

4 > Rheumatoid arthritis

KEY POINTS

- Rheumatoid arthritis is a chronic, inflammatory disease that can cause significant morbidity, joint damage, early disability and premature mortality. It is the most common autoimmune disease in Australia.
- Almost 438,000 Australians are reported to have rheumatoid arthritis. These self-report based estimates are much higher than those reported from other parts of the world.
- Rheumatoid arthritis occurs more commonly among females than males; its prevalence increases with age, a feature common to many chronic diseases.
- Disability associated with rheumatoid arthritis starts early in life and can be highly insidious. Over time, it can seriously compromise the individual's quality of life.
- Effective treatment can reduce the individual and societal costs of rheumatoid arthritis. Early diagnosis is central to the current treatment paradigm.
- Rheumatoid arthritis has low survival rates. It is not, however, a major underlying cause of death.

Rheumatoid arthritis is an autoimmune, systemic chronic disease that involves inflammation of multiple joints. More common among females than males, it is a major cause of morbidity and disability, resulting in substantial activity limitation and ongoing need for care and assistance. More often it affects the small and large joints in a symmetrical pattern; however, the disease also affects other organs of the body, including the heart, lungs and eyes.

More than 1% of the disease burden in Australia is accounted for by rheumatoid arthritis alone (AIHW: Mathers et al. 1999). Most of this burden is disability, although the disease also contributes to premature mortality (Pincus 1995). Recent advances have made rheumatoid arthritis more amenable to treatment (Goldbach-Mansky & Lipsky 2003). The disabling impact of rheumatoid arthritis on an individual can be reduced through early diagnosis and treatment.

In view of its high individual and societal costs (see Chapter 7 for health system costs) and the potential for these to be reduced by effective management, rheumatoid arthritis has been chosen for focused attention under the National Health Priority Areas Initiative for Arthritis and Musculoskeletal Conditions (NAMSCAG 2004).

This chapter describes the health impact of rheumatoid arthritis in terms of:

- incidence and prevalence
- disability
- health care service use, and
- mortality.

The nature of the problem and risk factors for the disease are also reviewed.

Nature of the problem

Rheumatoid arthritis is an autoimmune disease. In autoimmune diseases, the immune system fails to distinguish 'self' from 'non-self', targeting cells, tissues and various organs of the afflicted person's body.

In rheumatoid arthritis, the immune system mainly targets the synovial membrane. The pathological changes in the membrane result in inflammation that causes pain, swelling and stiffness of the joints. The disease causes progressive and irreversible joint damage, ultimately leading to cartilage destruction and deformity. The lungs, blood vessels or eyes may also be targeted.

The clinical manifestations and course of rheumatoid arthritis are extremely variable, characterised by exacerbations and remissions. The joint symptoms commonly include morning stiffness in and around the affected joints, pain on motion, local soft tissue swelling, warmth and redness. The joint involvement is often polyarticular, affecting three or more joints simultaneously. It also tends to be symmetrical.

Those with rheumatoid arthritis, or their children, are more likely to develop other autoimmune diseases, such as Type 1 diabetes and thyroid disease. Other diseases associated with rheumatoid arthritis include respiratory and infectious diseases, gastrointestinal disorders, and non-Hodgkin's lymphoma (Scott & Hochberg 1998). It is also the most common cause of secondary amyloidosis, in which deposits of a waxy, starch-like protein (amyloid) can decrease the function of tissues, including those in the heart and brain (Wollheim 1993).

Diagnosis

There is no one test for diagnosing rheumatoid arthritis. The diagnosis rests on a composite of clinical and laboratory observations. The American College of Rheumatology (ACR) has developed a set of criteria for diagnosing the disease (WHO Scientific Group 2003). At least four out of seven signs and symptoms, listed in Box 4.1, are required for a firm diagnosis.

Box 4.1: The 1987 revised ACR criteria for the classification of rheumatoid arthritis		
No.	Criterion	Comment
1	Morning stiffness	Duration > 1 hour; lasting > 6 weeks
2	Arthritis of at least 3 areas ¹	Soft tissue swelling or exudation lasting > 6 weeks
3	Arthritis of hand joints	Wrist, metacarpophalangeal joints or proximal interphalangeal joints lasting > 6 weeks
4	Symmetrical arthritis	At least one area, lasting > 6 weeks
5	Rheumatoid nodules	As observed by a physician
6	Serum rheumatoid factor	As assessed by a method positive in less than 5% of control subjects
7	Radiographic changes	As seen on anteroposterior films of wrists and hands

Source: WHO Scientific Group 2003.

Rheumatoid arthritis can be difficult to diagnose in its early stages, as symptoms vary considerably. The full range of symptoms develops over time (Sarau et al. 2001). Besides, some of the initial symptoms of the disease overlap with other types of arthritis and joint conditions, and it may take some time for those conditions to be ruled out.

Prognosis

Rheumatoid arthritis is extremely heterogenous in its rate of progression. But permanent remission is rare once the joint damage has set in. Radiographic evidence of joint destruction is present in over 70% of cases within the first two years of presentation and it continuously progresses over time (Goldbach-Mansky & Lipsky 2003). Functional deterioration occurs in most persons within 15 years (Rasker & Cosh 1989).

With persistent inflammation, a variety of characteristic deformities develop. This happens particularly in the hands and wrist, and in the feet. Deformities of the feet include eversion (a turning outwards) of the heel, widening of the forefoot (hallux valgus, a swelling or deformity at the head of the first metatarsal of the big toe), and lateral deviation and dislocation of the toes (Nuki 1998).

Causal and risk factors

The autoimmune nature of rheumatoid arthritis is best explained as the unleashing of genetic susceptibility by environmental agents. Both genetic and environmental factors are thus causal to its development. Defects in several biological intermediates, in particular those belonging to the immune system, are also implicated.

1 Possible areas: proximal interphalangeal joints, metacarpophalangeal joints, wrist, elbow, knee, ankle, metatarsophalangeal joints.

Several risk factors are identified, based mostly on causal mechanisms. These include, in particular, family members with rheumatoid arthritis, immunogenetic susceptibility, female sex and environmental factors.

Genetic factors

Family studies indicate the high inheritability of rheumatoid arthritis. Severe rheumatoid arthritis is found at approximately four times the expected rate in first-degree relatives of persons with the disease. Approximately 10% of persons with rheumatoid arthritis have an affected first-degree relative (Silman & Hochberg 2001). The disease also exhibits a higher concordance rate in identical twins than in fraternal twins (MacGregor et al. 1995).

HLA associations

An immunogenetic perspective to rheumatoid arthritis is provided by its strong association with Class II HLA (human leucocyte antigens) alleles. These genes are located within the major histocompatibility complex (MHC), on the short arm of chromosome 6 in man. The MHC houses several immune response genes, one or more of which may mediate autoimmune response in rheumatoid arthritis.

Individuals with HLA DRB1 alleles *0101, *0401, *0404 and *0405 have a much greater relative risk of developing rheumatoid arthritis (Weyand & Gronzy 2000). More than 90% of people with rheumatoid arthritis have these alleles, compared with about 35% in the general population. The risk ratio for some of these alleles exceeds 6.0.

The role of HLA DRB1 in the pathology of rheumatoid arthritis is unclear. It has been proposed that certain epitopes of HLA DRB1 may affect the function of HLA DQ molecules, which actually mediate autoimmunity. Genes for HLA DQ are also located within the MHC complex, adjacent to the HLA DR genes (Taneja & David 2000).

Other genes

HLA DRB1 associations do not fully explain the genetics of rheumatoid arthritis. Associations with other genes, located outside the MHC, have also been reported.

Gender (hormonal factors)

Rheumatoid arthritis is more common among females than males. This may be due to the role of female sex hormones, particularly in the peri-menopausal period (Kuiper et al. 2001). Androgen deficiency and prolactin excess may also, at least in part, explain the higher incidence of rheumatoid arthritis in females (Brennan & Silman 1995). Pregnancy also influences the timing of the disease, with the postpartum period being a high risk time for developing first symptoms (Silman et al. 1992).

In addition to the above-mentioned genetic, environmental and biochemical factors, several societal factors such as socioeconomic status, education and psychosocial wellbeing may play important roles in the development of rheumatoid arthritis (Callahan & Pincus 1988; Symmons 2003).

Environmental factors

The presence of high-risk genes is not sufficient to develop rheumatoid arthritis. A variety of environmental factors are considered to expose this susceptibility. Something must occur to trigger the onset of the disease. It may be an infectious agent such as a virus or bacteria. But the disease is not transmissible from person to person by contact.

Rheumatoid arthritis is less common in underdeveloped countries and rural areas (Symmons 2002), although the differences between rural and non-rural areas are small.

Incidence and prevalence

Incidence

Considering the difficulties involved in establishing early diagnosis, only a few studies have tried to estimate the incidence of rheumatoid arthritis. According to the WHO Scientific Group (2003), its global incidence ranges from 0.2 to 3 cases per 1,000 persons. Other studies also indicate highly variable incidence (0.1 to 1.2 per 1,000 persons), depending on sex, race/ethnicity and calendar year (Gabriel 2001). The incidence is reportedly higher in females than males (Silman & Hochberg 2001).

The Australian Burden of Disease Study, using DISMOD software, has estimated the incidence of rheumatoid arthritis in Australia to be 0.3 per 1,000 females and 0.1 per 1,000 males (AIHW: Mathers et al. 1999).

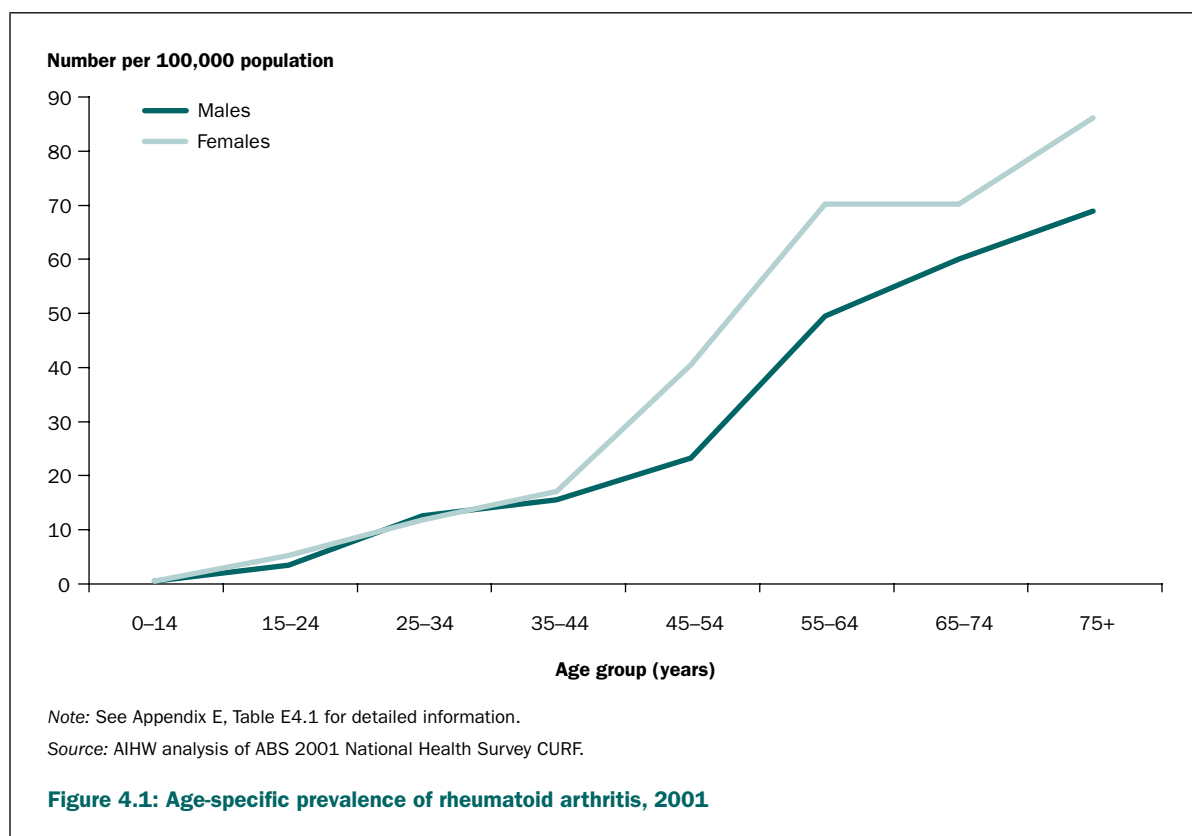
The incidence of rheumatoid arthritis may be declining, particularly among females (Gabriel 2001; MacGregor & Silman 2003). One explanation is the use of oral contraceptives; both pregnancy and the contraceptive pill are believed to protect against the development of the disease (Spector 1990).

Prevalence

Determining the prevalence of rheumatoid arthritis is equally problematic. A commonly used method is self-reports. However, the information so generated is not usually backed by clinical or laboratory evidence. The ACR criteria notwithstanding, diagnoses based on clinical features, radiological evidence and serological tests are also quite variable.

Almost 24 out of 1,000 Australians are estimated to have rheumatoid arthritis long term (ABS 2002). This translates to approximately 438,000 persons with the disease. The disease was reported more commonly by females (27 per 1,000 compared with 20 per 1,000 males).

The prevalence of rheumatoid arthritis rises sharply with age, with the female prevalence rate being greater at nearly all ages (Figure 4.1). The steep rise in its prevalence after the age of 45, particularly for females, is noteworthy.



Other studies

A 1995 sample survey of the South Australian population shows the prevalence of rheumatoid arthritis to be 32 per 1,000 males and 49 per 1,000 females among those aged 15 and over (Hill et al. 1999). These estimates are much higher than those reported commonly.

A characteristic feature of this study was the contrast in prevalence by country of birth. People of Asian origin reported virtually no rheumatoid arthritis compared with those born in Australia, United Kingdom, and other parts of Europe. This variation is in line with that noted from other studies worldwide (see the section on international comparisons on page 48).

Validity of self-reports

The validity of self-reported prevalence of rheumatoid arthritis has been questioned. Data obtained from clinical examination and diagnosis, as well as radiological evidence, suggest much lower prevalence than that obtained using self-reports.

Two validation studies from the United States and Norway were able to confirm the diagnosis in only 21% and 31% of the sub-sample, respectively (Star et al. 1996; Kvien et al. 1996). If those validations apply to the NHS sample, then the prevalence of rheumatoid arthritis in Australia is more likely to be between six and ten per 1,000 persons, in line with estimates obtained elsewhere through clinical diagnosis.

The prevalence of rheumatoid arthritis in United States is five per 1,000 males and ten per 1,000 females on the basis of clinical examination and diagnosis (Cunningham & Kelsey 1984). The radiological evidence, coupled with the presence of rheumatoid-factor, increases these estimates to seven per 1,000 males and sixteen per 1,000 females.

Using serology (rheumatoid factor) alone, the prevalence of rheumatoid arthritis in Michigan has been estimated to be three per 1,000 males and seven per 1,000 females (Mikkelsen et al. 1967).

Time trends

The prevalence of rheumatoid arthritis in Australia reportedly declined between 1995 and 2001. The overall prevalence, based on National Health Surveys, declined from 28 per 1,000 to 24 per 1,000 between 1995 and 2001. (The 1989–90 NHS did not distinguish between various forms of arthritis.) Not much can be made of time trends in the prevalence of rheumatoid arthritis on the basis of just two data points.

International comparisons

Rheumatoid arthritis shows some geographical variation (WHO Scientific Group 2003). Its prevalence is higher in the northern hemisphere, but contrasts strongly in the European and Asian populations.

Studies in several European and North American populations have reported the occurrence of rheumatoid arthritis as being between 0.5 and 1% (Silman & Pearson 2002). Its prevalence in India is similar to that reported by European countries, but higher than that reported by China, Indonesia and the Philippines.

The much higher prevalence of rheumatoid arthritis in Australia (compared with reported occurrence in European countries and North American populations) reflects mostly the use of disparate estimation procedures. The Australian estimates are based on self-reports; the validity of these reports in ascertaining rheumatoid arthritis prevalence is doubtful.

Disability and psychosocial impact

Rheumatoid arthritis is a highly disabling condition, with a major psychosocial impact. The functional limitations arrive soon after the onset of the disease and worsen with the passage of time. Loss of independence is the most important aspect (Young et al. 2000). Another important outcome is work disability—the inability to continue working, to work in the same occupation or to work the same number of hours (Barrett et al. 2000).

Functional limitations

Recent evidence suggests that more than 50% of people with rheumatoid arthritis are unable to perform household chores, and that the majority (60%) receive unpaid help (Maetzel et al. 2004). The impact of disability appears to be greater in younger and middle aged people than in the elderly (Sokka et al. 2003).

Although much can be accomplished in the treatment of rheumatoid arthritis through a combination of non-steroidal anti-inflammatory (NSAIDs) and disease-modifying anti-rheumatic drugs (DMARDs), the overall impact of the disease on functional limitations tends to be progressive, that is, worsens with time.

Work disability

Using a large series of clinical, laboratory and self-report measures, Wolfe and Hawley (1998) have estimated work disability in people with rheumatoid arthritis as being 25% six years after the onset of the disease and as 50% twenty-one years after disease onset. The most disability occurs late in the course of the disease.

Factors associated with work disability commonly are the nature of the job (the level of physical activity required and the degree of autonomy, particularly over the pace of work), the age at onset of the disease, marital status, level of formal education, duration of the disease and the level of disability.

National information on work disability in relation to rheumatoid arthritis is not available in Australia. The SDAC provides information on disability associated with arthritis and related disorders, but it does not distinguish between different forms of arthritis. Chapter 6 provides further information on work disability in relation to arthritis as a whole.

Psychosocial impact

Psychosocial changes are one of the significant adverse impacts of rheumatoid arthritis. The loss of positive body image is a serious problem for many. Meenan et al. (1981) found that 63% had experienced at least one major change in their life (marital status, employment) as a result of their disease. Of those surveyed, 83% of people between the ages of 21 and 65 had to make significant changes in their leisure activities.

Treatment and health service use

Rheumatoid arthritis is difficult to treat systematically. Although current treatments have been relatively successful in controlling the symptoms of chronic synovitis, true long-term remission in aggressive rheumatoid arthritis has not been achieved (WHO Scientific Group 2003). The complexities involved in treating the disease are outlined by Fries (2000).

The goal of treatment for rheumatoid arthritis is preventing or controlling joint damage, reducing functional loss, alleviating pain and maximising quality of life (ACR 2002). Since joint damage, loss of bone mass and disability occur quickly in the course of the disease, it is important to diagnose it early and treat it aggressively.

The disease is managed in a variety of settings, which include primary care by general practitioners (GPs); other allied health services such as physiotherapists, chiropractors and podiatrists; as well as treatment in hospital settings. A variety of procedures, including arthroplasty, is integral to the treatment and management of rheumatoid arthritis.

General practice visits

In 2003–04, rheumatoid arthritis accounted for 0.3% of all problems managed by GPs, as reported to the BEACH survey. One reason for this low consultation rate is that patients with rheumatoid arthritis are generally referred to rheumatology clinics after only a short duration of symptoms. Rheumatologists are more likely to make a timely and correct diagnosis of rheumatoid arthritis compared with GPs (Bellamy et al. 1988).

A variety of modalities is used by GPs to manage rheumatoid arthritis (Figure 4.2). The most common of these (in 92% of the cases) is medication—prescribed, advised or supplied.

Commonly prescribed medications for rheumatoid arthritis are disease-modifying anti-rheumatic drugs (DMARDs), non-steroidal anti-inflammatory drugs (NSAIDs) and low-dose corticosteroids. The medications prescribed by GPs for rheumatoid arthritis in 2003–04 are listed in Table 4.1.

The DMARD methotrexate—reported to be the best tolerated slow-acting anti-rheumatic in the medium term (Conaghan & Brooks 1996)—was the most commonly prescribed medication in 2003–04. Several other DMARDs were also prescribed. Many randomised controlled trials have shown that DMARDs influence the disease process and retard radiological destruction, at least in the short term (Mottonen et al. 1999).

The most common GP referral was to a rheumatologist (7%), followed by that to an orthopaedic surgeon. The most common pathology tests were for full blood counts (19%), erythrocyte sedimentation rate (14%) and liver function (11%).

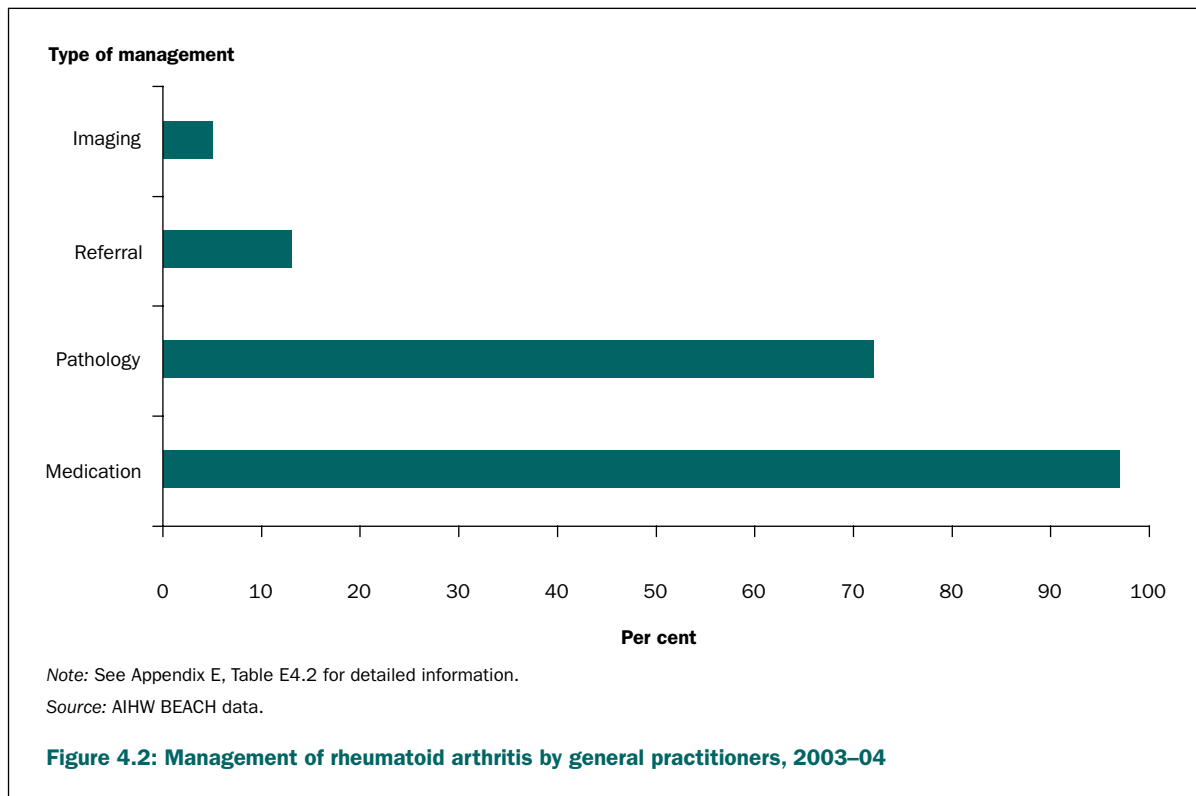


Table 4.1: Commonly prescribed medications for rheumatoid arthritis by general practitioners, 2003–04

Medication	Number of prescriptions	Per cent
Methotrexate	93	19.2
Prednisolone	53	10.9
Celecoxib	36	7.4
Paracetamol/codeine	30	6.1
Paracetamol	30	6.1
Sodium aurothiomalate	25	5.2
Rofecoxib	23	4.7
Tramadol	20	4.1
Other medications	175	36.1
Total	485	100.0

Source: AIHW BEACH data.

Hospitalisation

Much of the consultation for rheumatoid arthritis occurs in specialist clinics and as outpatient care. A large proportion of hospital separations in relation to rheumatoid arthritis is for procedures. Most of these are to restore a degree of functional capacity, effectively relieve pain and improve function (Saito 2002). The surgical treatment is for both joint protective surgery and joint reconstruction.

- Joint protective surgery inhibits rapid progression of joint destruction by removing the bulk of synovial tissue. It may be effective if performed early when articular cartilage and bone are minimally damaged (Shimizu & Yamamuro 1992).
- Joint reconstructive surgery compensates for functional deficit in an extremity by arthroplasty (both endoprostheses and arthrodeses) to improve the person's independence.

In 2003–04, a total of 3,762 surgical procedures were performed on people with the principal diagnosis of rheumatoid arthritis (Table 4.2). Of the 10 most frequently reported surgical procedures performed, arthroplasty was the most common, followed by arthrodesis.

Table 4.2: Top ten surgical procedures performed on people with rheumatoid arthritis, 2003–04

Procedure block	Principal procedure	Number of separations	Per cent ^(a)
Arthroplasty of knee	Total arthroplasty of knee, unilateral	401	10.7
Arthroplasty of hip	Total arthroplasty of hip, unilateral	176	4.7
Arthrodesis of ankle, foot or toe	Arthrodesis of first metatarsophalangeal joint	141	3.7
Excision procedures on other musculoskeletal sites	Excision of lesion of soft tissue, not elsewhere classified	129	3.4
Synovectomy of tendon of hand or wrist	Synovectomy of flexor or extensor tendon of hand	86	2.3
Arthroscopic excision of knee	Arthroscopic synovectomy of knee	74	2.0
Excision of bone of foot	Ostectomy of metatarsal bone	74	2.0
Arthrodesis of hand	Arthrodesis of interphalangeal joint of hand	63	1.7
Excision procedures on joints of other musculoskeletal sites	Excision of lesion of joint, not elsewhere classified	62	1.6
Repair of tendon of hand	Transfer of tendon of hand	59	1.6
Other procedures		2,497	66.4
Total		3,762	100.0

(a) Per cent of total procedures performed.

Source: AIHW National Hospital Morbidity Database.

Non-surgical procedures

In 2003–04, 10,496 non-surgical procedures were listed for people with the principal diagnosis of rheumatoid arthritis. These procedures, mainly non-invasive in nature, included cognitive, therapeutic or diagnostic interventions. The most common form was allied health intervention, mainly physiotherapy.

Visits to other/allied health professionals

Allied health services are an integral component of the management of rheumatoid arthritis. According to the 2001 NHS, about 26% of people with rheumatoid arthritis had consulted an allied or other health professional within the previous two weeks of the survey. The professionals most frequently consulted were chemists (6%), physiotherapists/ hydrotherapists, chiropodists/podiatrists, chiropractors and nurses, all accounting for around 3% of the consultations.

Recent studies also suggest the use of complementary medicine (Buchbinder et al. 2002) and occupational therapy (Steultjens et al. 2004) by persons with rheumatoid arthritis. The most commonly used complementary treatments were dietary and behavioural/cognitive therapies, homeopathy, aromatherapy, reflexology, massage and use of a copper bracelet. Occupational therapy was found to have a positive effect on the functional ability of some persons.

Mortality

Rheumatoid arthritis and its treatment significantly increase the risk for premature mortality. The survival rate for persons with rheumatoid arthritis is estimated to be lower than for those without the disease. Wolfe et al. (1994) estimated the death rate ratio for rheumatoid arthritis to be between 1.98 and 3.08.

The disease is not commonly the underlying cause of death. Most of the increased mortality is through its contribution to other causes of death. Wolfe et al. (1994) noted a specifically greater mortality due to infection, lymphoproliferative malignancy and digestive disorders. In 2003, rheumatoid arthritis was listed as the underlying cause in 184 deaths. It was listed as an associated cause of death in 632 cases (Table 4.3).

Table 4.3: Rheumatoid arthritis as an associated cause of death, 2003

Underlying cause of death	Number of deaths	Per cent
Cardiovascular disease	280	44.3
Cancer	116	18.3
Respiratory disease	69	10.9
Digestive disorder	26	4.1
Other causes	141	22.3
Total	632	100.0

Source: AIHW National Mortality Database.

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