-2 inhibitors for the short term
- Consider short term oral corticosteroids or injectable corticosteroids
- Increase or change DMARDs in consultation with a rheumatologist
- Lack of DMARD control in RA is associated with increased morbidity and mortality

WARNING: Treatment may cause serious adverse effects including death. Physicians and patients must monitor for signs and symptoms of potential toxicity through regular clinical and laboratory review.
Information for all medication is available on Australian Rheumatology Association's website at **www.rheumatology.org.au**

RA simplified algorithm – early diagnosis and management



SUMMARY OF RECOMMENDATIONS

There is one recommendation indicating extreme caution: Recommendation 22 *Tripterygium wilfordii* (Chinese herb) (highlighted in RED).

Note: Most of the recommendations below have specific good practice points in the body of the guideline.

RECOMMENDATION 1 – EARLY DIAGNOSIS (Grade A)
General practitioners should diagnose RA as early as possible in order to optimise outcomes for patients.

RECOMMENDATION 2 – REFERRAL (Grade A)
General practitioners should refer patients to a rheumatologist if there is persistent swelling beyond 6 weeks, even if RA is not confirmed. Early referral enables aggressive intervention with disease modifying drugs, reducing long term joint damage and disability.

RECOMMENDATION 3 – CLINICAL EXAMINATION (Grade B)
General practitioners should base a diagnosis of RA (and differential diagnosis) on clinical examination in the first instance. A strong suspicion of RA is indicated by:

- the presence of persistent joint pain and swelling affecting at least three joint areas, and/or
- symmetrical involvement of the metacarpophalangeal or metatarsophalangeal joints, and/or
- morning stiffness lasting more than 30 minutes.

RECOMMENDATION 4 – DIAGNOSTIC INVESTIGATIONS (Grade A)
For patients presenting with painful and swollen joints, GPs should support clinical examination with appropriate tests to exclude other forms of arthritis and other differential diagnoses, and to predict patients likely to progress to erosive disease. Base investigations should include:

- erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP)
- rheumatoid factor and anti-cyclic citrullinated peptide antibody levels.

RECOMMENDATION 5 – MULTIDISCIPLINARY CARE (Grade B)
General practitioners should encourage and support a management approach that is based on individual patient need and involvement of a multidisciplinary team of health professionals.

RECOMMENDATION 6 – CARE PLANS (Grade B)
General practitioners should aim to engage patients with RA in individualised care plans that include treatment goals and objective measures of disease.

RECOMMENDATION 7 – PATIENT INFORMATION (Grade B)
General practitioners should provide ongoing, tailored information to support patient understanding of their disease, treatment options, possible outcomes and their role in self management.

RECOMMENDATION 8 – PATIENT INFORMATION (Grade B)
General practitioners should encourage patients to seek appropriate information from relevant support agencies and encourage their participation in appropriate formal education opportunities according to their individual needs.

RECOMMENDATION 9 – PSYCHOSOCIAL SUPPORT (Grade C)
General practitioners should ensure access to appropriate psychosocial support for patients with RA, including support in managing relationship and sexuality issues.

RECOMMENDATION 10 – SLEEP (Grade D)
General practitioners should assess and manage sleep quality for patients with RA.

RECOMMENDATION 11 – SLEEP DISTURBANCES (Grade B)
General practitioners should consider the use of behavioural therapy, exercise, and tricyclic agents for early management of sleep disturbances.

RECOMMENDATION 12 – SIMPLE ANALGESICS (Grade B)
General practitioners should consider using simple analgesics (eg. paracetamol) where possible for pain relief in early arthritis.

RECOMMENDATION 13 – OMEGA-3 SUPPLEMENTATION (Grade A)

General practitioners should recommend omega-3 supplementation as an adjunct for management of pain and stiffness in patients with RA.

RECOMMENDATION 14 – GAMMA-LINOLENIC ACID SUPPLEMENTATION (Grade C)

General practitioners might recommend gamma-linolenic acid for potential relief of pain, morning stiffness and joint tenderness in RA patients.

RECOMMENDATION 15 – NSAIDS AND COX-2 INHIBITORS (Grade A)

General practitioners should consider using conventional NSAIDs or COX-2 inhibitors for reducing pain and stiffness in the short term treatment of RA where simple analgesia and omega-3 fatty acids are ineffective.

RECOMMENDATION 16 – NSAIDS AND COX-2 INHIBITORS (Grade A)

General practitioners should apply caution when using traditional NSAIDs and COX-2 inhibitors. Choice of NSAIDs or COX-2 inhibitors should be based on consideration of the patient's specific needs, baseline risk profile and concomitant medication. The potential benefits need to be measured in relation to potential harms. Caution is particularly required in those at risk, such as the elderly or patients who have gastrointestinal, renal or cardiovascular comorbidities.

RECOMMENDATION 17 – DMARD THERAPY (Grade A)

General practitioners must facilitate early treatment with DMARDs for patients diagnosed with RA as well as for those with undifferentiated inflammatory arthritis who are judged to be at risk of developing persistent and/or erosive arthritis. Ideally, DMARD therapy should be initiated by a rheumatologist in light of the potential toxicity of these agents.

RECOMMENDATION 18 – DMARD THERAPY (Grade A)

If initiating DMARD therapy, GPs should use methotrexate as the first line choice, particularly when the disease is judged to be moderate to severe, or when there is a high risk of erosive disease.

RECOMMENDATION 19 – CORTICOSTEROIDS (Grade A)

General practitioners should consider short term, low dose, oral corticosteroid treatment when simple analgesics, omega-3 fatty acids, and NSAIDs or COX-2 inhibitors have failed to achieve symptomatic relief. This should be undertaken in consultation with a rheumatologist and with a consideration of the patient's comorbidities and individual risk factors.

RECOMMENDATION 20 – CORTICOSTEROIDS (Grade B)

General practitioners should consider intra-articular corticosteroid injections for rapid symptomatic relief of inflammation in target joints, but no more than three injections per year for a specific joint.

RECOMMENDATION 21 – COMPLEMENTARY MEDICINES (Grade B)

General practitioners should inform patients about complementary medicines and the insufficient volume of evidence available on treating RA with these medicines. General practitioners should also inform patients of the potential adverse effects and interactions of these medicines.

RECOMMENDATION 22 – COMPLEMENTARY MEDICINES (TRIPTERYGIUM WILFORDII) (Grade B)

General practitioners should not recommend *Tripterygium wilfordii* (Chinese herb). While it may have beneficial effects on the symptoms of RA, it is associated with serious adverse effects (impaired renal function, haematotoxic and immunosuppressive effects, hair loss, diarrhoea and nausea).

RECOMMENDATION 23 – WEIGHT CONTROL (Grade B)

General practitioners should encourage dietary modification and weight control for all RA patients.

RECOMMENDATION 24 – EXERCISE (Grade C)

General practitioners should encourage patients with RA to engage in regular dynamic physical activity compatible with their general abilities in order to maintain strength and physical functioning.

RECOMMENDATION 25 – OCCUPATIONAL THERAPY (Grade B)
General practitioners should refer patients with RA experiencing limitations in function to a skilled occupational therapist for advice.

RECOMMENDATION 26 – OCCUPATIONAL THERAPY (Grade C)
Occupational therapy should be directed at assisting activities of daily living, including activities associated with work and leisure activities.

RECOMMENDATION 27 – FOOT CARE (Grade C)
General practitioners should support access to appropriate foot care for patients with RA.

RECOMMENDATION 28 – ALTERNATIVE PHYSICAL THERAPIES (Grade D)
General practitioners should inform patients about complementary and alternative physical therapies, particularly highlighting the insufficient volume of evidence that is available on treating RA with these therapies. General practitioners should also inform patients of the potential for adverse effects.

RECOMMENDATION 29 – DISEASE MONITORING AND COMORBIDITIES (Grade B)
General practitioners should be involved in monitoring disease progression, response to treatment, and comorbidities in conjunction with the treating rheumatologist and other members of the multidisciplinary team.

RECOMMENDATION 30 – DISEASE MONITORING AND COMORBIDITIES (Grade B)
Patients with RA should be assessed and treated for cardiovascular risk factors such as smoking, obesity, physical inactivity, hypercholesterolaemia, hypertension and diabetes.

RHEUMATOID ARTHRITIS RECOMMENDATIONS

Diagnosis of rheumatoid arthritis

Early diagnosis and referral

RECOMMENDATION 1 (Grade A)
General practitioners should diagnose RA as early as possible in order to optimise outcomes for patients.

RECOMMENDATION 2 (Grade A)
General practitioners should refer patients to a rheumatologist if there is persistent swelling beyond 6 weeks, even if RA is not confirmed. Early referral enables aggressive intervention with disease modifying drugs, reducing long term joint damage and disability.

Good practice points

- Refer to a rheumatologist immediately when there are many swollen joints, particularly if tests for rheumatoid factor (RhF) and/or anti-cyclic citrullinated peptide (anti-CCP) antibody are positive.
- If access to a rheumatologist is not possible, contact one by telephone to discuss appropriate treatment.

A 'window of opportunity' exists to initiate early treatment that will change the course of the disease. This window may be as little as 3–4 months.[19] The international guidelines identified as the basis for this guideline point to substantial evidence that, in RA, joint destruction begins within a few weeks of symptom onset and that early treatment decreases the rate of disease progression.[9,19] Therefore, it is important to diagnose RA and initiate disease modifying therapy as soon as possible.*

The EULAR guideline[19] stresses the importance of early referral (grade of recommendation B). The SIGN guideline[9] also supports early referral and early DMARD therapy (grade of recommendation B). The BSR guideline[20] and EULAR[19] stress that a lack of precise diagnostic criteria means that patients with undifferentiated inflammatory arthritis and strong predictors of persistence would be candidates for receiving DMARD therapy.

* *A recent article, identified after the search timeframe and not subjected to critical appraisal, reported on a validation study of a prediction rule for development of RA among patients presenting with recent onset undifferentiated arthritis. A weighted score was generated for the following factors (ie. predictive power): positive anti-CCP (2 pts); involvement of joints in both upper and lower extremities (1.5 pts); CRP ≥51 mg/L (1.5 pts); ≥11 tender or swollen joints (1 pt each); ≥60 minutes of morning stiffness (1 pt); positive RhF (1 pt); and female gender (1 pt). A score of ≥8 accurately predicted the risk of developing RA in 97% of individuals when tested in independent data collections. A score of ≤6 meant that it was possible to accurately reassure 83% of patients that they would not develop RA.*[29]

History and clinical examination

RECOMMENDATION 3 (Grade B)
General practitioners should base a diagnosis of RA (and differential diagnosis) on clinical examination in the first instance. A strong suspicion of RA is indicated by:

- the presence of persistent joint pain and swelling affecting at least three joint areas, and/or
- symmetrical involvement of the metacarpophalangeal or metatarsophalangeal joints, and/or
- morning stiffness lasting more than 30 minutes.

International guidelines[9,19,20] support the diagnosis of RA based primarily on careful history taking and clinical examination. In most patients, symptoms emerge over weeks to months.

Rheumatoid arthritis should be particularly suspected in patients who present with persistent joint pain and swelling affecting at least three joint areas; symmetrical involvement of the metacarpophalangeal or metatarsophalangeal joints; and/or morning stiffness lasting more than 30 minutes (grade of recommendation C,[20] grade of recommendation B[9,19]). The number of swollen/tender joints is an indicator of potentially serious progressive disease.[9,19,20] It is important to note that the number of swollen joints correlates better with radiographic progression in the later stages of RA.[19]

In addition to the above, systemic flu-like symptoms are also common.[9]

The BSR guideline[20] stresses that a lack of precise diagnostic criteria means that patients with undifferentiated arthritis and strong predictors of persistence would be candidates for early referral to a rheumatologist and commencement of DMARD therapy.

Rheumatoid arthritis can resemble any disorder causing acute or chronic polyarthritis. Elimination of other diseases is therefore a necessary step in RA diagnosis.[9,19,20]

Diagnostic investigations

RECOMMENDATION 4 (Grade A)

For patients presenting with painful and swollen joints, GPs should support clinical examination with appropriate tests to exclude other forms of arthritis and other differential diagnoses, and to predict patients likely to progress to erosive disease. Base investigations should include:

- ESR and/or CRP
- RhF and anti-cyclic citrullinated peptide antibody levels.

Good practice points

- Absence of any key symptoms, signs or test results does not necessarily rule out a diagnosis of RA.
- Depending on the clinical picture, additional investigations may be required to eliminate other causes of presenting symptoms. These may include full blood count (FBC), urinalysis, plain X-rays of hands and feet, anti-nuclear antibody (ANA) and others according to the context and patient history.

The diagnosis of RA requires a number of tests. The EULAR guideline[19] (grade of recommendation C) recommends that in every patient presenting with early arthritis, the following factors predicting persistent and erosive disease should be measured: number of swollen and tender joints; ESR or CRP; levels of RhF and anti-cyclic citrullinated peptide (anti-CCP) antibodies, and radiographic damage.

The RACGP Working Group suggests using plain X-rays as a prognostic indicator and for monitoring disease progression. The Working Group also suggests the use of synovial fluid analysis, including cell count, differential count, multiple chemical sensitivity and crystal deposition.

The recommended tests and practice points are described below. Tests are useful in increasing diagnostic certainty, excluding other forms of arthritis, predicting patients likely to progress to erosive disease, and monitoring disease progression. However, no single test accurately diagnoses RA.

The ESR and CRP indicate an inflammatory process but have low specificity for RA. One or other of these tests is usually performed (grade of recommendation C).[19] These markers are usually elevated in RA, but may be normal. High ESR or CRP levels independently predict long term radiographic progression. They may be useful in monitoring disease activity and response to treatment.[9]

The RhF test is not conclusive and may indicate other chronic inflammatory diseases (false positive). It may not show as seropositive in some RA cases (false negative). RhF is positive in 60–70% of RA patients. However, when present in combination with other factors (especially anti-CCP), the level of RhF indicates the severity of the disease.[19]

The anti-CCP antibody test is a relatively new and useful test, especially in early diagnosis of early RA. Recent research indicates that the test has similar sensitivity to RhF but considerably higher specificity, and is a strong predictor of progression to erosive disease. Nishimura et al[30] conducted a good quality meta-analysis of studies from 1987 to 2006 that involved a total of 30 235 participants compared the accuracy of anti-CCP antibody and RhF as markers in the diagnosis and prognosis of RA. The authors concluded that the presence of anti-CCP antibody is more specific than RhF for diagnosing RA and early RA. The study supports a role for anti-CCP antibody testing in the standard evaluation of early inflammatory polyarthritis, to achieve early accurate diagnosis of RA and, in turn, support early intervention with DMARD therapy.

Both EULAR and the RACGP Working Group support measuring RhF and anti-CCP antibody levels in every patient presenting with early arthritis.

A FBC is usually undertaken to provide general information relating to inflammation and anaemia and is useful as a prognosis indicator. (Working Group)

Plain X-rays of the hands and feet have been key investigations in identifying erosions and predicting disease; however, erosions are not often apparent in disease of less than 3 months duration. Serial X-rays over years may show disease progression and therefore indicate the need for a change in treatment strategy. EULAR[19] suggests that in very doubtful cases, ultrasound, power Doppler and magnetic resonance imaging might be helpful to detect synovitis.

The ANA test may be useful in distinguishing between RA and lupus and should be used for differential diagnosis. Some RA patients with severe disease test positive for ANA, so other criteria should be applied to determine an accurate diagnosis of RA.

General management of rheumatoid arthritis

Multidisciplinary care and care planning

RECOMMENDATION 5 (Grade B)
General practitioners should encourage and support a management approach that is based on individual patient need and involvement of a multidisciplinary team of health professionals.

RECOMMENDATION 6 (Grade B)
General practitioners should aim to engage patients with RA in individualised care plans that include treatment goals and objective measures of disease.

Good practice points

- Each person with RA should be cared for by more than one health professional.
- GPs may utilise Enhanced Primary Care (EPC) items to facilitate access to appropriate services (www.health.gov.au/epc). Eligible services include, but are not limited to, those provided by occupational therapists, physiotherapists, hand therapists, nurses, podiatrists, psychologists, mental health workers, Aboriginal health workers, chiropodists and exercise physiologists.
- Consider referral to a consultant pharmacist for a Home Medicine Review (MBS Item 900).

The role of multidisciplinary input in the management of chronic disease is strongly emphasised in national strategic policy relating to CDM. There are a number of recent federal government initiatives for the prevention or delay in onset, early detection, and evidence based management of chronic disease, including RA. These focus on improving capacity, effectiveness and efficiency of multidisciplinary collaboration.[2]

There is strong support from the existing guidelines[9,20] that the successful timely management of patients with RA depends on involvement of a range of health care professionals, according to the individual patient's need. These health care professionals include, but are not limited to, GPs, rheumatologists, physiotherapists, occupational therapists, pharmacists, psychologists, dieticians and social workers.

The BSR guideline[20] emphasises the importance of ongoing involvement of both primary and secondary care in the long term management of patients with RA, particularly in view of the multisystem involvement of RA as the disease progresses. The guideline recommends primary care physicians remain closely involved in the care of these patients and be responsible for their general health, particularly with regard to cardiovascular risk. The role of the primary care physician also includes encouraging patients to exert more control over their disease and disease management.

The RACGP Working Group supports the notion that the GP, rheumatologist and multidisciplinary team should aim to engage the patient in an individualised care plan, agreeing on treatment goals that include an objective measure of disease.

Patient information and education

RECOMMENDATION 7 (Grade B)
General practitioners should provide ongoing, tailored information to support patient understanding of their disease, treatment options, possible outcomes and their role in self management.

RECOMMENDATION 8 (Grade B)
General practitioners should encourage patients to seek appropriate information from relevant support agencies and encourage their participation in appropriate formal education opportunities according to their individual needs.

Good practice points

- Joint protection, energy conservation and problem solving skills training should be taught early in the disease course.
- GPs can access medication information for patients from the Australian Rheumatology Association's website (www.rheumatology.org.au or www.rheumatology.org.au/community/PatientMedicineInformation.asp#medicine) or refer patients to the site.
- Referral to Arthritis Australia is recommended for general disease and treatment information, as well as support services (www.arthritisaustralia.com.au).
- Lifestyle advice should be given to all RA patients to encourage smoking cessation, dietary modification, weight control and exercise.

While evidence of the impact of patient information and education remains limited, international guidelines[9,19,20] agree that this is an important aspect of general management of RA and should be encouraged among all members of the multidisciplinary team.

There is evidence that RA patients should be helped to contact support organisations (grade of recommendation B).[20] Patients with RA should also be provided with a plan of care from diagnosis that outlines the principles of management, including a commitment to training patients to self manage some aspects of their disease (grade of recommendation B).[20]

Education programs

There is evidence that education programs, aimed at helping patients to cope with pain and disability and to maintain work ability and general functionality, may be employed successfully as an adjunct intervention (grade of recommendation B).[19] The BSR[20] guideline stresses that patient education needs to be individually tailored in terms of content and format, and should be delivered at various times during the course of the disease (grade of recommendation A).[20] This guideline also recommends a cognitive behavioural approach to patient education in order to promote long term adherence to management strategies (grade of recommendation C).[20] It further identifies psychological issues as likely to be important in determining how receptive patients are to education opportunities to learn about their disease.[20]

The EULAR guideline[19] cites three RCTs which demonstrate that written information may increase knowledge about disease.

Overall, patient education has a small short term effect on disability, joint counts, patient global assessment, psychological status and depression; there is no evidence of significant long term benefits in adults with RA. However, education plays a role in terms of patient knowledge gain, improved self confidence, desirable behaviour and improved functional status.

Self management programs

Self management programs are designed to give patients more control over their chronic condition and to enable them to make more efficient use of primary and secondary care services. Evidence from EULAR[19] shows that self management programs can result in improved clinical outcome in RA patients, producing short term effects on disability and joint count, as well as on patient global assessment, anxiety and depression, but without any evidence of long term benefit (grade of recommendation B).

Psychosocial support

RECOMMENDATION 9 (Grade C)

General practitioners should ensure access to appropriate psychosocial support for patients with RA, including support in managing relationship and sexuality issues.

Good practice points

- Utilise EPC items to facilitate access to appropriate services (www.health.gov.au/epc). Eligible services include psychologists and mental health workers.
- Utilise mental health care items (www.health.gov.au/internet/wcms/publishing.nsf/Content/health-pcd-gp-mental-health-care-medicare).
- Refer patients to Arthritis Australia for information and services relating to psychosocial support (www.arthritisaustralia.com.au).

Given the potential for disability and reduction in quality of life, psychological and social support is an important aspect of the assessment and management of RA.[20] Such support is required early in the disease, in terms of coping with the diagnosis, and throughout disease progression as the impact of the disease becomes more evident.

The BSR guideline[20] identifies a shared role for all members of the multidisciplinary team in providing guidance on coping with the disease and encouraging positive attitudes toward self management and adjustment to the diagnosis of RA. It recommends that individuals should have social and psychological support to help them to stay at work and participate in normal activities of living. This may be accessed through a range of means including patient based support agencies. The BSR guideline[20] identifies evidence (although not high levels of evidence) of the effectiveness of support initiatives such as telephone help lines and the involvement of rheumatology nurses.

The BSR guideline also makes a specific recommendation regarding the need to address sexuality and relationship issues with patients, identifying that health care professionals should provide opportunities to discuss these issues and refer patients for appropriate support (grade of recommendation C).[20] Health care professionals should be alert to issues such as the impact of pain, dysfunction and dependence on relationships and self esteem.

A considerable body of literature relating to chronic disease in general is relevant to this area but has not been reviewed in this literature review.

Sleep patterns and fatigue

RECOMMENDATION 10 (Grade D)
General practitioners should assess and manage sleep quality for patients with RA.

RECOMMENDATION 11 (Grade B)
General practitioners should consider the use of behavioural therapy, exercise and tricyclic agents for early management of sleep disturbances.

Good practice points

- Refer patients to Arthritis Australia for information and services relating to sleep (www.arthritisaustralia.com.au) or to Sleep Disorders Australia (www.sleepoz.org.au).
- Initiate tricyclic therapy at the lowest dose and gradually increase to the maximum tolerable dose or minimal effective dose (whichever is lower).
- Maintain tricyclic therapy for at least 4 weeks before assessing efficacy of treatment.
- After 3–6 months of symptom remission, gradually decrease the dose with regular pain assessment.

The BSR guideline[20] identifies sleep disturbance as a common feature of RA, particularly during disease flares. Fatigue is also found to be a significant problem. A full review of the literature relevant to this consensus recommendation was not undertaken.

The BSR[20] recommends that health providers give consideration to the impact of fatigue on the quality of life in early RA. The guideline cites a survey in which 40% of patients reported severe fatigue. The BSR[20] recommends that the sleep patterns of patients with RA should be specifically assessed (grade of recommendation A). Early management of sleep disturbance may include behavioural therapy and the use of exercise (grade of recommendation B).

The BSR guideline[20] also recommends the consideration of tricyclic agents in sleep management for patients with RA. Antidepressants may be used to improve symptoms and quality of life in patients with chronic pain (particularly pain impacting upon sleep quality) in conjunction with other pharmacological management. Tricyclic agents are recommended as the first choice of antidepressants for use in pain management.[20,31] A good quality SR[31] of 77 RCTs and 12 meta-analyses provided support for the use of tricyclics in managing pain impacting upon sleep in patients with RA. In an analysis of the general analgesic effects of antidepressants that included two previous SRs (98 RCTs), the authors reported that the analgesic effects of tricyclics are independent of antidepressant effects and superior to selective serotonin re-uptake inhibitors (SSRIs). Sub-analysis of results reported from eight good quality, placebo controlled RCTs specifically in populations with inflammatory rheumatic diseases, including RA, supported these findings. The authors of the SR provide a number of recommendations for using tricyclic agents, including initiating therapy at the lowest dose; increasing to the maximum tolerable dose or minimal effective dose (whichever is lower); maintaining therapy for at least 4 weeks before assessing efficacy; and gradually decreasing the dose after 3–6 months of symptom remission and regular pain assessment.[31]

It is the opinion of the RACGP Working Group that monitoring of sleep patterns and fatigue by GPs is important in the management of RA. The Working Group recommends consulting the Therapeutic Guidelines (www.tg.com.au) and the National Prescribing Service (www.nps.org.au) for detailed prescribing information, including adverse effects.

Pharmacological interventions for RA

Prior to commencing pharmacological interventions, check drug sensitivities.

The RACGP Working Group recommends consulting the Therapeutic Guidelines (www.tg.com.au) and the National Prescribing Service (www.nps.org.au) for detailed prescribing information, including adverse effects.

Simple analgesics (eg. paracetamol)

RECOMMENDATION 12 (Grade B)
General practitioners should consider using simple analgesics (eg. paracetamol) where possible for pain relief in early arthritis.

Good practice points

- Paracetamol should be prescribed in regular divided doses to a maximum of 4 g/day for treating persistent pain in people with RA.
- Simple analgesics should be used in place of NSAIDs if possible, and DMARDs should be introduced early to suppress disease activity.
- Paracetamol is the analgesic of choice in the presence of pregnancy, peptic ulcer disease, or significant cardiac, renal, and other comorbidities.
- Paracetamol has few side effects, but dosing is limited by possible hepatotoxicity.

The use of simple analgesia is generally accepted for managing pain in early RA; however, only a small number of patients receive sufficient pain relief from simple analgesia alone.[9] Paracetamol has an excellent safety profile and remains the analgesic of choice, particularly in mild to moderate pain. Around the clock pain control depends on taking adequate doses regularly.[32] There is some evidence supporting the effectiveness of simple analgesia for RA,[9,33] however, much of the evidence is old and contains methodological weaknesses.[33]

In established RA, both conventional NSAIDs and COX-2 inhibitors are more effective than simple analgesics in relieving the signs and symptoms of active disease.[19,33] However, this must be balanced against the potential gastrointestinal, renal and cardiovascular side effects of NSAIDs and COX-2 inhibitors.

Simple analgesics can be added safely to more specific anti-inflammatory medication and may enable a reduction in the dose of NSAIDs required.[32]

The RACGP Working Group recommends that simple analgesics should be the first choice for pain management.

Fatty acid supplements (omega-3 and gamma-linolenic acid)

RECOMMENDATION 13 (Grade A)
General practitioners should recommend omega-3 supplementation as an adjunct for management of pain and stiffness in patients with RA.

RECOMMENDATION 14 (Grade C)
General practitioners might recommend gamma-linolenic acid for potential relief of pain, morning stiffness and joint tenderness in RA patients.

Good practice points

- GPs should ask their patients about their use of supplements/complementary medicines so that this can be considered in care planning. Recommendations 21 and 22 also refer to complementary/alternative medicines.
- Higher doses of omega-3 are likely to be of greatest benefit (up to 12 g/day).
- Fatty acid interventions may provide supplementary or alternative treatment to NSAIDs for some patients. They can also enable a reduction of NSAID doses.

- The recommended dosage for gamma-linolenic acid (GLA) is 1400 mg/day of GLA or 3000 mg of evening primrose oil.

Omega-3 supplementation

A recent good quality meta-analysis[34] of the analgesic effects of omega-3 polyunsaturated fatty acids provides good evidence for a role of omega-3 in pain management in RA. Seventeen RCTs involving 823 patients were included. A meta-analysis of 16 of the studies at 3–4 months showed significant effects for four out of six pain outcome measures, including patient assessed pain, morning stiffness, number of painful and/or tender joints and NSAID consumption. In contrast, significant effects were not detected for physician assessed pain and the Ritchie Articular Index. Eleven of the 16 studies used high doses (>2.7 g/day omega-3). Significant improvements were noted in patient assessed pain and morning stiffness among studies providing high dose, but not low dose omega-3. The results suggest a potential role for omega-3 supplements as adjunctive treatment for pain and stiffness associated with RA. The results differ from previous meta-analyses, showing a stronger effect than that reported by Fortin, et al[35] and a beneficial effect compared to lack of effect for patient assessed pain by Maclean et al.[36] The authors attribute the differences to the different outcomes measured and the inclusion of eight additional trial results.

The SIGN guideline[9] identifies a benefit in terms of a reduction in tender joints and duration of morning stiffness based on a meta-analysis of patients using omega-3 supplements.[35] Supplementation is practical and can be easily achieved with encapsulated or, less expensively, bottled fish oil.

Gamma-linolenic acid

In a Cochrane review of RCTs of herbal interventions in RA compared to placebo, Little and Parsons[37] assessed the effectiveness of various herbal therapies in the treatment of RA. They found 11 suitable RCTs; seven of the studies compared GLA to placebo. All of the GLA studies found some improvement in clinical outcomes; however, drawing conclusive results proved to be difficult due to the varied methodologies used and the quality of the studies. However, the better quality studies suggest potential relief of pain, morning stiffness and joint tenderness. Further studies are required to establish optimum dosage and duration of treatment. Studies of GLA in the treatment of RA are promising and suggest that GLA may provide a supplementary or alternative treatment to NSAIDs for some patients.

Traditional non-steroidal anti-inflammatory drugs and COX-2 inhibitors

RECOMMENDATION 15 (Grade A)

General practitioners should consider using conventional NSAIDs or COX-2 inhibitors for reducing pain and stiffness in the short term treatment of RA where simple analgesia and omega-3 fatty acids are ineffective.

RECOMMENDATION 16 (Grade A)

General practitioners should apply caution when using traditional NSAIDs and COX-2 NSAIDs. Choice of NSAID or COX-2 inhibitor should be based on consideration of the patient's specific needs, baseline risk profile and concomitant medication. The potential benefits need to be measured in relation to potential harms. Caution is particularly required in those at risk, such as the elderly or patients who have gastrointestinal, renal or cardiovascular comorbidities.

Good practice points

- Simple analgesics should be used in place of NSAIDs if possible, and DMARDs should be introduced early to suppress disease activity.
- NSAIDs and COX-2 inhibitors should be used for the shortest possible duration.
- Long term use of NSAIDs should be at the lowest effective dose.
- Only one NSAID or COX-2 inhibitor should be prescribed at a time.
- Avoid NSAIDs and COX-2 inhibitors in patients taking anticoagulants or corticosteroids.
- Avoid celecoxib in patients who are allergic to sulphonamides.
- Avoid COX-2 inhibitors in patients who have been asthmatic or have had an allergic reaction to NSAIDs.
- Blood pressure and renal function should be monitored, particularly in older people and others at risk.
- If NSAIDs and COX-2 inhibitors are not suitable and paracetamol, omega-3 and non-pharmacological interventions have failed to achieve symptomatic relief, consider use of low dose corticosteroid therapy in consultation with a rheumatologist.

- If NSAIDs or COX-2 inhibitors are required beyond 6 weeks, referral to a rheumatologist is strongly advised.
- NSAIDs and COX-2 inhibitors should be avoided during pregnancy where possible, and should be stopped in women planning to become pregnant. They can be continued until the second trimester if the woman becomes pregnant while taking them. However, they should be discontinued before the third trimester as they interfere with the onset of labour and ductus closure.
- NSAIDs and COX-2 inhibitors should be stopped at least 7–10 days before any major surgical procedure.
- Addition of gastrointestinal protective drugs to conventional NSAIDs can significantly reduce complications, such as the incidence of gastrointestinal bleeding,[19,20] and is recommended for RA patients over 65 years of age, as well as for those with a past history of peptic ulcer disease.[9]

There is substantial evidence that conventional NSAIDs and COX-2 inhibitors have both analgesic and anti-inflammatory effects in RA. However, there is no evidence that they prevent joint damage.[9,19,20] Some evidence shows that NSAIDs and COX-2 inhibitors may be more effective than simple analgesics in relieving the signs and symptoms of active disease; however, the number and quality of trials is poor.[33] Substantial evidence also points to significant side effects for these groups of drugs, including gastrointestinal, renal and cardiovascular effects, as well as many potential drug interactions.[9,19,20] Studies suggest that the risk of cardiovascular and gastrointestinal tract (GIT) events is associated with the dose and duration of NSAID use.

COX-2 inhibitors are equally effective analgesics when compared with conventional NSAIDs, and may cause fewer GIT side effects. A good quality SR of three RCTs involving 15 187 patients with RA or osteoarthritis identified that the selective COX-2 inhibitor, celecoxib, is associated with significantly less GIT side effects compared to conventional NSAIDs. There was insufficient evidence on the safety and efficacy of this medication beyond 12 weeks.[38]

There is strong evidence[9,19] that long term use of NSAIDs and COX-2 inhibitors should be at the lowest effective dose compatible with symptom relief (grade of recommendation A).[20] They should be reduced and, if possible, withdrawn when a good response to DMARDs is achieved (grade of recommendation A).[20]

Compared to non-selective NSAIDs in Australia, COX-2 inhibitors have been demonstrated to be cost effective in arthritic patients at high risk of serious upper GIT events. In average risk patients, COX-2 inhibitors may not be cost effective, as higher costs relative to alternatives are not matched with commensurate benefits.[4]

Side effects

The BSR[20] and EULAR guidelines[19] cite evidence that the use of COX-2 inhibitors is associated with increased risk of cardiac and cerebrovascular events and they should be used only after careful evaluation of cardiovascular status. These effects are likely to extend to conventional NSAIDs. Concern over the potential cardiovascular toxicity of COX-2 inhibitors and NSAIDs generally suggests they should be avoided in high risk individuals. They should also be used with caution in others who cannot be managed with analgesia, steroid injections and one or more DMARDs.

A recent meta-analysis[39] estimates that taking a COX-2 selective NSAID is associated with a 42% increase in the relative risk of a first serious vascular event compared with placebo. This was chiefly attributable to an increased risk of myocardial infarction, with little apparent difference in other vascular outcomes. Overall, the incidence of serious vascular events was similar between a selective COX-2 inhibitor and any traditional NSAID; however, studies with naproxen showed it was not associated with increased vascular events.

The consensus of the RACGP Working Group is that the choice of NSAID and COX-2 inhibitor should be tailored to the patient's specific needs and baseline risk profile.

Disease modifying antirheumatic drugs

RECOMMENDATION 17 (Grade A)

General practitioners must facilitate early treatment with DMARDs for patients diagnosed with RA, as well as for those with undifferentiated inflammatory arthritis who are judged to be at risk of developing persistent and/or erosive arthritis. In light of the potential toxicity of these agents, DMARD therapy should be initiated by a rheumatologist.

RECOMMENDATION 18 (Grade A)

If initiating DMARD therapy, GPs should use methotrexate as the first line choice, particularly when the disease is judged to be moderate to severe, or when there is a high risk of erosive disease.

Good practice points

- If access to a rheumatologist is not possible, consider commencing single drug therapy with MTX or sulphasalazine, based on a consideration of individual patient preference and comorbidities. Consult with a rheumatologist as soon as possible.
- Before commencing DMARDs, organise a baseline chest X-ray, FBC, renal tests, LFTs, CRP, and hepatitis B and C status.
- Be aware of the dosage and monitoring schedules. For example, MTX is given as a weekly oral dosage, usually with a folic acid supplement throughout the week and blood tests for monitoring FBC and LFTs at least monthly.
- Physicians and patients must monitor for signs and symptoms of toxicity through regular clinical and laboratory review as treatment may cause serious adverse effects.
- All DMARD therapy should be reviewed in women planning to conceive, and in pregnant and lactating women. For example, there is evidence that sulfasalazine and hydroxychloroquine can be used safely during pregnancy. However, MTX and leflunomide should not be used in pregnancy. There is some evidence that potential fathers should stop using MTX at least 3 months before planning a pregnancy.
- Monitor for continuing efficacy (ESR/CRP, number of tender and swollen joints, duration of morning stiffness and ADL).
- Alcohol use should be reviewed for people being prescribed MTX as the danger of liver cirrhosis rises significantly with high alcohol intake.
- Smoking cessation should be highly recommended.

It is well established that joint damage commences early in RA and that early treatment with disease modifying drugs is the foundation of a best practice approach to disease management.[9,19,20] DMARDs suppress the inflammatory disease process and have been shown to reduce the rate of erosive change. Therefore they have the potential to alter the disease course, reduce morbidity and mortality, and improve quality of life. Three international guidelines[9,19,20] recommend that patients should be established on disease modifying therapy as soon as possible after a diagnosis of RA has been established. The EULAR guideline supports the concept of a 'window of opportunity' for effective treatment, which may be as short as 3–4 months. This guideline recommends that patients at risk of developing persistent and/or erosive arthritis should be started on DMARD therapy as early as possible, even if they do not yet fulfil established classification criteria for inflammatory rheumatologic diseases.[19]

MTX has become the most popular first line DMARD agent because of its early onset of action (4–6 weeks), good efficacy, favourable toxicity profile, ease of administration, and relatively low cost. One SR and subsequent RCTs have found no consistent differences in efficacy between MTX versus leflunomide, parenteral gold, or etanercept.[40] In addition to the disease modifying effect in relation to joints, there is also evidence that treatment with MTX can reverse the cardiovascular risk associated with active RA.[20]

The guidelines[9,19,20] support MTX as a first line choice, particularly where disease is judged to be moderate to severe or where there is a high risk of erosive disease. Leflunomide or sulphasalazine are identified as alternatives where MTX may be contraindicated.[9,19,20] Hydroxychloroquine is considered an appropriate choice for mild disease.[20] In Australia, leflunomide only attracts a Pharmaceutical benefits Scheme (PBS) subsidy when MTX is ineffective or contraindicated. A recent SR and subsequent RCTs have found no consistent differences in efficacy between MTX, leflunomide, parenteral gold and etanercept.[41]

The adverse effects of conventional DMARDs are well established, as is the need for careful monitoring to identify and manage these effects. Adverse effects may include severe anaemia, liver damage, lung disease and death. Combination therapy appears to have a similar risk profile to monotherapy. Alcohol use during MTX therapy may increase the risk of liver cirrhosis.

The basis for first agent selection is the risk/benefit ratio. One meta-analysis of early placebo controlled trials suggests that sulphasalazine, MTX, leflunomide, intramuscular gold and pencillamine are equally effective in reducing radiological progression in RA.[10]

Combined therapies

Existing guidelines[9,10,19,20] identify clear evidence for the disease modifying effects of MTX, sulfasalazine, leflunomide and intramuscular gold. They point to less compelling evidence, in terms of effect on reduction of erosions, for hydroxychloroquine, penicillamine, oral gold, cyclosporin and azathioprine. There is increasing evidence that combination therapy is more effective than monotherapy for many patients. One guideline[10] cites evidence that low dose, once weekly MTX combined with most other DMARDs is more beneficial than treatment with a single drug. One SR and subsequent RCTs have found that combining certain DMARDs is more effective than using individual drugs alone. However, the balance between benefit and harm varies among combinations.[42] This has been supported by a good quality meta-analysis of 36 RCTs. This meta-analysis found that combination DMARD therapy was more effective in reducing disease severity than monotherapy, both in patients with an early diagnosis of RA and in those with established RA.[43] Combination therapy appears to have no greater toxicity than monotherapy, although individual combinations vary in terms of toxicity.

The RACGP Working Group would consider monotherapy appropriate in mild to moderate RA.

Corticosteroids

RECOMMENDATION 19 (Grade A)

General practitioners should consider short term, low dose, oral corticosteroid treatment when simple analgesics, omega-3 fatty acids, and NSAIDs or COX-2 inhibitors have failed to achieve symptomatic relief. This should be undertaken in consultation with a rheumatologist, and with a consideration of the patient's comorbidities and individual risk factors.

RECOMMENDATION 20 (Grade B)

General practitioners should consider intra-articular corticosteroid injections for rapid symptomatic relief of inflammation in target joints, but no more than three injections per year for a specific joint.

Good practice points

- Oral corticosteroids are not recommended for routine use and should be withdrawn slowly to avoid rebound flare of symptoms.
- Inform patients of the risks of using corticosteroids before prescribing.
- Monitor bone density and ensure osteoporosis protection if there is prolonged use.
- Avoid NSAIDs in patients taking corticosteroids.
- When administering intra-articular injections, always consider possible septic arthritis in the differential diagnosis of mono/oligo flare in RA. Adverse reactions of intra-articular injection (eg. injury, infection, bruising) are minimised and clinical efficacy is increased by accuracy of needle placement and adherence to an appropriate sterile technique during the injection procedure.[44,45]

Corticosteroids are used in RA both for their effects on symptom control (reducing pain and swelling) and for their potential disease modifying action. Systemic corticosteroids, either alone or as part of a DMARD combination strategy, are effective in the short term relief of signs and symptoms, and are probably effective in retarding radiographic progression in early and established RA (grade of recommendation A).[19]

Two SRs and one subsequent RCT have found benefit from both short and long term treatment (more than 3 months) with low dose, oral corticosteroids. Short term treatment reduces disease activity and joint inflammation. Long term treatment may reduce radiological progression while treatment continues. However, long term use is associated with considerable adverse effects.[21] All four guidelines[9,10,19,20] recommend that systemic corticosteroids be considered as short term therapy as part of a DMARD strategy. 'Bridge' corticosteroids (usually intramuscular or intravenous) can be used to provide symptomatic relief while awaiting the effects of DMARDs. Rebound flare of symptoms following cessation is experienced in some patients.[9]

There are few controlled trials on the use of intra-articular corticosteroids in RA, although it is widely accepted that they provide short term relief in pain and swelling. (Working Group)

All guidelines[9,10,19,20] also recommend that intra-articular corticosteroid injections should be considered for the relief of local symptoms of inflammation (grade of recommendation A).[19] Local injections of corticosteroids into joints can directly suppress synovitis and prevent the development of erosions in early RA.[20] Large cohort trials suggest that complications such as joint sepsis are rare, and that aspiration of synovial fluid at the time of joint injection reduces relapse rate.

Intra-articular corticosteroids and bridging therapy with intramuscular and possibly intravenous corticosteroids are useful strategies to rapidly suppress inflammation when starting and increasing DMARDs.[20] In Australia, corticosteroids (combined with DMARDs) have been shown to be cost saving relative to NSAIDs (combined with DMARDs).[4]

Complementary medicines

RECOMMENDATION 21 (Grade B)

General practitioners should inform patients about complementary medicines and the insufficient volume of evidence available on treating RA with these medicines. General practitioners should also inform patients of the potential adverse effects and interactions of these medicines.

RECOMMENDATION 22 (Grade B)

General practitioners should not recommend *Tripterygium wilfordii* (Chinese herb). While it may have beneficial effects on the symptoms of RA, it is associated with serious adverse effects (impaired renal function, haematotoxic and immunosuppressive effects, hair loss, diarrhoea and nausea).

Good practice point

- GPs should ask their patients about use of complementary medicines when prescribing treatment for RA. Recommendations 13 and 14 also refer to complementary/alternative medicines.

Complementary medicines are widely used by patients with RA to support control of symptoms and assist general wellbeing. With the exception of omega-3 fatty acids, and to a lesser extent GLA (refer to recommendations 13 and 14), there is limited evidence of the effect of complementary/herbal medicines in RA. The studies are few and are generally of poor quality.[9,19,20]

In a Cochrane review of 11 RCTs of herbal interventions in RA compared to placebo, Little and Parsons[37] assessed the effectiveness of various herbal therapies (GLA, feverfew, *Tripterygium wilfordii*, topical capsaicin and Reumalex). Drawing conclusive results proved difficult because of the small number of studies, varied methodology and the quality of the studies. Good tolerance of most of the herbal remedies was demonstrated, although caution is warranted in interpreting safety due to the small sample sizes in some of the studies. The review did, however, raise concerns about the potential serious side effects of *T. wilfordii*, a Chinese herb with immunosuppressive effects and an established history of use in the treatment of RA. While it may have beneficial effects on the symptoms of RA, *T. wilfordii* is associated with serious adverse effects that include impaired renal function, haematotoxic and immunosuppressive effects, hair loss, diarrhoea and nausea.[37*]

In another good quality SR, Canter, et al[46] investigated the efficacy and safety of *T. wilfordii*. Based on findings from two RCTs of moderate to good quality, the authors concluded that *T. wilfordii* extract was effective in improving symptoms and functional outcomes in RA patients with active symptoms. However, it was associated with significantly higher rates of serious adverse events than placebo and its use could not be recommended.

A good quality review by Park, et al[47] investigated the effect and tolerability of Ayurvedic medicines (182 patients) on symptoms including pain, morning stiffness and joint swelling, as well as effects on the general health questionnaire. Of the seven RCTs reviewed, only one was of good quality. This RCT showed Ayurvedic medicines to have no effect above placebo in improving symptoms in patients who have had RA for at least 6 months. Minor adverse events were reported.

The RACGP Working Group highlights the need for vigilance with respect to potential toxicity and interactions of complementary and alternative medicines, and the need for primary care physicians to be alert to such medicines that their patients may be taking.

* Further supporting evidence, identified after the search time frame and not subjected to critical appraisal, was available from conference presentations of an update to this Cochrane review. One additional moderate to good quality RCT involving 30 participants investigated *T. wilfordii* in two doses (360 mg/day and 180 mg/day) compared with placebo. The results showed that more participants in the high dose *T. wilfordii* group met ACR[20] criteria than those in the low dose *T. wilfordii* group or the placebo group. (No placebo participants met ACR[20] criteria.) However, the safety profile of *T. wilfordii* remained concerning and the product was not recommended.[48,49]

Non-pharmacological interventions for rheumatoid arthritis

Weight control

RECOMMENDATION 23 (Grade B)
General practitioners should encourage healthy diet and weight control for all RA patients.

Good practice points

- Healthy diet and regular exercise are important in long term weight control.
- The diet recommended for arthritis is similar to that for good health generally, with special emphasis on cardiovascular risk prevention. This includes:
  - eating plenty of fruit, vegetables and whole grain cereal foods
  - eating foods rich in fish oil (omega-3)
  - eating a diet low in fat
  - maintaining a healthy body weight
  - limiting alcohol intake
  - eating only a moderate amount of sugars and foods containing added sugars, and
  - choosing low salt foods and using salt sparingly
- Appropriate exercise is discussed in recommendation 24.

While there is limited evidence of the effect of diet on RA, there is general acceptance of the need to encourage patients to adopt a healthy diet and maintain a healthy weight. The SIGN guideline[9] highlights the importance of maintaining a health weight and body mass index (BMI) in the general management of patients with RA. Weight reduction in RA patients who are overweight or obese reduces impact on weight bearing joints and reduces risk factors for cardiovascular disease. SIGN[9] cites several studies that suggest RA patients with a BMI below healthy range have poorer functional status, highlighting the importance of maintaining BMI within the normal range. The EULAR and BSR[20] guidelines also identify weight control as an important aspect of general disease management.

There have been insufficient studies on the effectiveness of specific diets in managing RA and studies that have investigated diet have not reported BMI as an outcome measure. The SIGN[9] and EULAR[19] guidelines reported that small RCTs investigating a range of diets including gluten free, vegetarian, vegan and fasting, found evidence of significant effect on ACR[20] response and pain in patients with RA, however long term compliance and nutritional deficiencies reduced the acceptability and practicality of many dietary interventions.

It is the opinion of the RACGP Working Group that promotion of a sound diet and weight control by GPs is important in the management of RA.

Exercise

RECOMMENDATION 24 (Grade C)
General practitioners should encourage patients with RA to engage in regular dynamic physical activity compatible with their general abilities in order to maintain strength and physical functioning.

Good practice points

- GPs may utilise EPC items to facilitate access to appropriate services (www.health.gov.au/epc). Eligible services include, but are not limited to, those provided by physiotherapists, occupational therapists and exercise physiologists.
- GPs could refer patients to Arthritis Australia for information and services relating to exercise in RA (www.arthritisaustralia.com.au).
- Exercises such as tai chi may not show statistically significant improvement in body functions but tend to be enjoyable and have a strong social component.

Exercise therapy is well accepted as having a role in combating the adverse effects of RA on muscle strength, endurance and aerobic capacity. However, the effect of exercise in early inflammatory disease or early RA has not been fully investigated and has been primarily extrapolated from results in established RA.

Based on a Cochrane review conducted by van den Ende, et al,[50] the SIGN guideline[9] identified that dynamic exercise therapy (ie. exercises of low to moderate aerobic intensity) is effective in increasing aerobic capacity and muscle strength, with no adverse effects on disease activity or pain observed.

The BSR guideline[20] recommends that aerobic exercise should be encouraged while being mindful of minimising short term exacerbation of disease or joint destruction. The guideline cites two recent studies[51,52] that show exercise can be undertaken without exacerbation of disease in the short term. Long term effects are still not known.

In recommending that exercise can be applied as treatment adjuncts in early arthritis, the EULAR guideline[19] cites a number of RCTs and Cochrane reviews in support of dynamic exercise and hydrotherapy (grade of recommendation B). The effect is generally on improved strength and physical functioning, but may have symptom relieving effects.

Some studies have looked specifically at tai chi and its role in RA. A Cochrane review by Han, et al[53] examined four trials involving 206 participants. The comparative studies measured improvements in ambulatory adults suffering from RA who participated in 8–10 week tai chi programs. In three studies, the programs had no clinically important or statistically significant effect on most outcomes of disease activity, including ADL, tender and swollen joints, and patient global overall rating. In one small study, the most notable results were a significantly increased range of motion in the ankle, hip and knee, and an increased enjoyment of exercise. No detrimental effects were reported. Preserving range of motion in affected joints is particularly important for RA sufferers to maintain functionality.

The RACGP Working Group reached consensus that general physical activity and exercise therapy should be encouraged in RA. Specifically, exercise should be tailored to the needs and preferences of the patient to combat the adverse effects of the disease on muscle strength, endurance and aerobic capacity.

Occupational therapy

RECOMMENDATION 25 (Grade B)

General practitioners should refer patients with RA experiencing limitations in function to skilled occupational therapists for advice.

RECOMMENDATION 26 (Grade C)

Occupational therapy should be directed at assisting activities of daily living, including activities associated with work and significant leisure activities.

Good practice points

- Splints, including hand/wrist resting splints and functional wrist splints, may be offered by an experienced health care professional when hands and wrists are painful and/or swollen; however, the role of splinting remains uncertain.
- Joint protection, energy conservation, and problem solving skills should be taught early in the disease course.
- GPs may utilise EPC items to facilitate access to appropriate services (www.health.gov.au/epc).

The international guidelines[9,19,20] support the role of occupational therapy (OT) interventions in maintaining function for RA patients, while accepting there is an absence of evidence from RCTs. Occupational therapy interventions include training of motor function, skills training, instruction on joint protection and energy conservation, counselling, instruction about assistive devices, and provision of splints

The SIGN guideline[9] recommends that skilled OT should be available to those experiencing limitation in function (grade of recommendation C). The BSR[20] guideline also recommends that joint protection, energy conservation and problem solving skills should be taught early in the course of the disease (grade of recommendation B). It also specifically recommends a continuing OT role in maintaining hand function, utilising devices for assisting hand function, and in aiding alternative work methods (grade of recommendation C).

A further moderate quality review, Steultjens, et al,[54] identified three SRs of occupational therapy interventions in RA. The review concluded that OT improved functional ability in RA patients. However, its effect on other outcome measures was unclear.

Foot care

RECOMMENDATION 27 (Grade C)
General practitioners should support access to appropriate foot care for patients with RA.

Good practice points

- An annual foot assessment and review is recommended for patients at risk of developing serious complications in order to detect problems early.
- GPs may utilise EPC items to facilitate access to appropriate services (www.health.gov.au/epc). Eligible services include podiatrists and chiropodists.

The value of appropriate foot care for RA is well recognised in practice but there is little evidence based research to support recommendations in early arthritis. Both the SIGN[9] and BSR[20] guidelines identify podiatry input and appropriate foot orthoses as important and effective interventions in RA. A further review of the literature relevant to this consensus recommendation was not undertaken.

It is the opinion of the RACGP Working Group that access to appropriate foot care for patients with RA is important in the management of the disease.

Alternative physical therapies

RECOMMENDATION 28 (Grade D)
General practitioners should inform patients about complementary and alternative physical therapies, particularly highlighting the insufficient volume of evidence that is available on treating RA with these therapies. General practitioners should also inform patients of the potential for adverse effects.

Good practice points

- GPs should be alert to alternative physical therapies used by their patients.
- Patient information about physical therapies is available from Arthritis Australia (www.arthritisaustralia.com.au).
- The choice of physical therapies should be guided by patient preference.

According to the BSR guideline,[20] the evidence for the effectiveness of complementary therapy is conflicting and no firm recommendations can be made (grade of recommendation B). For many specific interventions there is insufficient evidence available regarding effectiveness. However, complementary therapies can play an important role in encouraging positive changes in lifestyle and outlook and the majority of these forms of therapy are not harmful.[20]

In a good quality SR of five RCTs, low level laser therapy (LLLT) for up to 4 weeks had a clinically relevant effect in reducing pain and morning stiffness in patients with RA of the hand; however, it did not appear to have long lasting effects. There appeared to be no significant difference between dosage, wavelength and method of delivery.[55] The SIGN guideline[9] suggests that the evidence for use of LLLT is conflicting or insufficient to make conclusions on its use.

The EULAR guideline[19] describes a number of therapies, including acupuncture, laser therapy, use of compression gloves, transcutaneous electrical nerve stimulation (TENS), ultrasound, thermotherapy, and use of splints and orthoses. The BSR guideline[20] also refers to a range of alternative therapies including massage and the Alexander technique. While some studies reported short term pain relief for some of these interventions, there is no evidence for long lasting benefits, and recommendations for use of such interventions are only as adjuncts to pharmaceutical therapies.

A Cochrane review[56] evaluated the effectiveness of thermotherapy on objective and subjective measures of disease activity in RA. Seven studies and 328 participants were included. The review found no significant effect on objective measures (joint swelling, pain, pain medication intake, range of motion, grip strength or hand function) for hot or cold pack application, cryotherapy or faradic baths. There was also no difference in patient preference and no harmful effects were reported. The review concluded that thermotherapy may be used as palliative therapy.

There is evidence from a Cochrane review[57] on the use of acupuncture and electro-acupuncture by rehabilitation specialists as an adjunct therapy for the symptomatic treatment of RA. Two studies involving a total of 84 people were included; one used acupuncture while the other used electro-acupuncture.

In the acupuncture study, there were no statistically significant differences between groups for ESR, CRP, patient's global assessment on visual analogue scale, number of swollen and/or tender joints, general health questionnaire, modified disease activity scale, or for a decrease in analgesic intake. Pain in the treatment group improved more than in the placebo group but the difference was not statistically significant. In the electro-acupuncture study, a significant decrease in knee pain was reported in the experimental group 24 hours post-treatment when compared with the placebo group. This effect was sustained at 4 months post-treatment. Even though electro-acupuncture seems beneficial for reducing symptomatic knee pain in patients with RA, the reviewers precluded its recommendation due to poor quality methodology and a small sample size. They concluded that acupuncture has no effect on any of the outcome measures in the trials. These conclusions are limited by methodological considerations such as the type of acupuncture (acupuncture vs. electro-acupuncture), the site of intervention, the low number of clinical trials and the small sample size of the included studies.[57]

According to the EULAR guideline,[19] acupuncture is among several non-pharmaceutical interventions of which controversial effects have been reported in RCTs. If positive, the RCTs demonstrated short term relief of pain rather than an effect on disease activity.

The BSR guideline[20] states that acupuncture-like TENS (AL-TENS) is beneficial for reducing pain intensity and improving muscle power scores over placebo, while conversely, conventional TENS (C-TENS) resulted in no clinical benefit on pain intensity compared with placebo. The SIGN guideline,[9] citing the same Cochrane review as above, states that acupuncture showed no benefit in one meta-analysis but the quality of the analysis was limited.

Many other 'natural' therapies are used, such as capsaicin, wintergreen and magnet therapy. While they are generally harmless, benefit has not always been rigorously demonstrated and products can often be costly.[10]

Disease monitoring and comorbidities

RECOMMENDATION 29 (Grade B)

General practitioners should be involved in monitoring disease progression, response to treatment and comorbidities in conjunction with the treating rheumatologist and other members of the multidisciplinary team.

RECOMMENDATION 30 (Grade B)

Patients with RA should be assessed and treated for cardiovascular risk factors such as smoking, obesity, physical inactivity, hypercholesterolaemia, hypertension and diabetes.

Good practice points

- Arthritis activity should be assessed at least three times per year. Treatment should be adjusted to keep the swollen and tender joint count, and the CRP levels, as low as possible.
- Patients should be monitored for potential toxicity and adverse events of medications.
- Frequency and type of monitoring will depend on the DMARD prescribed, but most require FBC (to monitor for marrow suppression) and LFTs (to look for raised transaminases as a sign of hepatotoxicity) approximately monthly.
- Cardiovascular risk factors should be assessed at least three times per year.

The RACGP Working Group recommends that GPs review Therapeutic Guidelines (www.tg.com.au) and the National Prescribing Service (www.nps.org.au) for detailed prescribing information, including ongoing monitoring requirements, toxicity and adverse effects.

Ongoing monitoring of RA patients is important in assessing progress against overall management goals. Treatment efficacy, including disease activity, comorbidities, ADL, and quality of life should be monitored just as seriously as the monitoring of toxicity and medication adverse effects.[21]

Monitoring requirements vary depending on disease severity, disease activity and the drug regimen used. The EULAR[19] (strength of recommendation A) and SIGN[9] guidelines provide recommendations relating to disease activity monitoring including tender and swollen joint count, patient and physician global assessments, ESR and CRP, as well as X-rays to monitor structural damage, and functional assessment. The GP has an ongoing role in monitoring for adverse events and toxicity associated with medication, which is discussed under relevant pharmacological management recommendations.

The BSR guideline[20] addresses the specific management/monitoring of cardiovascular risk for RA patients, and recommends that, in light of the fact that RA is an independent risk factor for ischaemic heart disease, patients should be screened for cardiovascular risk factors. These factors should be actively addressed by primary care services. The guideline recommends that lifestyle advice should be given to all RA patients to encourage smoking cessation, dietary modification, weight control and exercise. In addition, regular blood pressure monitoring and treatment of hypertension, diabetes screening and treatment, and screening and treatment of hyperlipidaemia is advised.

It is the opinion of the RACGP Working Group that GPs have an important role in ongoing monitoring of RA patients.

RESOURCES

A full detail of the evidence on which the guideline is based is presented in the companion documents *Recommendations for the diagnosis and management of early rheumatoid arthritis* (www.racgp.org.au/guidelines/rheumatoidarthritis/recommendations) and *Early rheumatoid arthritis: a literature review of recent evidence* (www.racgp.org.au/guidelines/rheumatoidarthritis/literaturereview).

The Process Report (*Appendix A*) outlines the full method used to develop these recommendations.

Appendix B contains additional resources, as well as contact details for organisations providing services and support to people with RA.

The RACGP Working Group recommends consulting the Therapeutic Guidelines (www.tg.com.au) and the National Prescribing Service (www.nps.org.au) for detailed prescribing information including:

- indications
- drug dosage
- method and route of administration
- contraindications
- supervision and monitoring
- product characteristics.

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APPENDIX A. PROCESS REPORT

This report outlines the process used for the development of the evidence based *Clinical guideline for the diagnosis and management of early rheumatoid arthritis*. The process consisted of the following major phases.

- Formation of a disease focused, multidisciplinary expert Working Group (see *Appendix C*)
- Development of a scoping document outlining the scope and objectives of the project, including the process to be used during guideline development
- Identification and appraisal of relevant existing clinical guidelines, leading to the selection of existing guidelines for use as the primary references
- Systematic literature searches to identify the most recent evidence
- Synthesis of new evidence and evidence from the primary reference guidelines into graded clinical recommendations and algorithms
- Peer review and appraisal through a public consultation process
- Response to feedback and completion of final guideline.

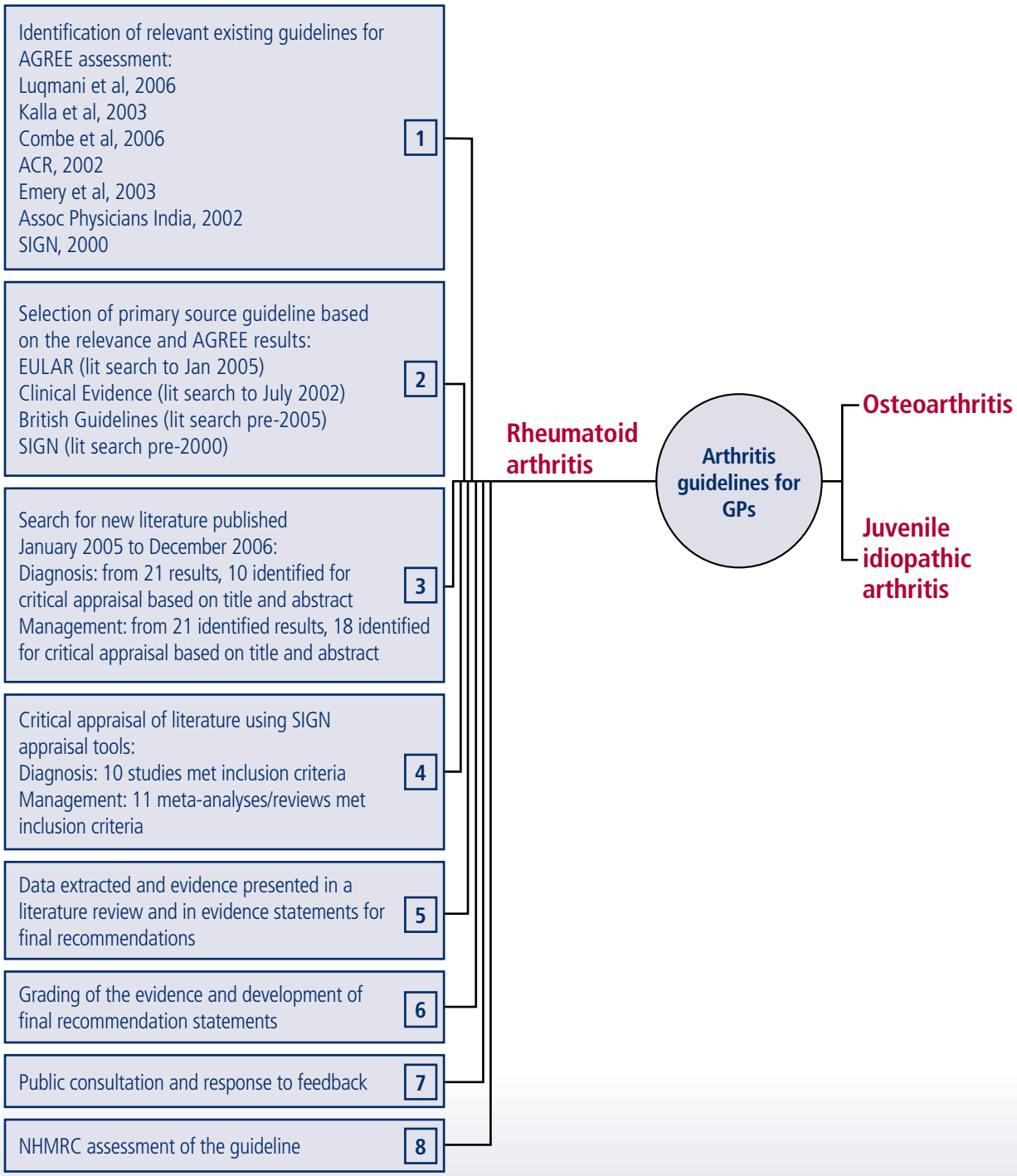

Figure 1. Process of guideline development

Identification of the guideline focus

A process model developed by The Royal Australian College of General Practitioners (RACGP) Steering Committee was used to identify the primary focus of the guideline (see *Background*). The RACGP Rheumatoid Arthritis Working Group reached consensus opinion on the primary focus of the guideline through discussion of the most important areas to cover for the primary audience (Australian GPs), with consideration to the feasibility of completing the guideline within the prescribed timeframe and budget. Clinical questions relevant to the scope of guideline were developed to focus the search for relevant literature.

Identification, appraisal and selection of existing clinical guidelines

Due to extensive research that has been published on RA and its management, it was not feasible for the Working Group to conduct appraisals and a review of all the relevant research within the time and budget constraints of this project. Because several guidelines were available on the management of RA, it was determined that the most feasible methodology would be to use appropriate existing guidelines as primary references and conduct literature searches limited to new research published after the selected primary guidelines.

Existing guidelines were identified through database searches and those known to the experts in the Working Group. Those considered to be the most relevant to the focus of this project were selected for broad appraisal of quality using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument.[1] Developers of the AGREE tool propose its use to assess '…the confidence that the potential biases of guideline development have been addressed adequately and that the recommendations are both internally and externally valid, and are feasible for practice'.[1]

The AGREE tool includes 21 questions organised into six quality domains:

- scope and purpose
- stakeholder involvement
- rigour of development
- clarity and presentation
- applicability
- editorial independence.

Reviewers score each question on a 4-point Likert scale (strongly agree, agree, disagree and strongly disagree). The scores from multiple reviewers are used to calculate an overall quality percentage for each domain.

Literature searches conducted in 2005 and 2006 by the Working Group identified a number of relevant existing guidelines. Seven identified guidelines were assessed by two independent reviewers using the AGREE tool. The following seven guidelines were assessed and the results are presented in *Table 1*:

- Scottish Intercollegiate Guidelines Network (SIGN). Management of early rheumatoid arthritis: A national clinical guideline. December 2000[2]
- Emery P, Suarez-Almazor M. Rheumatoid arthritis. Clinical Evidence 2003[3]
- Kalla AA, Stanwix A, Gotlieb D, et al. Rheumatoid arthritis: Clinical guideline. South African Med J 2003[4]
- Combe B, Landewé R, Lukas C, et al. European League Against Rheumatism (EULAR) recommendations for the management of early arthritis: Report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). 2006[5]
- Luqmani R, Hennell S, Estrach C, et al. British Society for Rheumatology (BSR) and British Health Professionals in Rheumatology. Guideline for the management of rheumatoid arthritis (the first 2 years). 2006[6]
- The Association of Physicians of India. Indian guidelines for the management of rheumatoid arthritis. 2002[7]
- American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis. 2002 update.[8]

Table 1. AGREE domain scores for identified guidelines

(Shaded guidelines were selected as primary sources)

Guideline	AGREE domain scores					
	Domain 1. Scope and purpose	Domain 2. Stakeholder involvement	Domain 3. Rigour of development	Domain 4. Clarity and presentation	Domain 5. Applicability	Domain 6. Editorial independence
SIGN, 2000	61%	58%	40%	75%	17%	8%
Clinical evidence, 2003	64%	8%	86%	58%	33%	66%
South African guidelines, 2003	44%	58%	24%	17%	0%	67%
Indian guidelines, 2002	11%	0%	4%	33%	0%	0%
ACR guidelines, 2002	8%	0%	4%	0%	22%	33%
EULAR, 2006	72%	25%	52%	71%	0%	0%
BSR, 2006	72%	67%	52%	75%	83%	92%

The following four international guidelines were selected as the primary sources of information for the RA guideline for the following reasons:

1. EULAR recommendations for the management of early arthritis.[5] This guideline was selected as a primary resource due to its high rigour of development and overall clarity.
2. BSR. Guideline for the management of rheumatoid arthritis (the first 2 years).[6] This guideline was elected because of its overall high scoring on the AGREE tool, and specifically for its strong GP focus, making this guideline particularly applicable to this project.
3. SIGN. Management of early rheumatoid arthritis.[2] This guideline was selected because of its high rigour of development, high scores, and overall clarity based on research published up to mid 2000.
4. Rheumatoid arthritis. Emery P, Suarez-Almazor M. Clinical evidence, 2003;(9):1349–71.[3] This guideline was selected as a primary source on medications as it provided a comprehensive review of the pharmacological management of RA based on research published up to 2002.

Identification, appraisal and synthesis of new evidence

Following the selection of existing guidelines, literature searches were conducted to identify new evidence published since the selected guidelines. The Working Group conducted extensive literature searches to identify the most recent available evidence under the guidance of experienced librarians, research consultants, and a National Health and Medical Research Council (NHMRC) consultant. The process used for the literature search is reported in more in detail in *Early rheumatoid arthritis: a literature review of recent evidence* (www.racgp.org.au/guidelines/rheumatoidarthritis/literaturereview).

Search strategy

The MEDLINE, EMBASE and CINAHL databases and the Cochrane Library (including CENTRAL Cochrane Controlled Trial Register) were searched to identify studies for inclusion. As this literature review intended to update previous guidelines, only papers published between January 2005 and December 2006 were included, and inclusion was limited to English language literature. Reference lists in review articles and trials were also retrieved. An additional manual search was used to identify evidence for interventions not represented in the initial search or not covered by the primary guidelines. Further grey literature was also identified through personal contact with the authors. In specific areas where randomised controlled trials (RCTs) or systematic reviews (SRs) were not available, lesser levels of evidence and expert opinion were sourced. The following search strategies were applied to the MEDLINE database and were adapted to apply to the other databases.

Search of evidence on diagnosis of RA

1. Arthritis, Rheumatoid/bl, cf, di, ra, ri, us [Blood, Synovial Fluid, Diagnosis, Radiography, Radionuclide Imaging, Ultrasonography] (13155)
2. Early Diagnosis/ or Diagnosis/ or Diagnosis, Differential/ (301051)
3. (sensitivity and specificity).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (202073)

4. sensitivity.tw. (302016)
5. specificity.tw. (198517)
6. ((pre test or pre-test) adj probability).tw. (157)
7. ((pre-test or pretest) adj probability).tw. (576)
8. predictive value$.tw. (12)
9. predictive value$.tw. (36002)
10. likelihood ratio$.tw. (3573)
11. 3 or 4 or 5 or 7 or 9 or 10 (545298)
12. 1 and 2 and 11 (111)
13. limit 12 to (humans and English language and yr='2005 - 2006') (21).

Search for evidence on management of RA

1. Arthritis, Rheumatoid/di, dh, pc, dt, ra, ri, rt, rh, su, th, us [Diagnosis, Diet Therapy, Prevention & Control, Drug Therapy, Radiography, Radionuclide Imaging, Radiotherapy, Rehabilitation, Surgery, Therapy,] (10573)
2. 'Practice Guideline [Publication Type]'/ (8111)
3. 'Review Literature'/ or Meta-Analysis/ (6343)
4. 'Guideline [Publication Type]'/ (9399)
5. 2 or 3 or 4 (16730)
6. 1 and 5 (60)
7. limit 6 to (humans and English language and yr='2005 - 2006') (24)
8. from 7 keep 1-18 (18).

Diagnosis inclusion/exclusion criteria

Types of studies

Only studies considered to be of NHMRC Level I–III evidence (*Table 3*) that evaluated diagnostic strategies for RA were considered for inclusion. Studies reported in SRs already selected for inclusion were not subjected to individual critical appraisal to prevent replication of data.

Types of participants

Studies that included individuals aged 16 years or over with disease duration of 2–5 years.

Management inclusion/exclusion criteria

Types of studies

Only studies considered being of NHMRC Level I evidence (*Table 2*) that evaluated the effectiveness and/or safety of pharmacological and non-pharmacological interventions for RA were considered for inclusion.

Types of participants

Studies that included individuals aged 16 years or over with a diagnosis of RA.

Table 2. NHMRC levels of evidence for intervention studies[9]

Level of evidence	Intervention studies	Diagnosis
I	Evidence obtained from a systematic review of all relevant randomised controlled trials	A systematic review of level II studies
II	Evidence obtained from at least one properly designed randomised controlled trial	A study of test accuracy with independent blinded comparison with a valid reference standard, among consecutive patients with a defined clinical presentation
III–I	Evidence obtained from well designed pseudo-randomised controlled trials (alternate allocation or some other method)	A study of test accuracy with independent blinded comparison with a valid reference standard, among non-consecutive patients with a defined clinical presentation
III–2	Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case control studies, or interrupted time series with a control group	A comparison with reference standard that does not meet the criteria for Level II or Level III–1 evidence
III–3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group	Diagnostic case control evidence
IV	Evidence obtained from case series, either post-test or pre-test and post-test	Study of diagnostic yield (no reference standard)

Critical appraisal

Critical appraisals were conducted for all studies that met the inclusion criteria, with the exception of Cochrane reviews, for which critical appraisal was not considered to be warranted (NHMRC advisor). One reviewer critically appraised all studies that met the inclusion criteria, with a second reviewer appraising 40% of the papers. There was a high level of consensus between reviewers, with minor discrepancies in SIGN scoring resolved by a third reviewer.

The following critical appraisal tools were used where appropriate by the appraisers:

- SIGN appraisal tool for SRs (www.sign.ac.uk/guidelines/fulltext/50/checklist1.html)
- SIGN appraisal tool for RCTs (www.sign.ac.uk/guidelines/fulltext/50/checklist2.html)
- NHMRC diagnostic study appraisal form (www.nhmrc.gov.au)
- Textual paper score designed for this project.

Studies were graded as being of good, moderate or low quality based on the results of appraisal using the SIGN tools. The appraisal tools and their use are described in detail in the methodology in *Early rheumatoid arthritis: a literature review of recent evidence* (www.racgp.org.au/guidelines/rheumatoidarthritis/literaturereview).

Data extraction

Data extraction tools and tables were used to systematically identify and extract evidence. The following data extraction tools were used where appropriate by the appraisers:

- SR data extraction form developed by the Joanna Briggs Institute (JBI) (available on request from JBI or NHMRC)
- NHMRC intervention data extraction form (www.nhmrc.gov.au)
- Textual paper data extraction form.

For diagnosis studies the primary and secondary reviewers used a tabulated format to extract the relevant data. On combining data from the two reviewers, no discrepancies were found. For intervention studies the primary reviewer used the JBI data extraction tool for SRs to extract data from the included studies in a systematic manner.[10] The second reviewer checked and tabulated the data and no discrepancies were found. *Early rheumatoid arthritis: a literature review of recent evidence* presents the new evidence from included studies in a descriptive and tabulated format.

Special populations

The search strategy was designed to retrieve all available evidence meeting the inclusion criteria for the literature review, including research specific to the identified special populations – Indigenous Australians (Aboriginal and Torres Strait Islanders), rural and remote communities, Muslim Australians, and Vietnamese Australians. The literature searches identified minimal to no evidence directly related to these populations, thus a broader search was conducted to identify any research that addressed management of arthritis in the special population groups.

The following search was conducted in MEDLINE, CINAHL, EMBASE and Cochrane Library to identify relevant information:

1. Aboriginal.mp. OR Aborigine.mp. OR koori.mp. OR indigenous.mp. OR torres strait.mp. OR Vietnam/ OR Vietnamese.mp. OR rural health centers/ OR Hospitals, Rural/ OR Rural Health/ OR Rural Health Services/ OR Rural Areas/ OR Rural Health Nursing/ OR muslim.mp. OR Islam/
2. Arthritis, Rheumatoid/ OR Arthritis/ OR Arthritis.mp
3. 2 and 3.

Ten papers were identified for retrieval – five papers related to Indigenous Australians, three papers related to rural health and two focused on Muslim populations. Nine papers were excluded as they did not directly relate to arthritis, or contained purely historical health information.

Development of the recommendations

Through group meetings, email circulation and feedback, the Working Group used the information from new evidence, together with recommendations from the primary source guidelines and expert opinion to develop recommendations relevant to general practice within Australia.

Evidence statements were developed that represented a summary of the most relevant research from the literature or, where there had been no newly published research, from the primary resource guidelines. The NHMRC body of evidence assessment matrix[9] (*Table 3*) was used to make an assessment of the volume and consistency of the literature on which the evidence statement was based. Additional assessments included clinical impact, generalisability, and applicability of the recommendation.

Each recommendation was given a final grading (*Table 4*) representing its overall strength. The gradings reflect implementability in terms of confidence practitioners can use in a clinical situation. The overall grade of each recommendation was reached through consensus and is based on a summation of the grading of individual components of the body of evidence assessment. In reaching an overall grade, recommendations did not receive a grading of A or B unless the volume and consistency of evidence components were both graded either A or B.

Where appropriate, recommendations are followed by good practice points. The good practice points are essential tips on how to effectively implement the recommendations.

Table 3. NHMRC body of evidence assessment matrix[9]

Component	A	B	C	D
	Excellent	Good	Satisfactory	Poor
Volume of evidence	Several Level I or Level II studies with low risk of bias	One or two Level II studies with low risk of bias or a SR/multiple Level III studies with low risk of bias	Level III studies with low risk of bias or Level II studies with moderate risk of bias	Level IV studies or Level I to III studies with high risk of bias
Consistency	All studies consistent	Most studies consistent, and inconsistencies may be explained	Some inconsistency reflecting genuine uncertainty around clinical question	Evidence is inconsistent
Clinical impact	Very large	Substantial	Moderate	Slight or restricted
Generalis-ability	Population(s) studied in body of evidence are the same as the target population for the guideline	Population(s) studied in the body of evidence are similar to the target population for the guideline	Population(s) studied in the body of evidence different to the target population for the guideline, but it is clinically sensible to apply this evidence to the target population (eg. results obtained in adults that are clinically sensible to apply to children)	Population(s) studied in the body of evidence different to the target population for the guideline and hard to judge whether it is sensible to generalise to the target population
Applicability	Directly applicable to Australian health care context	Applicable to Australian health care context with few caveats	Probably applicable to Australian health care context with some caveats	Not applicable to Australian health care context

Table 4. NHMRC grade of recommendations[9]

Grade	Description
A	Excellent evidence – body of evidence can be trusted to guide practice
B	Good evidence – body of evidence can be trusted to guide practice in most situations
C	Some evidence – body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Weak evidence – body of evidence is weak and recommendation must be applied with caution

Note: A recommendation cannot be graded A or B unless the volume and consistency of evidence components are both graded either A or B

Consultation phase

Draft versions of the *Clinical guideline for the diagnosis and management of early rheumatoid arthritis; Recommendations for the diagnosis and management of early rheumatoid arthritis;* and *Early rheumatoid arthritis: a literature review of recent evidence*, were presented for public feedback via the RACGP website. An interactive survey was designed to collect comments from all potential stakeholders. The public consultation period was advertised in a major national newspaper, information was sent to almost 20 000 GPs, and over 200 known stakeholders (eg. members of RACGP musculoskeletal groups, arthritis foundations, departments of general practice, consumer groups) were sent personal invitations to review the material. Feedback collected from the survey and independent submissions were collated and addressed by the Working Group.

The Working Group would like to thank respondents who provided feedback during the consultation phase of the project. The Working Group acknowledges the contribution of Dr Melainie Cameron, who provided

access to new evidence[11,12] relevant to this project via the consultation process.

Dissemination

Final versions following consultation of *Clinical guideline for the diagnosis and management of early rheumatoid arthritis; Recommendations for the diagnosis and management of early rheumatoid arthritis;* and *Rheumatoid arthritis: a literature review of recent evidence*, together with supporting resources, will be made available to Australian GPs and the public on the RACGP website.

The RACGP has submitted to the Australian Department of Health and Aging (DoHA) a detailed dissemination plan based on the NHMRC standards. The dissemination process is based upon four lines of deliberate action:

- specified target groups
- the most appropriate media
- resources allocated for the design, production and distribution of materials
- the design, production and distribution process managed as a project, with appropriate evaluation and feedback.

Process report references

1. AGREE Collaboration. Appraisal of guidelines for research and evaluation (AGREE) instrument, 2001. Available at www.agreecollaboration.org [Accessed November 2006].
2. SIGN. Management of early rheumatoid arthritis: A national clinical guideline. SIGN Publication No. 48, 2000.
3. Emery P, Suarez-Almazor M. Rheumatoid arthritis. Clinical Evidence 2003;10:1454–76.
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5. Combe B, Landewé R, Lukas C, et al. EULAR recommendations for the management of early arthritis: Report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Diseases 2007;66:34–45. (Preview published online 2006).
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10. Joanna Briggs Institute Data Extraction Tool. Available at www.joannabriggs.edu.au/isearch/index.php. [Accessed 2007].
11. Cameron M, Chrubasik S, Parsons T, et al. Herbal therapies for treating rheumatoid arthritis: Update of a Cochrane review (abstract). Ann Rheum Diseases 2007;66(Suppl II):602.
12. Cameron M, Chrubasik S, Parsons T, et al. Updating the evidence for herbal therapies in osteoarthritis and rheumatoid arthritis. In: 3rd International Congress on Complementary Medicine Research. Sydney, Australia, 2008.

APPENDIX B. RESOURCES

Useful publications

National Health and Medical Research Council. Making decisions about tests and treatments: Principles for better communication between healthcare consumers and healthcare professionals. Canberra: NHMRC, 2005.

National Prescribing Service Limited. Indicators of quality prescribing in Australian general practice. Sydney: NPS, 2006.

National Health and Medical Research Council. Dietary guidelines for Australian adults. Canberra: NHMRC, 2003.

Symmons DPM, Silman AJ. Aspects of early arthritis. What determines the evolution of early undifferentiated arthritis and rheumatoid arthritis? An update from the Norfolk Arthritis Register 2006;8(4):214.

van Dongen H, van Aken J, Lard LR, et al. Efficacy of methotrexate treatment in patients with probable rheumatoid arthritis: A double-blind, randomized, placebo-controlled trial. Arthritis Rheumatism 2007;56(5):1424–32.

The RACGP Working Group recommends consulting the Therapeutic Guidelines (www.tg.com.au), the Australian Rheumatology Association (www.rheumatology.org.au) and the National Prescribing Service (www.nps.org.au) for detailed prescribing information, including adverse effects.

Useful electronic sources

Organisation	Website
Australian Rheumatology Association	www.rheumatology.org.au
National Health and Medical Research Council	www.nhmrc.gov.au
National Prescribing Service	www.nps.org.au
The Royal Australian College of General Practitioners	www.racgp.org.au
Therapeutic Guidelines	www.tg.com.au
ARA patient medication information sheets	www.rheumatology.org.au/community/PatientMedicineInformation.asp#medicine

Patient services

Organisation	Website	Telephone
Arthritis Australia	www.arthritisaustralia.com.au	1800 111 101 toll free
Australian Association of Occupational Therapists	www.ausot.com.au	+61 3 9415 2900 National office
Australian Hand Therapy Association	www.ahta.com.au	+61 8 9578 3348 National office
Australian Physiotherapy Association	www.physiotherapy.asn.au	+61 3 9092 0888 National office
Australian Rheumatology Association	www.rheumatology.org.au	+61 2 9256 5458 National office
Carers Australia	www.carersaustralia.com.au	1800 242 636 toll free Call put through to local branch
Independent Living Centres Australia	www.ilcaustralia.org	See website or phone directory for state branch contacts
Sleep Disorders Australia	www.sleepoz.org.au	See website or phone directory for state branch contacts

Note: website addresses and details were accurate at the time of publication.

Note:
Refer to the Medicare Benefits Schedule items/ notes for details of fees and requirements

Check that no EPC item numbers have been claimed in the past 12 months

Chronic disease management Musculoskeletal flow chart

Preparation of patient goal setting

GP Management Plan (GPMP) MBS Item 721

Team Care Arrangements (TCA) MBS Item 723

Home Medication Review (HMR) MBS Item 900 and Residential Medication Management Review (RMMR)

Consider for HMR/RMMR if:

- currently taking five or more regular medications
- taking more than 12 doses of medication per day
- recently (past 4 weeks) admitted to medical facility/hospital
- significant changes to medication regimen in past 3 months
- on medication with narrow therapeutic index or requiring therapeutic monitoring
- have symptoms suggestive of an adverse drug reaction
- have a subtherapeutic response to medication treatment
- suspected noncompliance or not managing medication related therapeutic devices
- manage own medications and/or at risk due to language difficulties, dexterity problems, impaired sight, confusion dementia or other diagnosis
- resident in residential aged care facility (RACF)

Review of GPMP MBS Item 725

(within 3–6 months)

Review progress to date and agreed goals

Consider involvement of community health service providers

Review of TCA MBS Item 727

Ongoing reviews and reassessment of patient

Role of practice nurse and/or allied health professional

Assists with:

- assessment of patient and documentation
- identification of patient needs
- provision of self management information and other patient education or exercise (eg BHSM or 'Active Scripts')
- preparation of GPMP
- contacting services outlined in GPMP
- GP needs to confirm and assess with patient present
- review and reassessment of patient
- referral to community health or community rehabilitation programs
- inform patient of any expenses likely to be incurred as a result of involving other providers (note: patients eligible for Medicare rebates for up to five allied health consultations per year)
- facilitation of communication between GP and allied heath professional to discuss their contribution to the TCAs – the treatment and services they will provide
- provision of copy of TCA to allied health professional, with patient's agreement

APPENDIX C. MEMBERSHIP AND TERMS OF REFERENCE OF RHEUMATOID ARTHRITIS WORKING GROUP

Aim of the RACGP Rheumatoid Arthritis Working Group

The aim of the Working Group was to undertake activities required to fulfil the aims of the project as outlined in the funding agreement, including:

- carrying out a review of literature as per NHMRC requirements
- developing clinical practice guidelines based on the evidence obtained within the literature review.

Establishment of the Working Group

In accordance with the project contract, membership of the Working Group endeavoured to include:

- three or more experts in each field – medical (including one GP) and allied health
- one expert National Arthritis and Musculoskeletal Conditions Advisory Group member
- one consumer representative
- one departmental representative
- a consultant appointed by the NHMRC.

In addition, a nominee of the Australian Rheumatology Association or the Australian and New Zealand Bone and Mineral Society was represented in accordance with the project contract.

Acknowledgments

The Working Group would like to acknowledge the contributions and dedicated work of the late Associate Professor Peter Waxman and the late Emeritus Professor Fay Gale.

Membership of RACGP Rheumatoid Arthritis Working Group

Member	Representation	Qualifications
Associate Professor Lyn March (Chair) Rheumatologist	Australian Rheumatology Association, NSW	MBBS, MSc(EpidemiolBiostats), PhD, FAFPHM, FRACP
Dr Claire Barrett	Rheumatologist, Qld	BSc, MBBS, MRCP, FRACP
Emeritus Professor Fay Gale Consumer representative (deceased)	Consumers' Health Forum of Australia, SA	AO, BA(Hons), PhD, DUniv(Hons), DLitt, FASSA
Associate Professor Marissa Lassere	Rheumatologist, NSW	MBBS, GradDipEpiN'cle, PhD UNSW, FAFPHM, FRACP
Jean McQuade Manager, Health Education and Research programs, Arthritis and Osteoporosis	Registered nurse/health educator, WA	RN, RHV, DipGrad(HV/PH), BSc(HlthPromEduc), GradDipArts (Counselling)
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