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The use of disease-modifying anti-rheumatic drugs for the management of rheumatoid arthritis

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Summary

Two different types of disease-modifying anti-rheumatic drugs (DMARDs) are used for the management of rheumatoid arthritis. These are referred to as conventional DMARDs and biologic DMARDs (bDMARDs). Since the introduction of bDMARDs in 2003, the government subsidy for DMARDs has increased markedly. This report examines the supply of, and increasing subsidy for, DMARDs through the Pharmaceutical Benefits Scheme (PBS) over a 5-year period, from 2003 to 2007.

What was the financial cost of DMARD treatment through the PBS?

- DMARDs supplied through the PBS cost $472 million over the 2003 to 2007 period. The annual cost increased three fold to $134 million over this time.
- Almost 84% of the expense for conventional DMARDs was paid for by the Australian Government under the PBS during the 5-year period. However, the proportion of the cost met by the patient increased from 13% in 2003 to 20% in 2007.
- During the 5-year period, bDMARD treatment cost $243 million; more than one-half of the total cost for all DMARDs. bDMARDs accounted for only 4% of DMARD prescription volume.

What DMARDs were supplied?

- More than 3.4 million DMARD prescriptions were subsidised by the PBS for the treatment of rheumatoid arthritis from 2003 to 2007.
- Conventional DMARDs accounted for 96% of all DMARDs supplied through the PBS, with bDMARDs accounting for the remaining 4%.

Who was supplied with DMARDs?

- Approximately 236,000 Australians were supplied with at least one conventional DMARD through the PBS during the 5-year period. Only 7,298 Australians received bDMARDs.
- Patients in the 55–64 years age group were the largest group of people receiving DMARDs.
- Almost two-thirds of those who received conventional DMARDs were females; a similar but slightly higher proportion of those who received bDMARDs were females.

Who were the DMARD prescribers?

- Almost three quarters of conventional DMARD scripts were written by general practitioners (GPs) and other primary care medical practitioners (OMPs).
- Only rheumatologists and clinical immunologists are authorised to prescribe bDMARDs.

Does starting treatment with bDMARDs change the supply of conventional DMARDs?

- Nine out of 10 people were supplied conventional DMARDs for the management of their rheumatoid arthritis in the 12 months prior to starting bDMARD treatment. The proportion reduced to three out of four people in the year following the start of bDMARDs.
- Supply of all conventional DMARDs, except methotrexate, decreased after the initiation of bDMARD treatment.

1 Introduction

The treatment of rheumatoid arthritis has changed considerably over the last two decades. This change came in light of findings that serious joint destruction takes place within the first year of disease onset. Early diagnosis and appropriate treatment is now recommended, preferably even before any damage is identified, to slow down the disease progression and alter the course of the disease (RACGP 2009).

Traditional treatment of rheumatoid arthritis, in its early phases, involved the use of paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) and other symptom-modifying drugs. In contrast, the current standard is to introduce disease-modifying anti-rheumatic drugs (DMARDs) early to achieve sustained improvement in physical function, decrease inflammatory synovitis, and minimise or prevent structural joint damage (Schuna 2009).

The optimal use of DMARDs, particularly the biologic DMARDs (bDMARDs), has dramatically enhanced the success of rheumatoid arthritis management in the recent years (Aletaha et al. 2010). Clinical adoption and the high cost of bDMARDs have, however, led to a marked increase in the cost of managing rheumatoid arthritis in many countries. In Australia, the cost of DMARDs for managing rheumatoid arthritis supplied through the Pharmaceutical Benefits Scheme (PBS) tripled in 5 years to $472 million in 2007–08.

Using the PBS data, this report provides an overview of the supply pattern of, and the PBS subsidy for, DMARDs used to manage rheumatoid arthritis. The report focuses on trends in the supply of DMARDs across population groups, changes in the supply patterns of DMARDs and increase in the PBS subsidy for these medications.

What is rheumatoid arthritis?

Rheumatoid arthritis is an inflammatory, autoimmune disease (Box 1.1) that affects the joint lining or synovium (Rheumatology Expert Group 2006). It affects multiple joints, and is the source of much pain, morbidity, disability and deformity and, eventually, premature mortality. The disease is systemic in nature in that it also involves various organs.

Box 1.1: The autoimmunity of rheumatoid arthritis

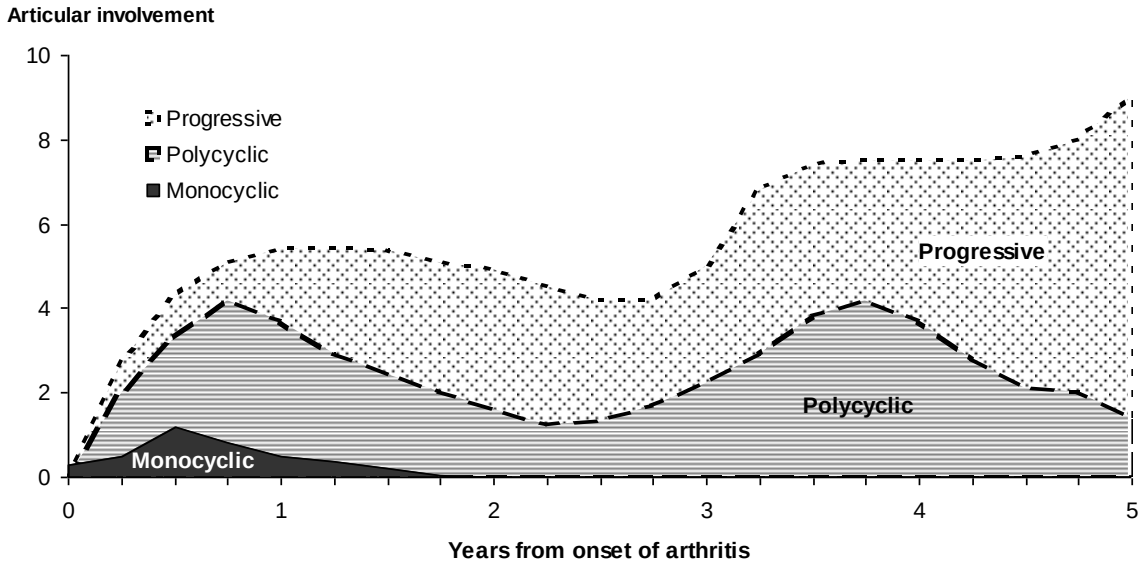
In autoimmune diseases such as rheumatoid arthritis, the body's tissues are attacked by its own immune system. Although not completely heritable, rheumatoid arthritis is said to have a strong genetic basis. Of the number of suspected genes implicated in rheumatoid arthritis, the associations with the human leukocyte antigen (HLA) genes are the best understood. HLA genes are located within the major histocompatibility complex on the short arm of chromosome 6 in humans. Several other genes that confer susceptibility for other autoimmune diseases have been named and are currently under investigation (Turesson & Matteson 2006). The exact role these genes play in the development and progression of rheumatoid arthritis is yet to be identified.

There is also a large environmental component to the development of rheumatoid arthritis. Infectious agents such as bacteria or viruses as well as cigarette smoking may trigger development of the disease in people with genetic propensity for autoimmunity. Gender-specific factors (almost two-thirds of Australians with rheumatoid arthritis are females) and the body's response to stressful events such as physical or emotional trauma may also contribute to its development.

Although tissues throughout the body are affected because of the systemic nature of the disease, the synovium bears the brunt of rheumatoid arthritis. (Synovium is the capsule around movable joints, filled with a lubricating fluid secreted by the surrounding synovial membranes.) The process that involves inflammation and thickening of the synovial membrane is called synovitis. Persistent inflammation causes tissue destruction, erodes cartilage and may rupture tendon fibres. Secondary osteoarthritis may be present in the end stages of rheumatoid arthritis.

Rheumatoid arthritis progresses rapidly. Within the first few months of its onset, a person can develop irreversible joint damage and deformities. The disease takes a variable and unpredictable course, but three basic courses (monocyclic, polycyclic and progressive) have been identified (Hadler & Gillings 1985), as illustrated in Figure 1.1.

Kaplan (2006) noted that people who follow a monocyclic course experience complete and permanent remission within 2 years of a disease onset. The polycyclic course is said to be the most common course, characterised by slow progression punctuated by flare-ups and remissions. Flare-up periods of the polycyclic course tend to become longer over time. The progressive course is the most aggressive course of rheumatoid arthritis. It is a constant and destructive form of the disease which causes deformity, disfigurement, and even death.



Note: Adapted from Hadler & Gillings (1985).

Figure 1.1: A diagrammatic representation of disease activity patterns in rheumatoid arthritis

Classification criteria for rheumatoid arthritis

The 1987 American College of Rheumatology classification criteria for rheumatoid arthritis has been in widespread international use for over 20 years. These criteria, however, describe the symptoms of fully developed late-stage rheumatoid arthritis, and are not sensitive to early phases of the disease. To overcome this shortcoming, revised criteria were published in 2010.

The new criteria focus on the features of earlier stages of the disease that are associated with persistent and/or erosive disease (Aletaha et al. 2010). The following presentations are taken into account in the new criteria:

- confirmed presence of synovitis in one or more joints
- absence of an alternative diagnosis that would better explain the synovitis
- number and sites of affected joints
- presence of antibodies in the blood (rheumatoid factor and/or anticitrullinated protein antibody)
- presence of acute inflammation or infection (abnormal C-reactive protein and/or erythrocyte sedimentation rate)
- duration of symptoms (6 weeks or more).

What are DMARDs?

Disease-modifying anti-rheumatic drugs (DMARDs) are a group of anti-inflammatory and immune-suppressing agents that are predominantly used to treat rheumatoid arthritis. The use of DMARDs is not entirely exclusive to rheumatoid arthritis as these may also be used to

treat other autoimmune diseases (e.g. systemic lupus erythematosus (SLE), Crohn's disease, psoriatic arthritis and Sjogren's syndrome). These agents have the potential to slow down the underlying disease process as well as reduce joint damage by minimising inflammation (van Gestel et al. 1997).

DMARDs include antimalarial drugs, anti-inflammatory metals, immunosuppressants, sulpha drugs and biologic agents (Lavelle et al. 2007). Two major types are recognised, conventional DMARDs and biologic DMARDs (bDMARDs or biologics). The term 'conventional DMARD' is reserved for small molecular drugs synthesised chemically that have broad effects upon the immune system. bDMARDs are produced by recombinant DNA technology, generally target cytokines or their receptors, or are directed against other cell surface molecules.

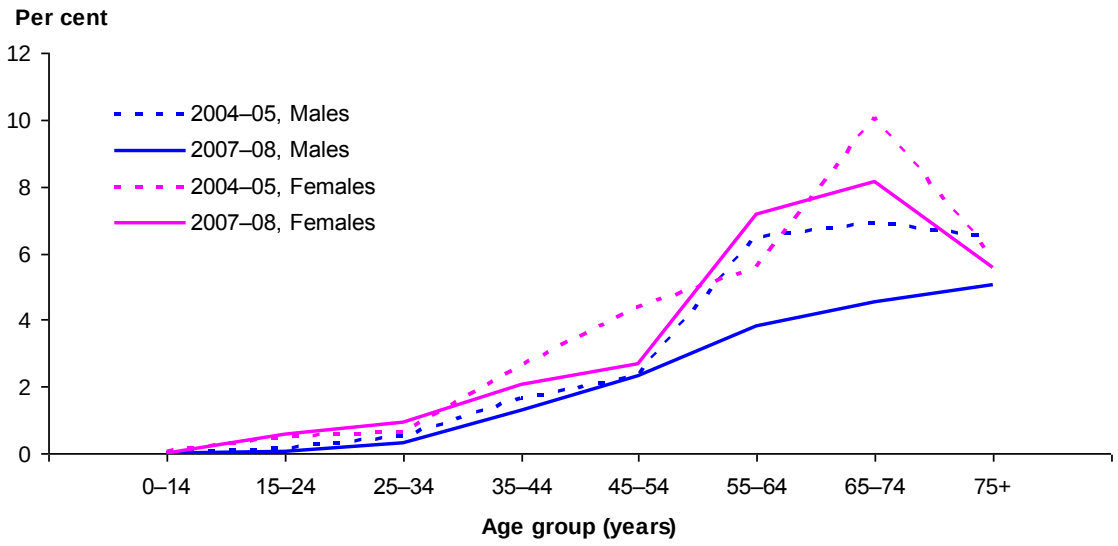
Extent of need

The National Health Survey (NHS) rheumatoid arthritis data are based on a statement by survey respondents that they have been diagnosed with the disease by a doctor and that they have had the disease for more than 6 months. No information is collected about the stage or severity of the disease in those surveys (ABS 2009).

According to the NHS data, an estimated 384,000 Australians had the disease in 2004–05 (AIHW 2008). The number increased to 428,000 in 2007–08. While the estimated number of people with the condition increased, the prevalence rate of rheumatoid arthritis in Australia declined from 2.4% in 2004–05 to 2.1% in 2007–08. This decline was not statistically significant.

Rheumatoid arthritis is more common in females than in males; about two-thirds of Australians with rheumatoid arthritis are females. The disease can start at a young age, with the highest incidence between the ages of 35 and 64 years. Rheumatoid arthritis taking place before the sixteenth birthday is referred to as juvenile arthritis and its prognosis varies greatly. Some children recover without significant damage to their joints while others continue to have active arthritis into adulthood and throughout life. Rheumatoid arthritis is more prevalent in the older population, and peaks at 65–74 years of age (Figure 1.2).

While the NHS provides valuable insights into the nation's health, there is some concern about the NHS self-report methodology leading to an overestimation. Rheumatoid arthritis shares a similar name with rheumatism and osteoarthritis and NHS respondents might not correctly recall what their diagnosis was or get confused at the time they respond. The latest NHS estimate is almost double the prevalence of rheumatoid arthritis found in other countries, at around 1% (Silman 1993).



Note: Based on self-reports of having a doctor's diagnosis of rheumatoid arthritis and still having the disease.

Source: AIHW analysis of 2004–05 and 2007–08 National Health Survey Confidentialised Unit Record Files (CURFs).

Figure 1.2: Age-specific prevalence of rheumatoid arthritis, 2004–05 and 2007–08

General practitioner (GP) consultations

Information about the management of rheumatoid arthritis by general practitioners (GPs) provides an important perspective on the extent of need. In Australia, this information is collected through the Bettering the Evaluation and Care of Health (BEACH) survey (Britt et al. 2009). The BEACH program is a continuous national study of general practice activity, based on a new sample each year of about 1,000 GPs, each of whom provides details for 100 consecutive GP–patient encounters.

The BEACH program began in 1998, and is ongoing. Data collected in the survey include reasons for GP–patient encounter, problems managed, and details of pharmacological and non-pharmacological management options. With regards to recommendation of pharmacological management, the survey records whether the GP wrote the prescription for the medicine, supplied the medicine or advised to purchase over-the-counter medicine.

The BEACH data suggest that rheumatoid arthritis remained steady at around 0.5 per 100 GP encounters in the 10-year period 1998–99 to 2007–08 (O'Halloran & Pan 2009).

Between 2003–04 and 2007–08, GP prescription of medications for rheumatoid arthritis declined from 100 scripts per 100 rheumatoid arthritis problems managed to less than 88 scripts per 100 rheumatoid arthritis problems managed. Some of this decline was offset by GP-supplied medications which doubled from 6 per 100 rheumatoid arthritis problems managed to 12 per 100 rheumatoid arthritis problems managed during this period (O'Halloran & Pan 2009).

There was also an increased emphasis on seeking expert advice from specialists in managing rheumatoid arthritis. Between 2000–01 and 2007–08, there was a significant increase in the referral of patients with rheumatoid arthritis to specialists (O'Halloran & Pan 2009). The number of specialist referrals increased from 8.0 per 100 rheumatoid arthritis problems managed to 15.5 per 100 rheumatoid arthritis problems managed. This trend is in accordance

with the recommended clinical guidelines for the management of rheumatoid arthritis, where regular expert input is recommended (RACGP 2009).

Treatment of rheumatoid arthritis

The key elements of the current approach to management of rheumatoid arthritis are (RACGP 2009; Rheumatology Expert Group 2006):

- early diagnosis and commencement with DMARD treatment
- stopping the disease process
- preventing deformity
- minimising functional loss
- alleviating or minimising pain
- regular monitoring for drug efficacy and toxicity
- active patient participation in management of the condition.

An important target in the management of rheumatoid arthritis is early diagnosis and immediate treatment (Symmons & Silman 2006). The use of NSAIDs and DMARDs is now recommended early in treatment (Schur & Maini 2010). Additional measures include the injection of long-acting corticosteroid preparations into inflamed joints.

Non-pharmacological treatment for rheumatoid arthritis includes physical therapy, weight loss and occupational therapy. Regular exercise is also important for maintaining joint mobility and making the joint muscles stronger.

Reconstructive surgery is often required in late stages of the disease. Procedures including arthrodesis (surgical fusion of joint), osteotomy (bone cutting to shorten, lengthen or change its alignment) and arthroplasty (joint replacement) all have their place (Solomon et al. 2005).

The provision of medical aids and adjustments to the work and living environment are also useful in improving the quality of life of people with rheumatoid arthritis (Koehn et al. 2002).

Rheumatoid arthritis and DMARDs

DMARDs can halt or slow down the disease process sufficiently to reduce joint destruction and disability associated with early rheumatoid arthritis. They are slow-acting, and could take several months to take effect, but can alter the disease course.

A variety of DMARDs have been used for the management of rheumatoid arthritis over the last several decades. Gold salts were the earliest form of conventional DMARDs, available since the 1920s. Although new DMARDs became available in the following years (sulfasalazine in the 1940s, hydroxychloroquine in the 1950s and methotrexate in the 1980s), it was not until the 1980s that DMARDs were widely used to treat rheumatoid arthritis. The development of bDMARDs in the late 1990s offered further opportunity to treat the disease.

Current clinical guidelines (RACGP 2009) recommend treatment of early rheumatoid arthritis with DMARDs, including those with undifferentiated inflammatory arthritis that is judged to be at risk of leading to persistent and/or erosive arthritis (RACGP 2009). Several factors have contributed to this change, prominent among which is the finding that joint destruction occurs in the first year of the disease in almost two-thirds of people with rheumatoid arthritis (van der Heijde et al. 1992). There is also an increasing body of evidence

that DMARD intervention during a critical period may reverse the disease process (RACGP 2009).

A brief overview of the clinical guidelines and best practice for the treatment of rheumatoid arthritis is given in Box 1.2.

Box 1.2: Clinical guidelines and best practice

Until recently, a so-called pyramidal approach was used to treat rheumatoid arthritis. Typically, people with early rheumatoid arthritis were treated with non-steroidal anti-inflammatory drugs (NSAIDs) for many months and even years; a disease-modifying anti-rheumatic drug (DMARD) was added to the treatment plan only after radiographic damage was confirmed. Even with DMARDs, physicians started those with established rheumatoid arthritis on the least toxic DMARD, and if after several months no improvement was observed, then another DMARD was introduced (Woolf & *v*an Riel 1997).

The RACGP now recommends that methotrexate, a conventional DMARD, be used as the first-line treatment for rheumatoid arthritis (RACGP 2009). In fact, methotrexate has become the most widely used first-line DMARD agent due to its early action (4–6 weeks), good efficacy, favourable toxicity profile, ease of administration and relatively low cost (Matsumoto et al. 2010).

If methotrexate is ineffective or intolerable, two other DMARDs, namely leflunomide and sulfasalazine, are often the first-change drugs. Combination therapy consisting of two or more DMARDs has also prove*n* successful in inducing disease remission and reducing joint damage (Klareskog et al. 2004). Hydroxychloroquine is considered an appropriate choice for mild disease.

Any of the conventional DMARDs may be used as single-line therapy or in combination with other conventional DMARDs, bDMARDs, NSAIDs anti-rheumatic or corticosteroids. Auranofin, cyclophosphamide, cyclosporine, sodium aurothiomalate and penicillamine are infrequently used, but may be employed when methotrexate, leflunomide and sulfasalazine have failed or cannot be tolerated. How and when these medications are used to manage rheumatoid arthritis depends on the person, their previous treatment and current stage of the disease.

In cases where DMARD mono or combination therapy does not produce a satisfactory response, bDMARDs may be added to the treatment.

While DMARDs have opened new therapeutic horizons for rheumatoid arthritis, they are potent drugs that can cause a variety of side effects such as stomach irritation and diarrhoea, loss of appetite, hair loss, liver damage and lung disease. Moreover, as bDMARDs are immunosuppressant, patients may develop infectious diseases such as pneumonia, listeriosis and tuberculosis (Rheumatology Expert Group 2006).

DMARDs on the PBS

Ten conventional DMARDs and five bDMARDs were available on the PBS for managing rheumatoid arthritis between 2003 and 2007. Brief descriptions of these agents, including the dates they became available on the PBS and average prices, are given in Appendix B (Tables B.1–B.3). Rituximab, a bDMARD, became available on the PBS in August 2007. As this report focuses on the use of DMARDs from 2003 to 2007, rituximab was not included in the analysis presented in this report because of the short duration of its availability on the PBS.

While there is considerable overlap in the use of both types of DMARDs, the bDMARDs are in the authority-required category of the PBS and are under stricter legislative control. The bDMARDs can only be prescribed by rheumatologists and clinical immunologists for patients who meet strict criteria including trial and failure of conventional DMARDs.

The application to initiate bDMARD treatment on the PBS must be submitted to Medicare Australia for prior approval. Continuation with bDMARD therapy through the PBS also needs to be pre-approved by Medicare Australia based on a positive response to the bDMARD as measured by improvements in blood chemistry levels and reduction in the number of affected joints. The conventional DMARDs, in contrast, can be and are widely prescribed by GPs and other primary care medical practitioners.

Information on the requirements that applied between 2003 and 2007 can be found in Appendix B. bDMARDs can be used in conjunction with conventional DMARDs, NSAIDs and corticosteroids but not with another bDMARD.

Structure of the report

The report is organised into six chapters. This introductory chapter provides background information about the use of DMARDs for managing rheumatoid arthritis, the extent of the problem that needs to be managed and various strategies used for the management of rheumatoid arthritis. Information about the PBS administrative data set used in the study and various analytical approaches used in this study are described in Chapter 2.

The supply of both conventional and biologic DMARDs on the PBS from January 2003 to December 2007 is described in Chapter 3. Interpopulation variation in the supply of both types of DMARDs is presented. Changes in the supply of various DMARDs are also tracked.

Chapter 4 explores treatment pathways for patients on bDMARDs. Analyses of DMARDs supplied before and after the initiation of bDMARDs are presented.

The extent of the PBS financial subsidy as well as patient co-payment for DMARDs on the PBS is quantified in Chapter 5.

Various issues emerging from the analysis of the PBS data on DMARD supply for rheumatoid arthritis are discussed in Chapter 6.

Detailed therapeutic and statistical information is provided as Appendixes A–D.

2 Data source and methodology

This study is based on Pharmaceutical Benefits Scheme (PBS) data. The study population includes all people for whom one or more DMARD prescription was processed on the PBS between January 2003 and December 2007.

A cohort of new enrollees for bDMARDs was also identified from this sample, and followed over 12 months to study the dynamics of the supply of DMARDs in conjunction with that of bDMARDs.

Pharmaceutical Benefits Scheme

The Australian Government subsidises the cost of medicines through the PBS and the Repatriation Pharmaceutical Benefits Scheme (RPBS) (collectively referred to as the PBS in this report). The subsidy is applied when the cost of a drug dispensed at a pharmacy exceeds the patient co-payment (Box 2.1).

Box 2.1: Patient co-payment on the PBS

The patient co-payment on the Pharmaceutical Benefits Scheme (PBS) is set each year by the Australian Government depending on income, age, health status and certain other factors. There are two major categories: general and concessional.

The holders of a health-care card, pensioner concession card, or Commonwealth seniors health card are entitled to concessional status and pay less for their medication than those in the general category.

In 2007, people in the concessional category paid up to $4.90 for a PBS-listed medication while those in the general category paid $30.70 (see Appendix C, Table C.1 for changes to the patient co-payment rates for general and concessional categories between 2003 and 2007). The PBS covers the gap between the full cost of the drug and the patient co-payment.

Safety net provisions apply once a family's co-payments exceed a set amount within a calendar year. General category patients are then entitled to the PBS medications at the concession price for the remainder of the calendar year, while concession patients are entitled to the PBS medications at no cost. In 2007, the safety net threshold was $1,059.00 for the general category and $274.40 for the concessional category.

Not all pharmaceutical medicines are PBS subsidised. These medicines are to be paid for fully by the patient (with or without private health insurance). The circumstances in which the cost of a medicine is not subsidised are when:

- drugs are not listed on the PBS
- the full cost of the drug is below the patient co-payment amount
- a restricted benefit category drug is not used to treat the conditions they are indicated for under the PBS
- authority is not given for the prescription of an authority-required medication under the PBS.

The list of drugs on the PBS is updated monthly with new drugs added or existing ones deleted, changes to prices and fees noted, and drug restriction information updated.

The data extract

The PBS data were obtained from the Australian Government Department of Health and Ageing, covering all records of DMARDs (conventional and biologic) processed from 1 January 2003 to 31 December 2007.

Data items

Each record (de-identified) in the PBS data extract included person and pharmaceutical information as well as pharmacy and prescriber details (Table 2.1).

Table 2.1: Data items in the PBS data extract

Person information	Pharmaceutical information	Pharmacy detail	Prescriber detail
Personal information number	PBS item number	Pharmacy identifier	Prescriber identifier
Date of birth	Government cost	Date of supply	Date of prescribing
Sex	Patient contribution	Postcode	Derived major speciality
Postcode	Number of scripts		
Co-payment category	Anatomical therapeutic code		

Record selection

Selecting DMARD prescriptions provided to manage rheumatoid arthritis out of PBS records faces two challenges:

- the conventional DMARDs are used to manage rheumatoid arthritis as well as other autoimmune diseases (SLE, Crohn's disease, psoriatic arthritis and Sjogren's syndrome)
- PBS records for DMARDs do not include information about the condition for which the medicine was prescribed.

These facts make it impossible to select DMARD data exclusive to rheumatoid arthritis management. Given this situation, the following data selection decisions were made to focus, as much as possible, on DMARD prescriptions for rheumatoid arthritis:

- all conventional DMARDs used for management of rheumatoid arthritis are included regardless of their possible use for other conditions
- the prescriber's major specialty was used to select DMARD prescriptions that were likely to have been provided for management of rheumatoid arthritis.

Six specialty types, listed below, were considered relevant to the prescription of DMARDs for rheumatoid arthritis:

- GPs
- other primary care medical practitioners (OMPs)
- immunologists
- rheumatologists
- geriatricians
- other specialists (such as those in rehabilitation medicine or occupational medicine).

The data set selected in this way still contains DMARD prescriptions for other conditions. While the extent of this is difficult to evaluate, it was believed that the selected data set was

adequate for the analysis on the basis that the other conditions are less common in the population compared to rheumatoid arthritis. The reported prevalence of SLE, Crohn's disease and Sjogren's syndrome is in the 0.03%–0.05% range (Anagnostopoulos et al. 2010; Bernstein et al. 2006; Johnson et al. 1995; Thomas et al. 1998), while that of psoriatic arthritis is in the 0.05%–0.35% range (Alamanos et al. 2003; Gefland et al. 2005; Helmick et al. 2008; Wilson et al. 2009).

Records with missing age or sex information were excluded from the analysis.

Population subgroups

To study interpopulation variation in the prescription and supply of DMARDs, the PBS data were disaggregated using remoteness of location and by socioeconomic disadvantage information.

Remoteness

Remoteness classification in this report is based on the Accessibility/Remoteness Index of Australia (Department of Health and Ageing & University of Adelaide 1999). This index is calculated based on how distant a place is by road from urban centres of different sizes, and therefore provides a relative indication of how difficult it might be for residents to access certain services, such as health care and education.

Using postcode information, the PBS records were assigned to five remoteness categories, namely *Major cities*, *Inner regional, Outer regional, Remote* and *Very remote* areas.

The records that could not be mapped to one of the five areas were excluded from analysis of remoteness in this report.

Socioeconomic status

Patient postcodes were classified in terms of relative socioeconomic status (SES) using the Index of Relative Socioeconomic Disadvantage (IRSD) developed by the Australian Bureau of Statistics (ABS).

The IRSD measures the average level of disadvantage across a geographical area in comparison to other areas. The index is a weighted summary of 17 different social and economic factors including income, educational attainment, levels of public sector housing and unemployment, and the availability of jobs in various occupations (ABS 2008).

IRSD scores were used to rank each area into one of five SES categories (or quintiles), with each category representing 20% of the total number of areas.

These categories have been labelled SES 1 through to SES 5, with SES 1 being the lowest SES areas and SES 5 being the highest SES areas.

The records that could not be mapped to an SES classification were excluded from the analyses of SES presented in this report.

Completeness of the supply of DMARD data

The coverage of prescriptions supplied might have been incomplete towards the end of 2007 in the PBS data extract used, on account of lag between the supply of medicine (and the pharmacy making the claim) and the processing of the claim by Medicare Australia (and adding the record to the PBS database). Pharmacies lodge a claim for the PBS payment with Medicare Australia either once a month or online each time medicine is dispensed (Medicare

Australia 2009). Online claiming was introduced in 2004, and has since been promoted and adopted widely as an improved way for claiming. Most of the PBS claims are now made online, however in 2007 there may have been some manual processing.

The cost of most of the conventional DMARDs and all the bDMARDs was above the patient co-payments (for both concessional and general categories) between 2003 and 2007. However, methotrexate (in the 2.5 mg tablet form), cyclophosphamide (50 mg tablets) and penicillamine (125 mg tablets) were, at some time during the study period, below the co-payment amount for the general category. The PBS data set used in this study therefore does not fully capture the supply of DMARDs in Australia.

While the incomplete coverage of the DMARDs is undesirable for the purpose of this report, the PBS data are the most informative available data. Also, the use of cyclophosphamide and penicillamine is rare. The implications of the lack of full coverage are discussed in the final chapter.

Between January 2003 and December 2007, the PBS-subsidised scripts for conventional DMARDs totalled 3,238,172; bDMARDs totalled 132,397. The number of individuals who received at least one script was 236,456 people for conventional DMARDs and 7,298 for bDMARDs.

3 Supply of DMARDs on the PBS

This chapter describes the supply of both conventional DMARDs and bDMARDs on the PBS between 2003 and 2007. In addition to information about the nature, type and trends in the supply of DMARDs, the chapter also focuses on sociodemographic and locational aspects of DMARD prescription and usage.

Conventional DMARDs on the PBS

Since the early 1990s, a variety of conventional DMARDs has been available on the PBS. Between 2003 and 2007, 10 different conventional DMARDs were subsidised (Table 3.1).

Table 3.1: Conventional DMARDs subsidised under the PBS, 2003 to 2007

DMARD	Abbre-viation	Year listed on the PBS	DMARD	Abbre-viation	Year listed on the PBS
Sulfasalazine	SSZ	1992[(a)]	Cyclosporine	CSP	2000
Methotrexate	MTX	1992[(a)]	Penicillamine	PEN	1992[(a)]
Leflunomide	LEF	2000	Cyclophosphamide	CPH	1992[(a)]
Hydroxychloroquine	HCQ	1992[(a)]	Auranofin	AUR	1992[(a)]
Azathioprine	AZA	1992[(a)]	Sodium aurothiomalate	ATM	1992[(a)]

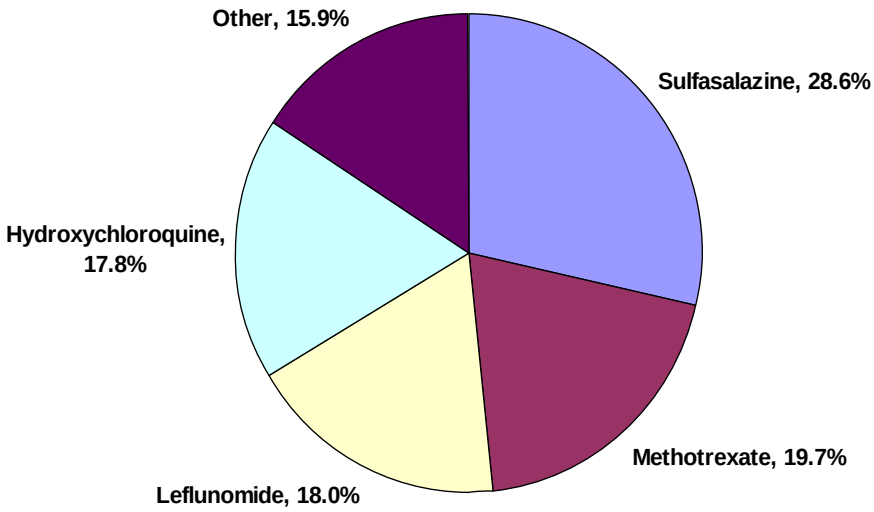
(a) DMARDs available before 1992.

More than 3.2 million DMARD prescriptions were dispensed between January 2003 and December 2007. Sulfasalazine was the most commonly supplied DMARD, accounting for more than a quarter of all DMARD prescriptions filled during the 5-year period, followed by methotrexate, leflunomide and hydroxychloroquine in that order (Figure 3.1). These top four DMARDs accounted for over 84% of all DMARDs supplied.

The methotrexate supply is likely to be an underestimate, as one form of this medicine was below the patient co-payment threshold. Methotrexate is usually the initial preferred medicine for treatment of rheumatoid arthritis (Kay & Westhovens 2009) and is likely to be more widely supplied than sulfasalazine.

Azathioprine was the fifth most commonly supplied conventional DMARD. While some patients may be supplied with azathioprine to manage rheumatoid arthritis, the current prescribing pattern in Australia would indicate that a significant proportion of the azathioprine is used for other conditions, such as vasculitis.

Cyclosporine, penicillamine, auranofin, cyclophosphamide and sodium aurothiomalate together accounted for less than 5% of all DMARD prescriptions filled between 2003 and 2007. Given the low supply of these DMARDs, and the likely supply of azathioprine for conditions other than rheumatoid arthritis, this chapter focuses mainly on the four most commonly dispensed conventional DMARDs.



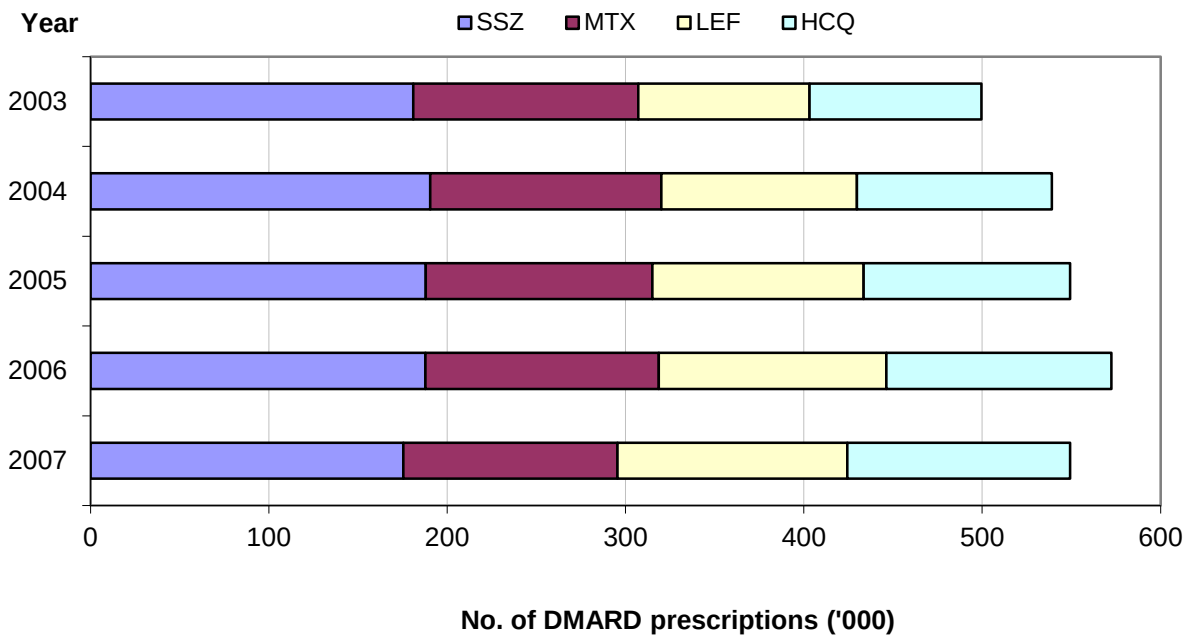
Note: 'Other' includes azathioprine, cyclosporine, penicillamine, cyclophosphamide, auranofin and sodium aurothiomalate.

Source: PBS data extract.

Figure 3.1: Distribution of conventional DMARD prescriptions on the PBS by drug, 2003 to 2007

There was no major change in the relative supply of the top four DMARDs between 2003 and 2007 (Figure 3.2). While the share of sulfasalazine and methotrexate dropped by 3–4 percentage points, the proportion of hydroxychloroquine and leflunomide increased. (Note: all top four DMARDs have been on the PBS by 2000.)

The total script volume peaked in 2006, then decreased slightly to the 2005 level in 2007.



Abbreviations: SSZ = sulfasalazine; MTX = methotrexate; LEF = leflunomide; HCQ = hydroxychloroquine.

Source: PBS data extract.

Figure 3.2: Trends in supply of the four most common DMARDs, 2003 to 2007

Prescribers

Two different groups of prescribers of conventional DMARDs through the PBS were identified:

- general practitioners (GPs) along with other primary care medical practitioners (OMPs)
- rheumatologists along with other specialists (see Appendix C, Table C.2 for more information).

Of more than 3.2 million DMARD prescriptions filled between 2003 and 2007, almost three-quarters (74%) were written by GPs and OMPs. Of the remaining, the large majority were prescribed by rheumatologists (24%), with only a small proportion of prescriptions generated by other specialists.

In the 5-year period, 158,095 people were provided with conventional DMARD prescriptions by GPs and OMPs; approximately 2 out of 3 of people (67%) who were provided with conventional DMARDs.

Sulfasalazine was the most commonly dispensed DMARD subsidised by the PBS prescribed by GPs and OMPs; it accounted for almost one-third of GP-prescribed DMARDs subsidised by the PBS during the 5-year period.

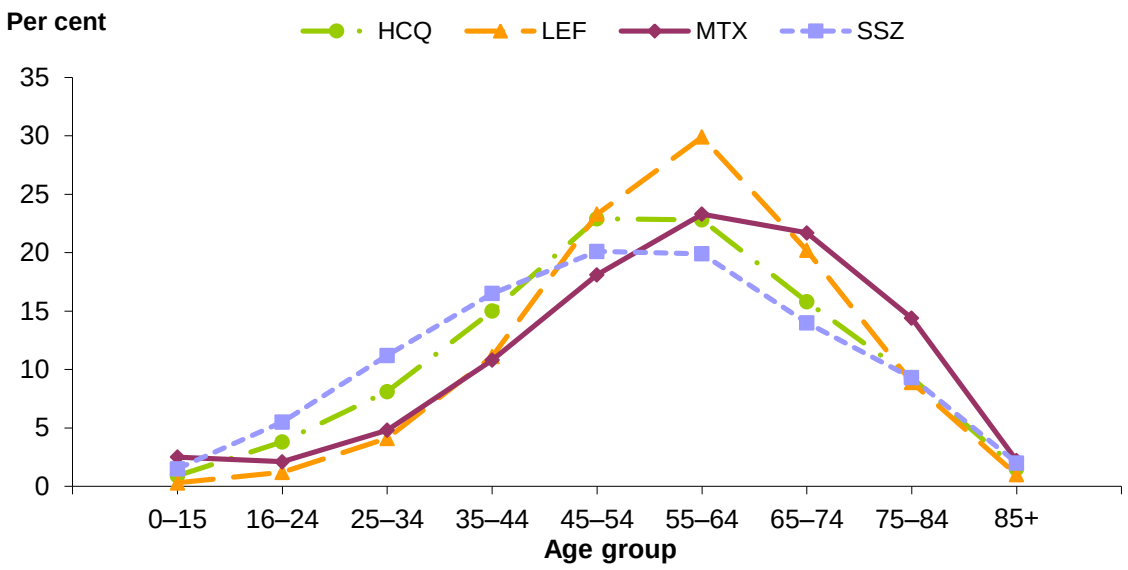
Conventional DMARD users

A total of 236,456 individuals filled a DMARD prescription on the PBS at least once during the 5-year period. There was an increase in the number of people using conventional DMARDs on the PBS between 2003 and 2007. This number increased from 617 per 100,000

population in 2003 to 675 per 100,000 population in 2007 (crude rates). Sociodemographic characteristics of people supplied with conventional DMARDs are given in Appendix D, Table D.1.

Almost two-thirds (62%) of Australians receiving conventional DMARDs via the PBS were females (Appendix D, Table D.2). This closely matches the self-reported, sex-specific distribution of rheumatoid arthritis in Australia (63%) (ABS 2009).

The number of people using DMARDs was the highest among those aged 55–64 years (Figure 3.3). All of the four major DMARDs were supplied most commonly in that age group. See Appendix D, Table D.3 for more detailed information about people who received each of the DMARDs.



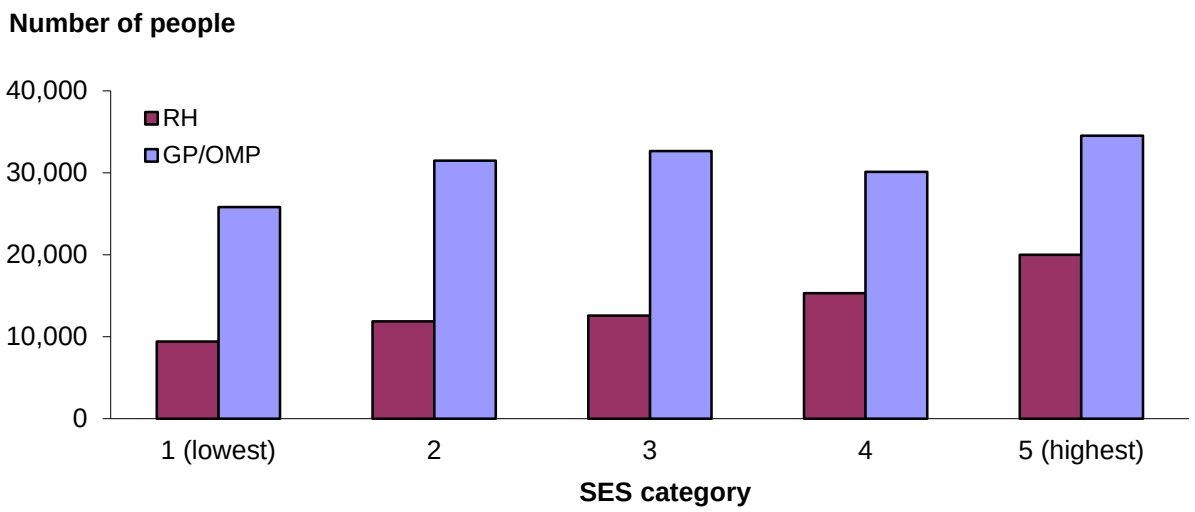
Abbreviations: HCQ = hydroxychloroquine; LEF = leflunomide; MTX = methotrexate; SSZ = sulfasalazine.

Source: PBS data extract.

Figure 3.3: Age-specific proportions of conventional DMARD supply by drug, 2003–2007

Socioeconomic profile

More people were prescribed with conventional DMARDs by GPs and OMPs than by rheumatologists in every SES category (Figure 3.4). However, the ratio of number of people receiving prescriptions from rheumatologists to those receiving prescriptions from GPs and OMPs differed across SES areas. In the lowest SES areas, for every one person who received a DMARD prescription from a rheumatologist, 2.7 people received a prescription from a GP. The ratio of number of people was down to 1.7 for the highest SES areas.



Abbreviations: RH = rheumatologist; GP = general practitioner; OMP = other primary care medical practitioner; SES = socioeconomic status.

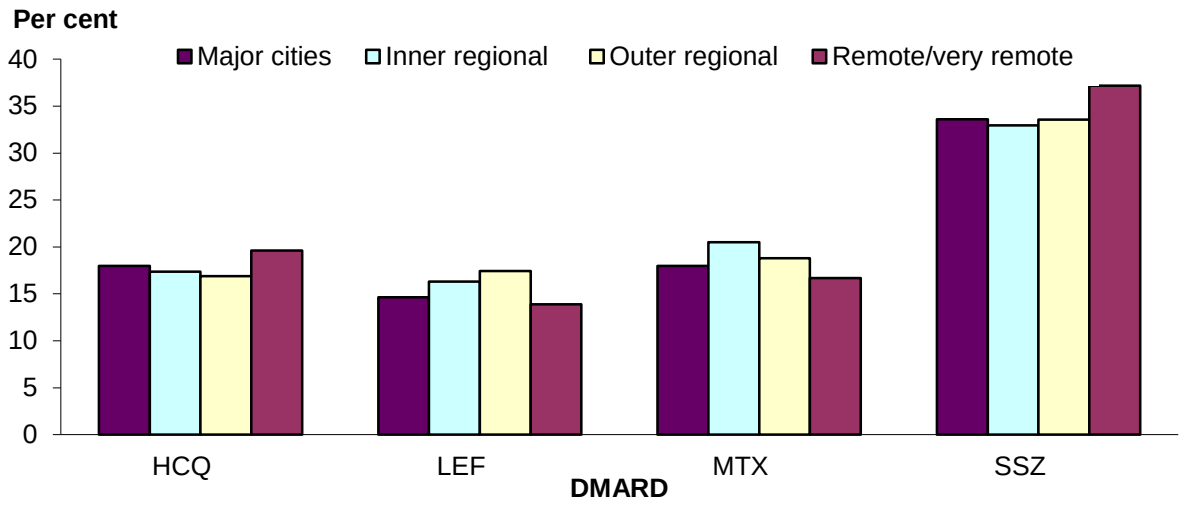
Source: PBS data extract.

Figure 3.4: PBS conventional DMARD prescriptions by socioeconomic group, 2003 to 2007

Regional profile

People living in *Major cities* (63%), *Inner regional* areas (25%) and *Outer regional* areas (11%) were the main receivers of conventional DMARDs on the PBS. Given the uneven geographical spread of medical practices with rheumatologists and other specialists who treat rheumatoid arthritis (these are more often in large cities), this analysis is based on GP-prescribed DMARDs on the PBS only (i.e. excludes prescriptions by specialists).

Sulfasalazine was the most commonly supplied DMARD on the PBS across all regional areas (Figure 3.5). The supply of methotrexate in all regions is likely to be underestimated due to one of the forms (2.5 mg tablet) being below the patient co-payment threshold.



Abbreviations: HCQ = hydroxychloroquine; LEF = leflunomide; MTX = methotrexate; SSZ = sulfasalazine.

Source: PBS data extract.

Figure 3.5: GP-prescribed conventional DMARDs dispensed on the PBS, by location of residence, 2003–2007

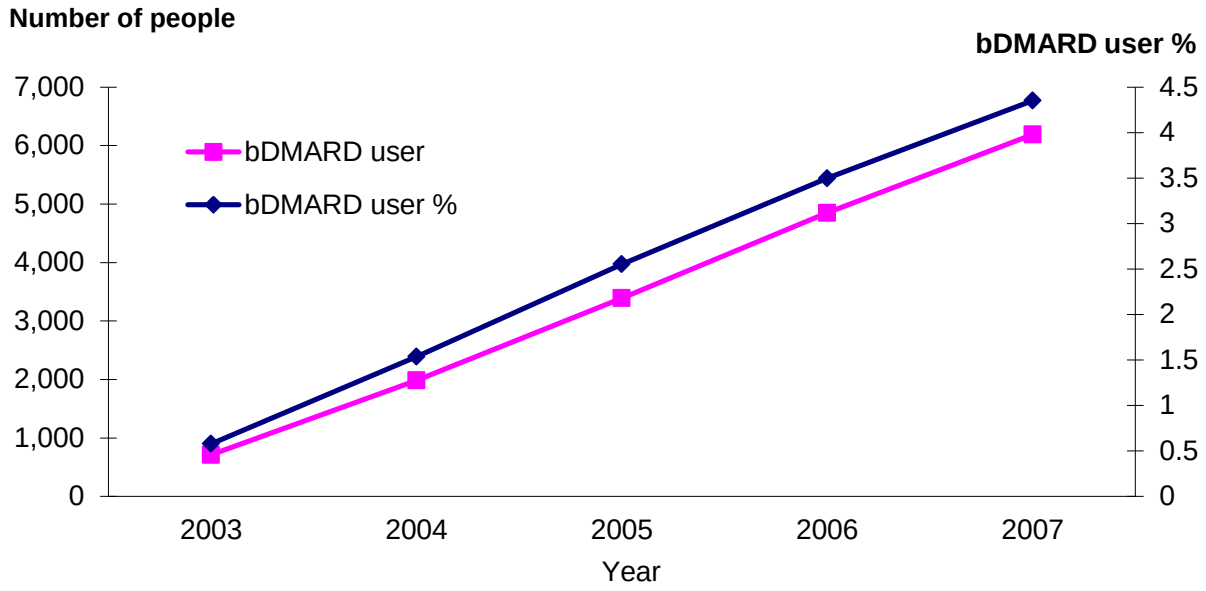
bDMARDs on the PBS

Four different bDMARDs were available on the PBS between 2003 and 2007, namely etanercept, infliximab, adalimumab and anakinra. The bDMARDs etanercept and infliximab first became available on the PBS in 2003. Adalimumab was listed on the PBS in mid-2004 and anakinra at the end of that year.

A total of 132,397 bDMARD prescriptions were filled at pharmacies across Australia by 7,298 people in the 5-year period. Given that etanercept and infliximab first became available in 2003, the total bDMARD supply was limited to 711 people in that year.

Between 2003 and 2007, the number of Australians receiving bDMARDs multiplied by around 9 times from 711 people to 6,190 (Figure 3.6).

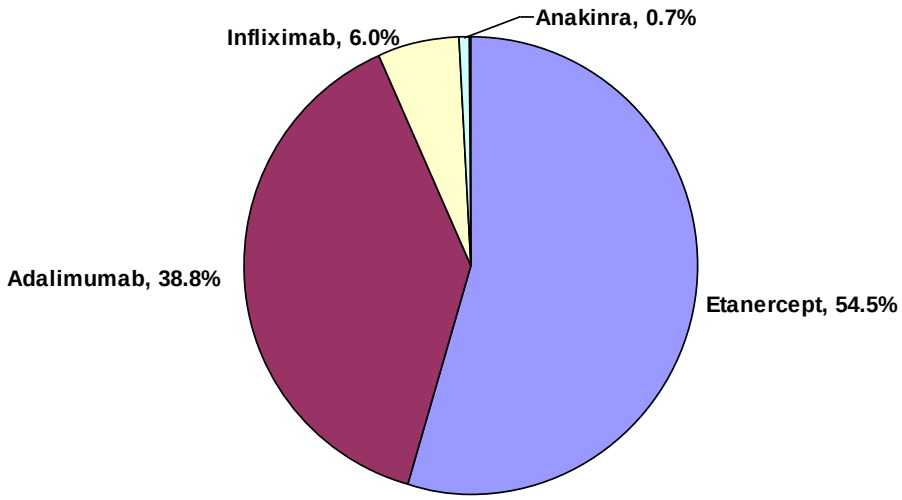
The proportion of bDMARD users among the conventional DMARD users increased 8-fold; from 0.6% in 2003 to 4.4% in 2007.



Source: PBS data extract.

Figure 3.6: Trends in biologic DMARD supply, 2003–2007

Etanercept and adalimumab accounted for most of the bDMARD supply during the 5-year period, accounting for 55% and 39% of prescriptions filled, respectively (Figure 3.7). As more bDMARDs became available on the PBS over time, the mix of bDMARDs supplied to treat rheumatoid arthritis changed.



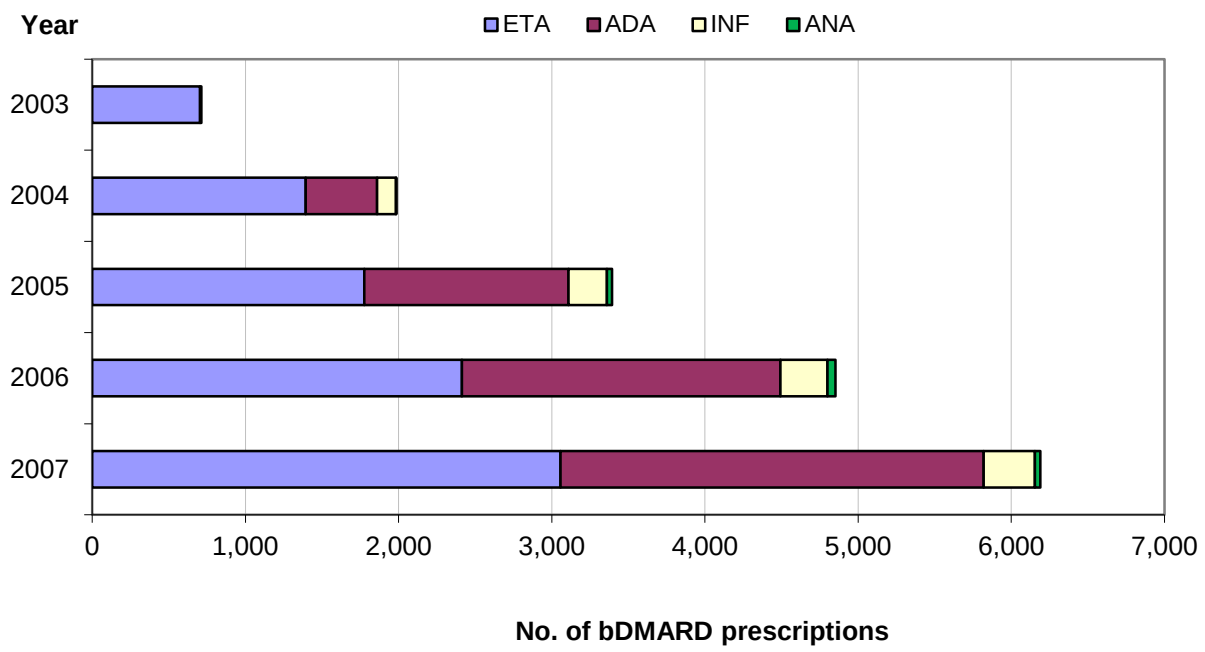
Source: PBS data extract.

Figure 3.7: Proportional distribution of biologic DMARDs supplied on the PBS, 2003–2007

In 2003, etanercept had a 99% share of bDMARD supply, with infliximab accounting for just 1% of the share (Figure 3.8). Infliximab first became available on the RPBS in June 2003 and on the PBS in December 2003; hence the low uptake that year. The supply of infliximab subsequently increased to around 6% by 2007.

Adalimumab, introduced on the PBS in 2004, grew its share steadily over the 5-year period, accounting for 45% of all bDMARDs supplied in 2007.

The share of anakinra, the most recent bDMARD on the PBS included in this study, remained limited during the study period.



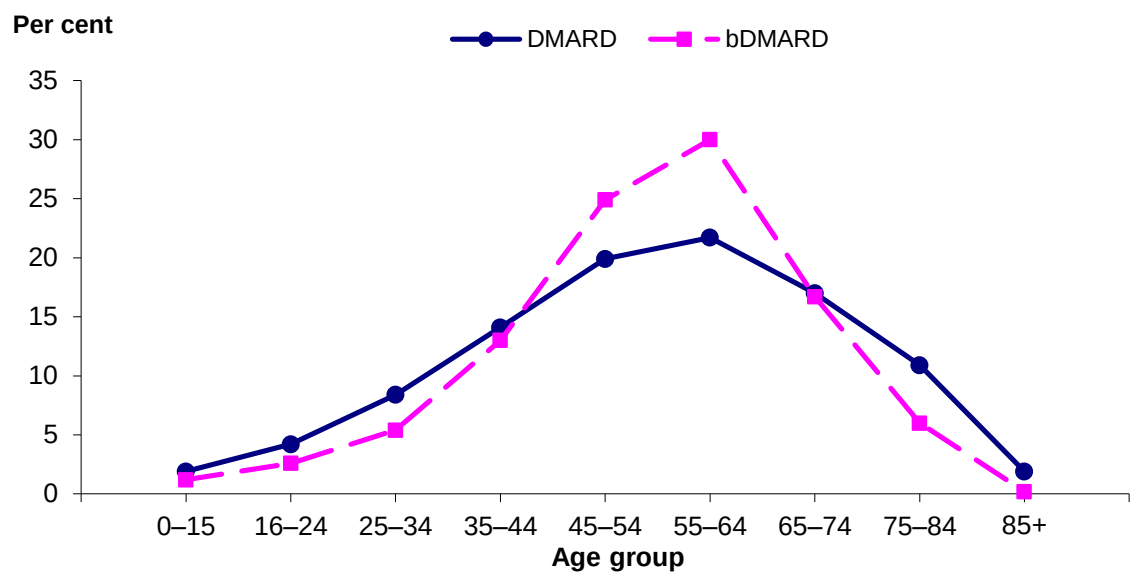
Abbreviations: ETA = etanercept; ADA = adalimumab; INF = infliximab; ANA = anakinra.

Source: PBS data extract.

Figure 3.8: Trends in biologic DMARD supply, 2003–2007

bDMARD users

The sociodemographic profile of biologic DMARD users was broadly similar to that of conventional DMARD users. A large proportion of both conventional DMARDs and bDMARDs were supplied to females (62% and 71%, respectively). Similar to the age-specific distribution of people receiving conventional DMARDs, people in the age group 55–64 years were proportionately the largest group of people receiving bDMARDs. The relative proportion of people in this age group was more marked for bDMARDs than for DMARDs (Figure 3.9). Similar to the findings for conventional DMARDs, bDMARDs were obtained more often by those living in *Major cities* (66%) or *Inner regional* areas (23%).The sociodemographic characteristics of individuals who were supplied bDMARDs on the PBS are given in Appendix D (Tables D.4 and D.5).



Source: PBS data extract.

Figure 3.9: Age-specific proportions of conventional DMARDs and biologic DMARDs supplied on the PBS, 2003–2007

Disease prevalence and DMARD prescriptions

An estimated 348,000 Australians—2.0% of the population—had doctor-diagnosed rheumatoid arthritis in 2004–05 (ABS 2006). Using this estimate, about two in five people with rheumatoid arthritis were supplied at least one DMARD in 2004 and 2005 (37% and 38%, respectively).

This low proportion of people on DMARD therapy does not necessarily reflect poor adherence to the treatment. As noted in Chapter 1, the NHS estimate of the prevalence of rheumatoid arthritis in Australia is likely to be an overestimate. The proportion of people with rheumatoid arthritis using DMARDs therefore may be much higher than the DMARD treatment rate of 37–38%.

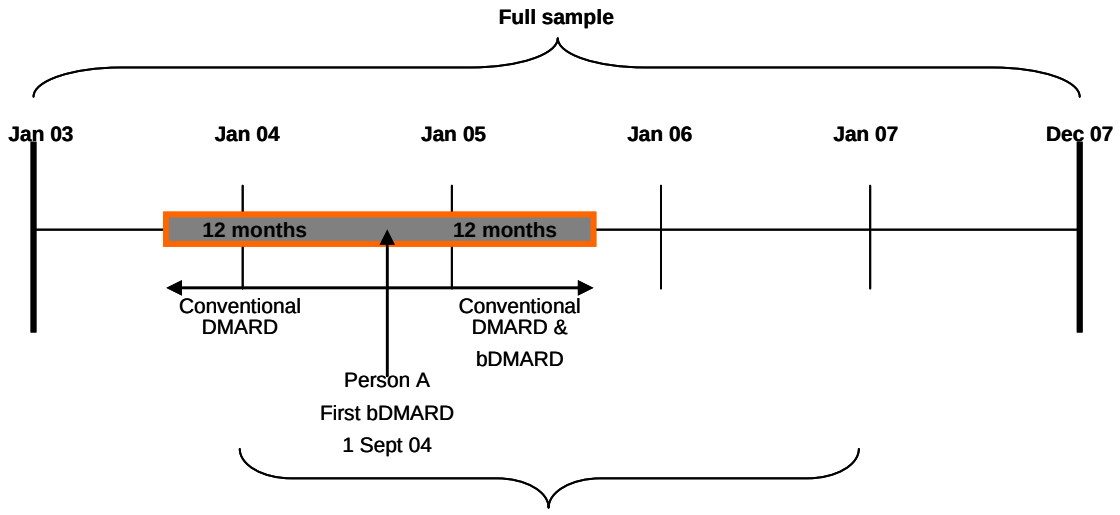
4 bDMARD treatment pathways

Biologic DMARDs may be effective when other therapies fail to achieve an adequate clinical response against rheumatoid arthritis. bDMARDs, however, are considerably more expensive than the conventional DMARDs (Appendix B, Table B.3). A variety of side effects have also been reported with their long-term use. These drugs are, therefore, recommended to be initiated only following other therapies. When used in conjunction with other conventional DMARDs, such as methotrexate, rather than as monotherapy, they are often effective in achieving an adequate response (Schuna 2009).

This chapter focuses on the introduction of bDMARDs for the treatment of rheumatoid arthritis in the context of, and in conjunction with, conventional DMARDs. The impact of the supply of bDMARDs on therapy with conventional DMARDs is also described. The supply of bDMARDs on the PBS was tracked over a 3-year period, from 2004 to 2006. Conventional DMARDs supplied in the 12 months before and after the initiation of bDMARD therapy were also followed.

The bDMARD cohort

The treatment pathways of a cohort of people initiated on bDMARDs between January 2004 and December 2006 were followed over for 12 months. Information on the supply of DMARDs in the 12 months before and after the introduction of bDMARDs was also generated from the PBS data set. The data selection for this cohort is shown in Figure 4.1. For detailed information about the cohort, see Appendix D, Table D.6.

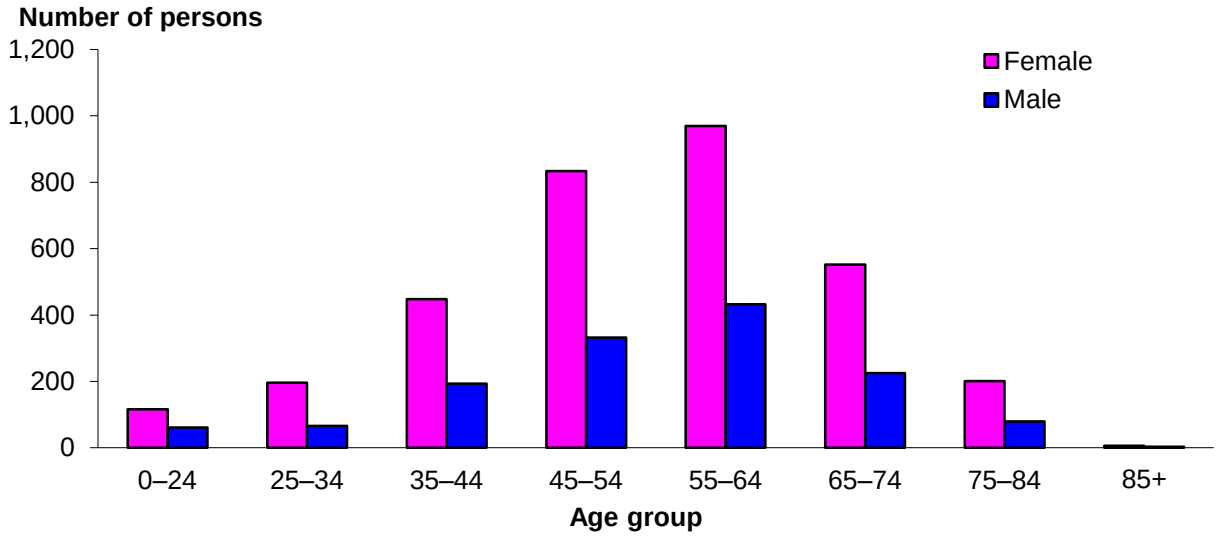


Note: This diagram shows an example of new enrollee, Person A, who received the first bDMARD on 1 September 2004. For Person A, 12 months of data, from 1 September 2003 to 31 August 2004, was used to track conventional DMARD usage before bDMARD treatment; another 12 months of data, from 1 September 2004 to 31 August 2005, was used to track conventional as well as biologic DMARD use.

Figure 4.1: Case selection for the bDMARDs cohort, 2004–2006

The first bDMARD

A total of 4,712 people were supplied with their first bDMARD in the 3-year period from January 2004 to December 2006. A large proportion of those initiated on bDMARD treatment (new enrollees) were females (71%), with an average age of 54 years. The number of new enrollees peaked in the age group 55–64 years (Figure 4.2).



Source: PBS data extract.

Figure 4.2: Age at the initiation of the bDMARD therapy, 2004–2006

The number of new bDMARD enrollees each year increased steadily over the 3-year period, from 1,314 to 1,806 (Table 4.1), an increase of 37%. The rate of enrolment increased from 6.5 per 100,000 to 8.7 per 100,000 population between 2004 and 2006.

Table 4.1: Initiation of bDMARD therapy, 2004–2006

	New bDMARD enrollees	
Year	**Number**	**Rate**
2004	1,314	6.5
2005	1,592	7.8
2006	1,806	8.7
Total	**4,712**	**–**

Note: The enrolment rates are expressed as crude rates, given as per 100,000 population.

Source: PBS data extract.

Etanercept (47%) and adalimumab (45%) were the two most common bDMARDs initiated (Table 4.2).

In most of the new enrollees (85%), only one type of bDMARD was supplied in the first 12 months of their treatment; two different types of bDMARDs were supplied to the remaining enrollees. Where two bDMARDs were supplied, the average number of days to change from one bDMARD to another was 196 days. Patients were eligible for PBS-subsidised treatment with only one bDMARD at any time. Those who used two types of bDMARDs did so consecutively and not concurrently.

Table 4.2: The first bDMARDs supplied on the PBS, 2004–2006

	Prescriptions filled	
bDMARD	**Number**	**Per cent**
Etanercept	2,219	47.1
Adalimumab	2,113	44.8
Infliximab	357	7.6
Anakinra	23	0.5
Total	**4,712**	**100.0**

Source: PBS data extract.

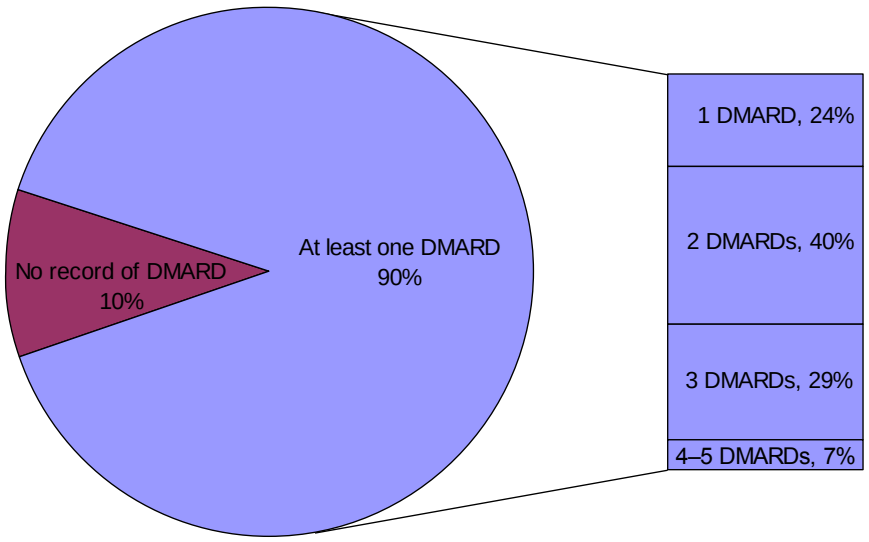
Conventional DMARDs before the supply of bDMARDs

Nine out of 10 enrollees (90%) during 2004–2006 were supplied with conventional DMARDs in the 12-months before their starting on bDMARDs (Figure 4.3).

Almost four out of nine (36%) people on DMARD treatment had filled prescriptions for three or more conventional DMARDs. Another 40% had received two different DMARDs.

A failed trial with conventional DMARDs is one of the conditions that a person must meet to start bDMARD treatment (see Appendix B for requirements to begin bDMARD treatment).

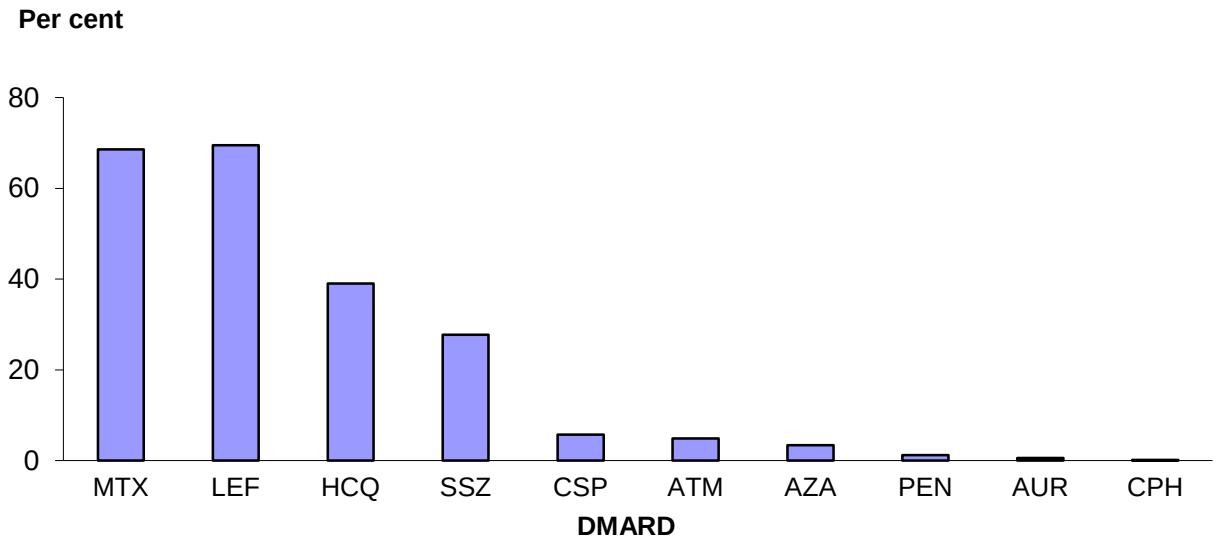
Those who did not have a record of supply of PBS-subsidised conventional DMARDs in the 12-months before initial bDMARD supply were likely to have been on methotrexate 2.5 mg or other non-PBS-subsidised conventional DMARD.



Source: PBS data extract.

Figure 4.3: Supply of conventional DMARDs before starting on biologic DMARD therapy, 2003–2006

Leflunomide and methotrexate were the two most common conventional DMARD prescriptions filled in the 12 months before starting on bDMARD therapy, with 69–70% of new bDMARD enrollees receiving one or both of these medications (Figure 4.4). Hydroxychloroquine and sulfasalazine were also commonly obtained, with 39% and 28% of people receiving these medications, respectively.



Abbreviations: MTX = methotrexate; LEF = leflunomide; HCQ = hydroxychloroquine; SSZ = sulfasalazine; CSP = cyclosporine; ATM = sodium aurothiomalate; AZA = azathioprine; PEN = penicillamine; AUR = auranofin; CPH = cyclophosphamide.

Note: The total sums to more than 100% as most people obtained more than one conventional DMARD during the 12-month period.

Source: PBS data extract.

Figure 4.4: Conventional DMARDs obtained in the year before starting on biologic DMARDs, 2004–2006

People supplied with only one type of conventional DMARD in the 12 months preceding the initiation of bDMARD therapy were more commonly prescribed leflunomide or methotrexate (37–38%). For detailed information, see Appendix D, Table D.7.

Of those who received two different conventional DMARDs during the period, the most common combinations were:

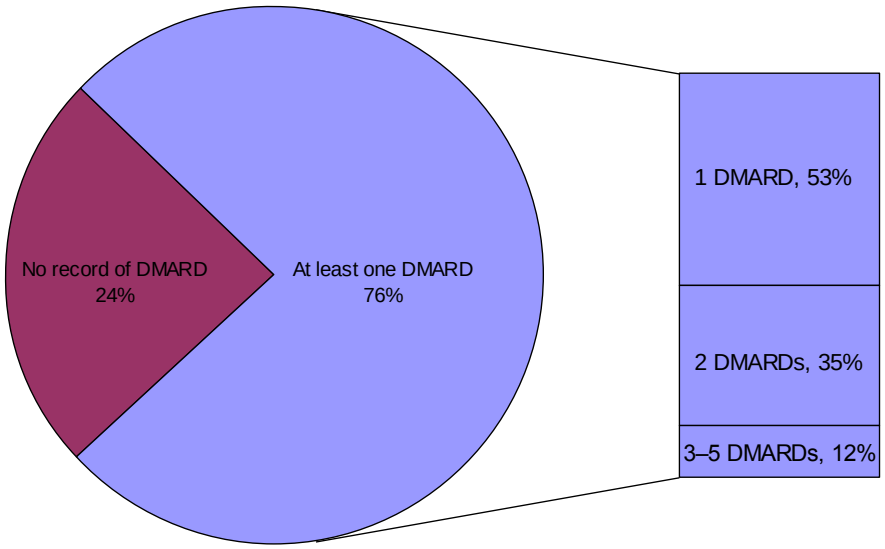
- methotrexate with leflunomide (48%)
- leflunomide with hydroxychloroquine (12%)
- methotrexate with hydroxychloroquine (10%).

These doublets were prescribed either concurrently or at different times in the 12 months before the initiation of bDMARD therapy. For detailed information on the distribution of various combinations of conventional DMARDs, see Appendix D, Table D.8.

Supply of conventional DMARDs following the initiation of bDMARD therapy

Over three-quarters (76%) of people starting on bDMARD therapy also received at least one conventional DMARD during the following 12 months (Figure 4.5). Over half of these were supplied with only one type of conventional DMARD, one-third were supplied with two different conventional DMARDs, and the rest were supplied with three to five conventional DMARDs.

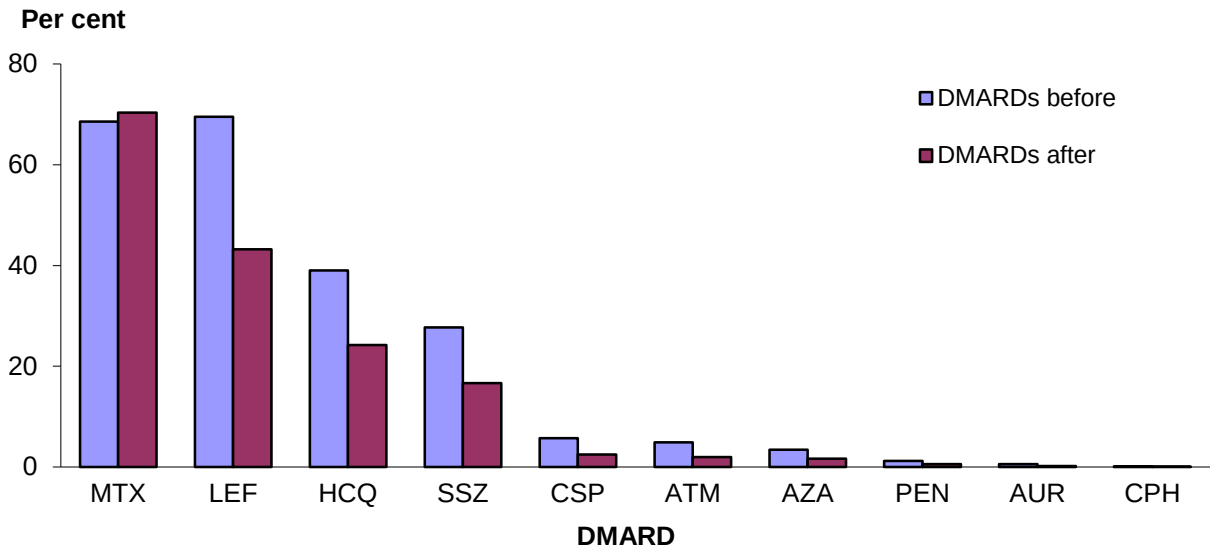
Compared to the 12 months before the initiation of bDMARD therapy, fewer people were supplied with conventional DMARDs through the PBS, and fewer people who had begun bDMARD therapy were supplied with multiple DMARDs.



Source: PBS data extract.

Figure 4.5: Supply of conventional DMARDs following biologic DMARD therapy initiation, 2004–2006

Commonly used conventional DMARDs in the year after starting therapy on the first bDMARD were methotrexate, leflunomide, hydroxychloroquine and sulfasalazine (Figure 4.6). Methotrexate was the only DMARD usage that did not decline after starting on a bDMARD. For detailed information, see Appendix D, Table D.9.



Abbreviations: MTX = methotrexate; LEF = leflunomide; HCQ = hydroxychloroquine; SSZ = sulfasalazine; CSP = cyclosporine; ATM = sodium aurothiomalate; AZA = azathioprine; PEN = penicillamine; AUR = auranofin; CPH = cyclophosphamide.

Note: The total sums up more than 100% as many people obtained more than one DMARD during the 12-month period.

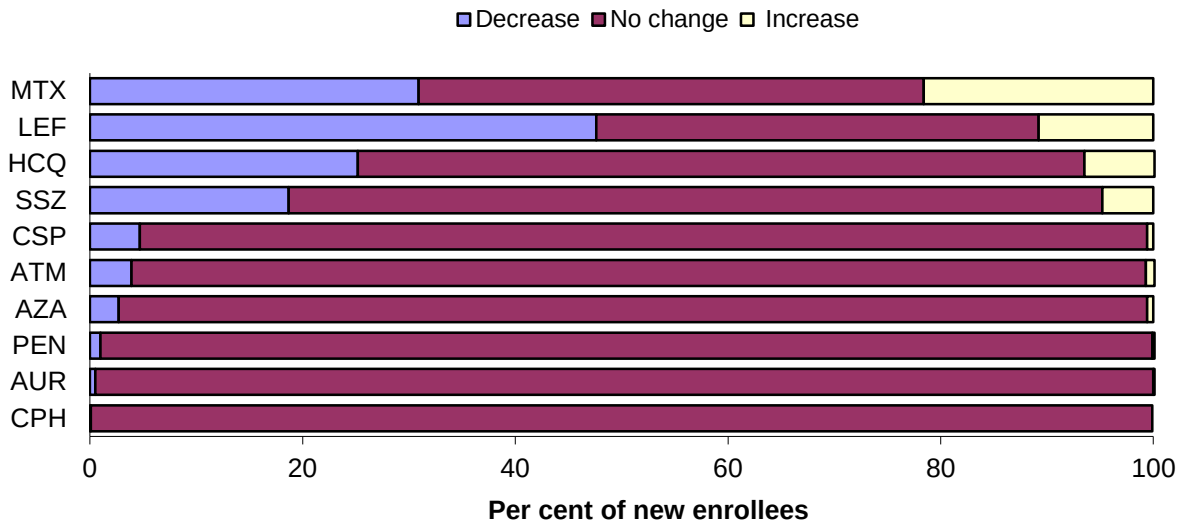
Source: PBS data extract.

Figure 4.6: Supply of conventional DMARDs in the 12 months before and after the start of biologic DMARD therapy, 2004–2006

Following the initiation of bDMARD therapy, the supply of conventional DMARDs generally reduced. The average number of DMARD scripts filled in the 12 months following the start of the bDMARD therapy was 1.6, a decrease from the average of 2.2 scripts in the 12 months preceding the start of this therapy.

In more than half the cohort (53%), the filling of DMARD prescriptions declined; no change was noted in 41% of the cases. In a small proportion (6%), the supply of conventional DMARDs increased.

Among those who were prescribed bDMARD therapy, 22% had an increased supply of methotrexate prescriptions in the following 12 months (Figure 4.7). On the other hand, in 31% of cases, the supply of methotrexate decreased. Leflunomide supply decreased most markedly; 48% of those who were on leflunomide reduced the supply of this conventional DMARD following being supplied with a bDMARD.



Abbreviations: MTX = methotrexate; LEF = leflunomide; HCQ = hydroxychloroquine; SSZ = sulfasalazine; CSP = cyclosporine; ATM = sodium aurothiomalate; AZA = azathioprine; PEN = penicillamine; AUR = auranofin; CPH = cyclophosphamide.

Source: PBS data extract.

Figure 4.7: Changes in the filling of conventional DMARD prescriptions following the initiation of biologic DMARD therapy, 2004–2007

5 PBS subsidy for DMARDs

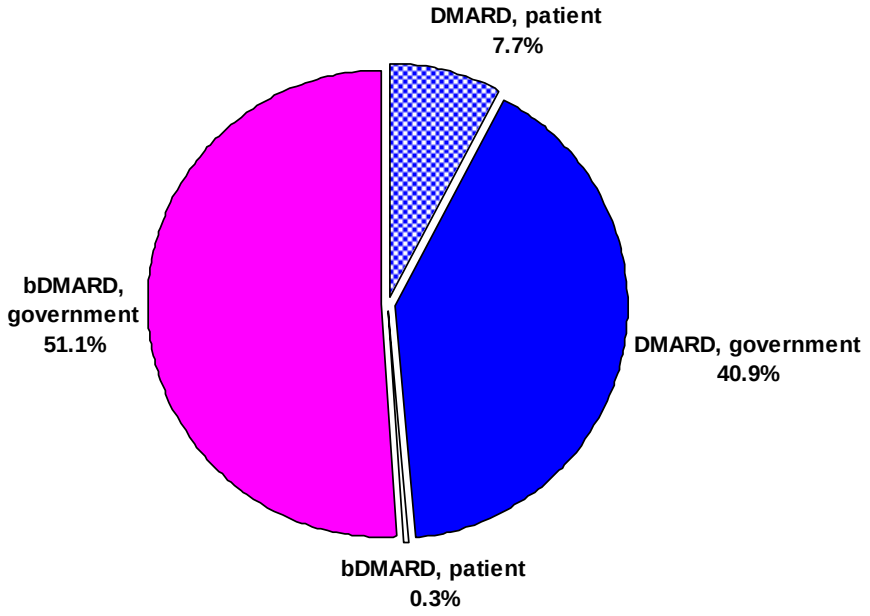
As described in Chapter 3, between 2003 and 2007 the supply of conventional DMARDs remained steady while the supply of bDMARDs increased markedly. Although the supply of bDMARDs was still relatively small compared to that of the conventional DMARDs, the pharmaceutical cost to the government to manage rheumatoid arthritis has increased due to the high cost of bDMARDs.

This chapter reports on the extent of the PBS subsidy for the supply of both conventional DMARDs and bDMARDs over the 5-year period, 2003–2007. Information is also provided about patient co-payments.

The expenditure described in this section does not cover those DMARDs that cost less than the patient co-payment threshold. For further details on patient co-payment thresholds, see Appendix C, Table C.1.

Overall expenditure

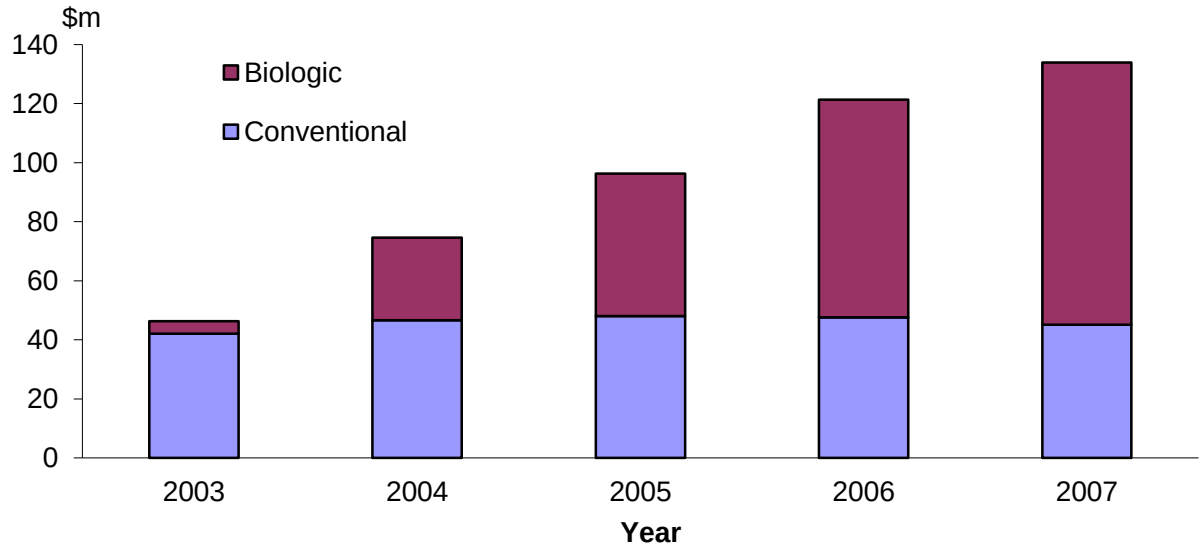
The overall expenditure (including both PBS subsidy and patient co-payments) for DMARDs, both conventional and biologic, over the 5-year period (2003 to 2007) was $472.4 million. Although much smaller in script volume (4% of DMARD scripts were for bDMARDs), bDMARDs accounted for 51% of the total costs (Figure 5.1).



Source: PBS data extract.

Figure 5.1: Expenditure for conventional DMARDs and biologic DMARDs through the PBS, 2003–2007

While the total expenditure on conventional DMARDs remained steady over the 5-year period, bDMARD expenditure increased by around $20 million each year (Figure 5.2). In 2007, the cost of bDMARDs was $89 million, more than 20 times the cost in 2003. The combined cost of conventional and biologic DMARDs almost tripled, from $46.3 million in 2003 to $133.9 million in 2007.

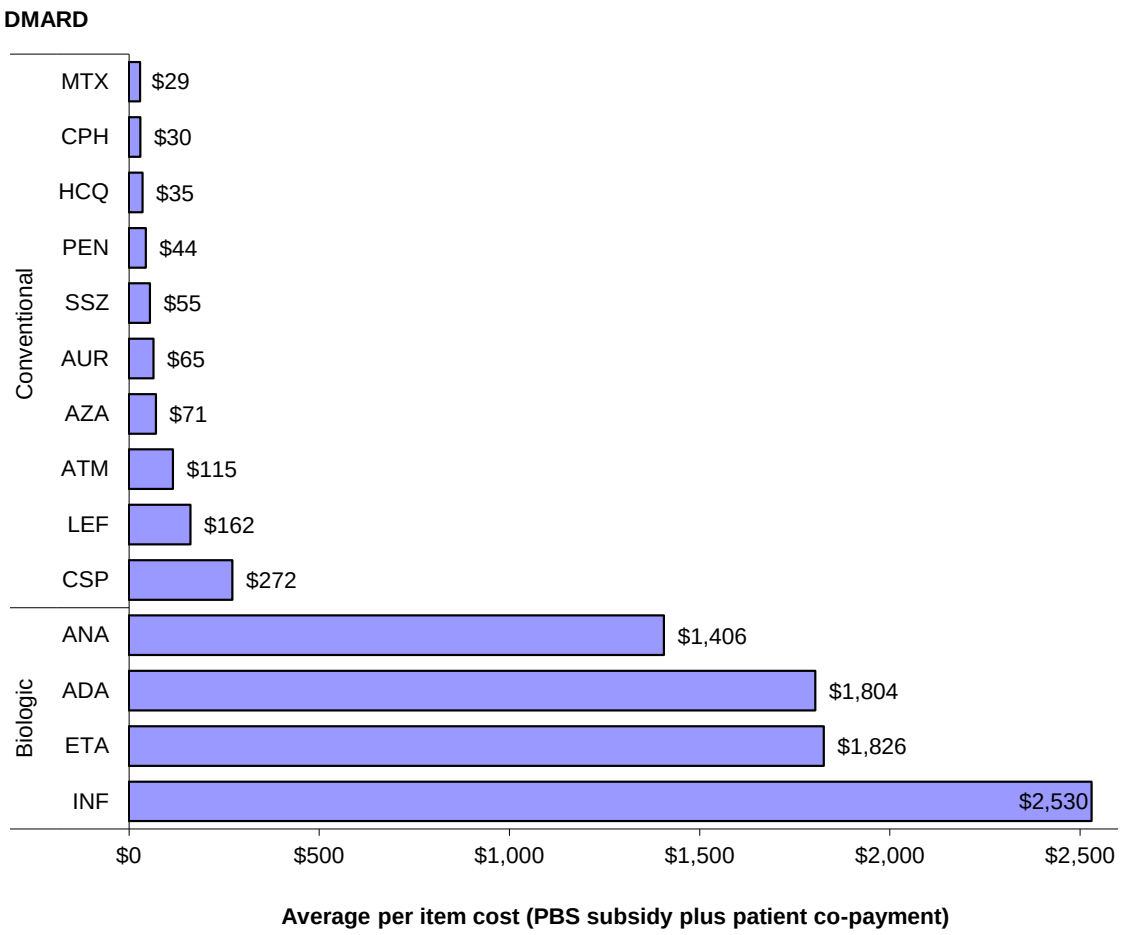


Source: PBS data extract.

Figure 5.2 Trends in PBS subsidy for conventional and biologic DMARDs, 2003–07

Close to 92% of DMARD expenditure was met through PBS subsidy, with the patient co-payment making up the rest (Figure 5.1).

The proportion of patient co-payment was much larger for conventional DMARDs than bDMARDs. This difference is explained by the higher cost of bDMARDs compared to conventional DMARDs (Figure 5.3).



Abbreviations: MTX = methotrexate; CPH = cyclophosphamide; HCQ = hydroxychloroquine; PEN = penicillamine; SSZ = sulfasalazine; AUR = auranofin; AZA = azathioprine; ATM = sodium aurothiomalate; LEF = leflunomide; CSP = cyclosporine; ANA = anakinra; ADA = adalimumab; ETA= etanercept; INF= infliximab.

Note: Current prices are reported.

Source: PBS data extract.

Figure 5.3: Item costs of the PBS-listed DMARDs, 2003–2007

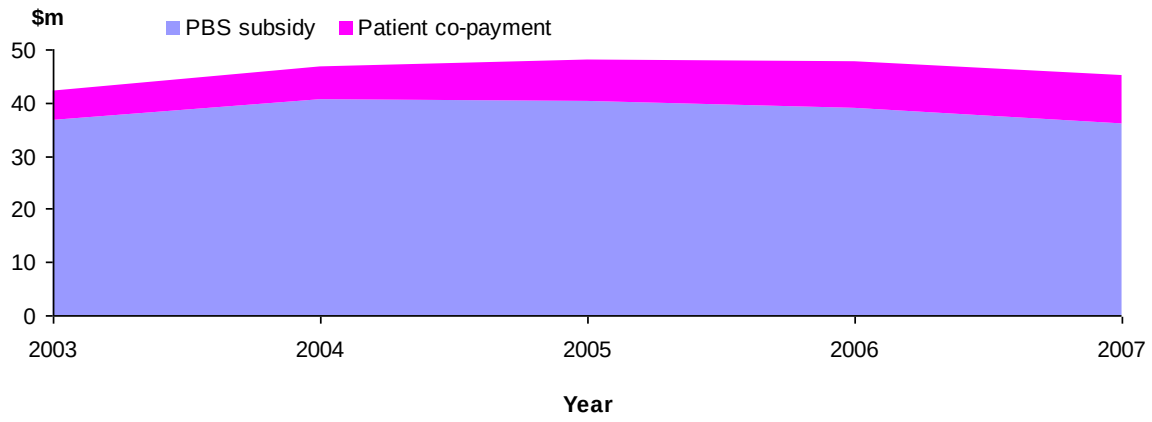
Based on PBS records, the average full cost of bDMARDs was $1,800 per item while conventional DMARDs averaged around $70.

The average yearly cost (PBS subsidy and patient co-payment) of conventional DMARDs per individual was $960 and $506 before and after bDMARD initiation, respectively. In comparison, a year's worth of bDMARD supply was much higher: approximately $14,000 for infliximab and anakinra, $19,000 for etanercept and $20,000 for adalimumab.

Expenditure on conventional DMARDs

The total cost of conventional DMARDs supplied on the PBS was $229.6 million between 2003 and 2007. The expenditure averaged around $46 million annually, and it remained relatively stable over the 5-year period.

Almost 84% of the expense for conventional DMARDs was paid for by the PBS, however, during this period the proportion paid for by the PBS subsidy steadily decreased. The proportion accounted for by patient co-payment increased from about 13% in 2003 to more than 20% in 2007 (Figure 5.4). The average patient cost for conventional DMARDs across the 5-year period was $11.32 per item, with an upward trend of $8.96 per item in 2003 to $14.00 in 2007.



Note: Current prices are reported.

Source: PBS data extract.

Figure 5.4: Trends in PBS subsidy and patient co-payment for conventional DMARDs, 2003–2007

Expenditure on bDMARDs

Based on PBS records, the total cost of bDMARDs during the 5-year period amounted to $242.8 million. This cost does not include supply from health services outside the PBS.

Almost all of the cost of bDMARDs supplied through the PBS was met through the PBS, with the patient contribution at less than 1%. Similar to the conventional DMARDs, the 5-year average cost to patient was $12.02 per item, with an upward trend of $5.95 per item in 2003 to $13.84 in 2007. The high price of bDMARDs explains the high PBS subsidy component of bDMARD expenditure.

6 Discussion

This report described the pattern of DMARD supply for the 5-year period from 2003 to 2007. Since 2003, the year bDMARDs first became available through the PBS to manage rheumatoid arthritis, much has changed in the way DMARDs are used for rheumatoid arthritis.

Key findings

The following were the key characteristics of the DMARD supply pattern over the 5-year period (2003–2007):

- By 2007, the overall expenditure for conventional DMARDs and bDMARDs grew to $134 million, 3 times higher than the 2003 level. Most of the increase was accounted for by an increase in bDMARD expenditure (see Figure 5.2).
- The yearly supply of conventional DMARDs remained relatively stable over the 5-year period (see Figure 3.2).
- The supply of bDMARDs for management of rheumatoid arthritis began modestly in 2003, and has increased rapidly in terms of total prescriptions and people supplied (see Figures 3.6 and 3.8).
- The majority of people continued to be supplied with conventional DMARDs after the commencement of bDMARD treatment, although the number of conventional DMARDs supplied to a person decreased on average (see Figures 4.3, 4.5 and 4.7).

This report found that approximately 4.4% of people who were supplied with conventional DMARDs also trialled bDMARDs in 2007. The number of bDMARD users is likely to have increased since 2007, and may still be increasing today. However, the estimated number of people who are eligible for bDMARD treatment in Australia is not readily available.

In recognition of these trends, the Pharmaceutical Benefits Advisory Committee reviewed the clinical evidence for bDMARDs and their cost-effectiveness in December 2009. The review concluded that a significant price reduction was warranted for all bDMARDs listed on the PBS for rheumatoid arthritis (Department of Health and Ageing 2009).

Following this assessment, an agreement was reached between the Australian Government and the suppliers of bDMARDs to reduce the price of bDMARDs from December 2010 (an exception to this was anakinra, which was taken off the PBS list in December 2010). The total expenditure, however, might still increase as more patients are identified to benefit from bDMARDs and are prescribed with them.

Notes on the data

The PBS data set contains considerable information about pharmaceutical use in Australia and is a valuable source of information to explore medicinal use. Every PBS record has a unique person identification number that can be used to track supply of medication to individuals over time. Because the PBS subsidy is available to all Australians, the data are free from sampling bias. Relevant sociodemographic information, such as age and sex, location of usual residence and socioeconomic disadvantage, is also available in the PBS

records. Information about prescribers in the PBS database helps analysis of the prescribing practice of various professionals.

Despite these advantages, the use of the PBS data for monitoring the supply of pharmaceutical medicines in Australia has several limitations. Efforts were made to circumvent these shortcomings in the way the data were analysed, nevertheless the findings of this report need to be viewed in light of these limitations.

First, as an administrative data set, the PBS database is not specifically designed for monitoring the supply of medicines for a specific disease. The PBS records do not generally have information about the disease or condition for which the medicine was supplied. In many cases, the PBS records cannot be identified exclusively in relation to a particular disease or condition. The PBS data for conventional DMARDs were included in the analyses only if the scripts were written by any of the six specialist categories likely to be treating rheumatoid arthritis as outlined in Chapter 2. While this method is likely to have eliminated many cases in which DMARDs were supplied to treat conditions other than rheumatoid arthritis, some uncertainties inevitably remain.

The second limitation of the PBS records is that they do not capture information about medicines that cost less than the patient co-payment threshold. Consequently, the PBS data under-enumerate less-costly medicines and total costs. For example, although a large variety of DMARDs dispensed during 2003–2007 exceeded the co-payment threshold, methotrexate (in the 2.5 mg tablet form), cyclophosphamide (50 mg tablets) and penicillamine (125 mg tablets) did not. The use of these as inferred from the PBS data therefore is significantly underestimated.

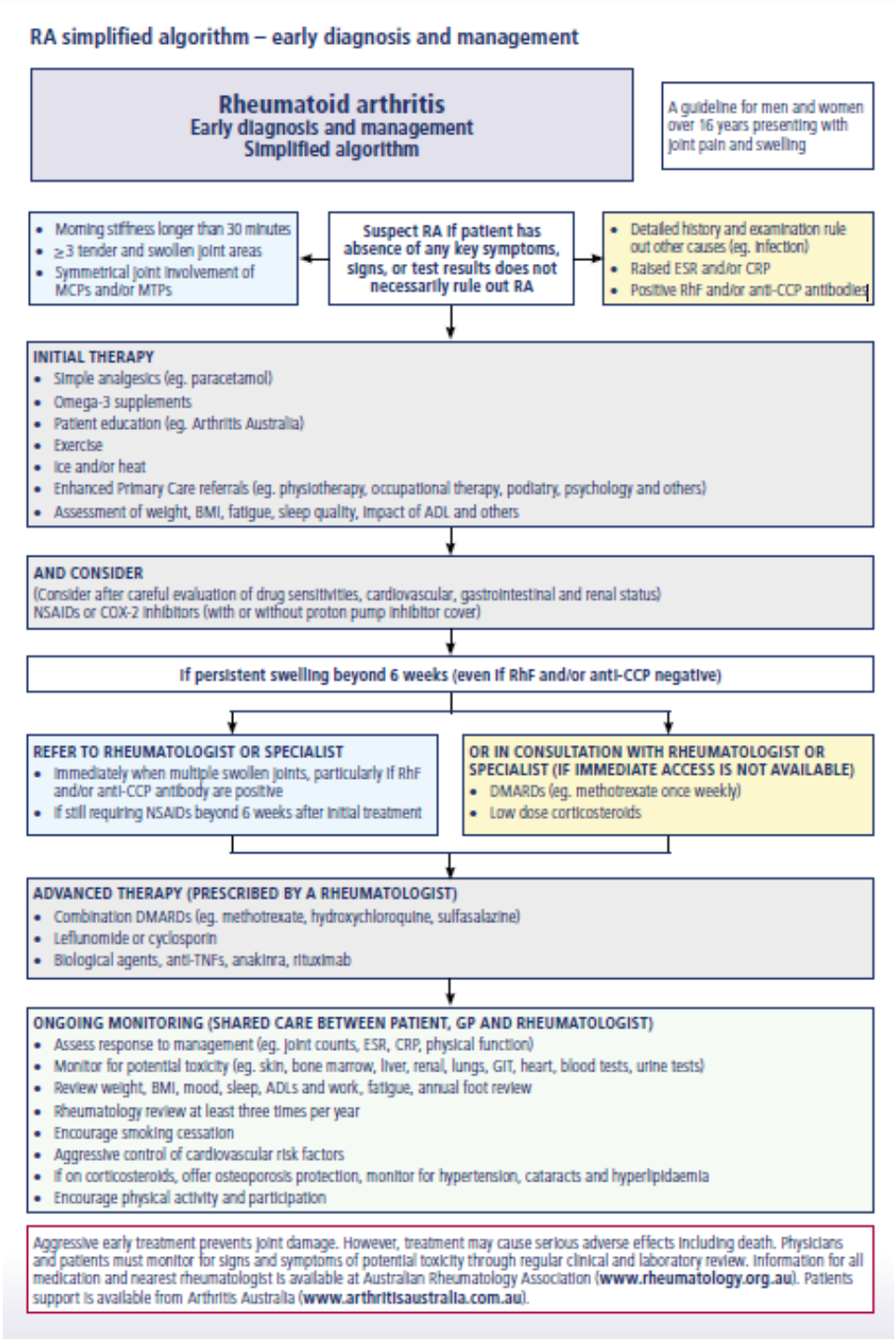
These limitations of the PBS data mean that:

- some number of the DMARD records captured in this report may in fact have been supplied for conditions other than rheumatoid arthritis
- some number of DMARDs supplied for rheumatoid arthritis may have been excluded from this report and
- the supply of and cost associated with conventional DMARDs (particularly methotrexate) are underestimated.

Notwithstanding the above issues, the following observations can be made from the PBS data:

- it is clear that the bDMARDs were rapidly adapted as a way to manage rheumatoid arthritis
- owing primarily to the growth of bDMARD supply, the PBS subsidy for management of rheumatoid arthritis has tripled in the 5-year period.

Appendix A: DMARD treatment pathways



Source: Clinical guideline for the diagnosis and management of early rheumatoid arthritis (RACGP 2009).

Figure A.1: Rheumatoid arthritis simplified algorithm—early diagnosis and management

Appendix B: DMARDs on the PBS, 2003–2007

A variety of DMARDs, both conventional and biologic, were available on the Pharmaceutical Benefits Scheme (PBS) during 2003–2007. Tables in this appendix show the nature and type of DMARDs and their pharmacological mechanisms (Table B.1), PBS codes and month and year of listing on the PBS (Table B.2) and average PBS costs (Table B.3).

Table B.1: Clinical pharmacology of DMARDs

DMARD type	Active components, pharmacological mechanisms and side effects	DMARDs
Anti-inflammatory metals	Gold is effective in the treatment of rheumatoid arthritis when it is given intramuscularly. Intramuscular gold salts were, until the 1990s, the most often used DMARD agents but have been replaced by methotrexate and other DMARDs as the preferred agents to treat rheumatoid arthritis. Injectable compounds and the oral gold compound are now rarely used due to their numerous side effects and monitoring requirements, limited efficacy and very slow onset of action.	auranofin sodium, aurothiomalate
Antimalarial drugs	Several antimalarial drugs, including chloroquine, have been used to treat rheumatoid arthritis for decades. The mechanism of their action is broad, and it is difficult to define. Antimalarial drugs have limited ability to prevent joint damage on their own, and these are used for mild cases of rheumatoid arthritis. The antimalarial are considered to be safe and most economical to treat rheumatoid arthritis.	hydroxychloroquine
Sulfa drugs	Sulfa drugs are generally used to treat bacterial and some fungal infections, but have also been used for the treatment of rheumatoid arthritis. Sulfasalazine is thought to inhibit the tumour necrosis factor (TNF) as well as a nuclear factor; but may cause hypersensitivity and allergic reactions in patients who are allergic to sulfur.	sulfasalazine
Immunosuppressants	Immunosuppressants reduce the activity of the immune system. Their basic mechanism is to increase the activity of suppressor cells.	azathioprine, cyclophosphamide, cyclosporine, leflunomide, methotrexate, D-penicillamine
Biologics (bDMARDs)	A valuable new class of medications that not only slows the progression of rheumatoid arthritis but also places it in a remissive state. This class of DMARDs inhibits various cytokines, such as TNF, interleukin-1 and CD 20, to attach to the receptors on the surface of the cells which in turn stops the inflammatory process.	adalimumab, anakinra, etanercept, infliximab

Note: The bDMARD rituximab was not included in the analysis as it was only added to the PBS late in the reporting period.

Sources: Lavelle et al. 2007; Matsumoto et al. 2010.

Table B.2: Listing of DMARDs on the PBS, 2003–2007

DMARD	PBS item code	Added to the PBS
Conventional DMARDs		
Auranofin	1095P	Before Jan 1992
Azathioprine	2687K	Before Jan 1992
	2688L	Dec 1992
Cyclophosphamide	1266P	Before Jan 1992
Cyclosporine	6125J	Nov 2000
	6232B	Dec 2000
	6352H, 6354K	Aug 2002
	6353J	Sep 2002
	8657P, 8658Q, 8659R, 8660T, 8661W	Aug 2003
Hydroxychloroquine	1512N	Before Jan 1992
Leflunomide	8373Q, 8374R, 8375T	Feb 2000
	8685D, 8686E	Feb 2004 (deleted May 2004)
Methotrexate	1622J, 1623K	Before Jan 1992
Penicillamine	2721F, 2838J	Before Jan 1992
Sodium aurothiomalate	2016D, 2017E, 2018F	Before Jan 1992
Sulfasalazine	2093E, 2096H	Before Jan 1992
Biological DMARDs		
Adalimumab	8737W, 8741C	May 2004
	9099X, 9100Y	Sep 2007
Anakinra	8773R, 8774T	Dec 2004
Etanercept	8637N	Aug 2003
	8638P	Sep 2003
	8861J, 8862K	Dec 2005
	9089J, 9090K	June 2007
Infliximab	4284L (RPBS)	June 2003
	6397Q	Dec 2003
Rituximab	9611W	Aug 2007

Note: The bDMARD rituximab was not included in the analysis as it was only added to the PBS late in the reporting period.

Source: Medicare Australia 2008.

Table B.3: Average price of DMARDs, 2003–2007

DMARD	Mode of administration	Pack size	Dose	Average PBS price
Conventional DMARDs				
Sodium aurothiomalate	Injection	10 × 10 mg	1× week/fortnight/month	$51.77
		10 × 20 mg		$79.19
		10 × 50 mg		$123.52
Auranofin	Tablet	60 × 3 mg	1–3 daily	$62.28
Azathioprine	Tablet	100 × 25 mg	50–100 mg daily	$45.14
		100 × 50 mg		$71.93
Cyclophosphamide	Tablet	50 × 50 mg	75–200 mg daily	$28.94
Cyclosporine	Capsules/liquid	120 × 10 mg	75–100 mg twice daily	$93.15
		60 × 25 mg		$104.79
		60 × 50 mg		$210.54
		60 × 100 mg		$403.77
		Liquid (100 mg per mL), 50mL		$30.70
Hydroxychloroquine	Tablet	100 × 200 mg	1 tab twice daily	$34.96
Leflunomide	Tablet	30 × 10 mg	10–20 mg daily	$96.60
		30 × 20 mg		$144.08
Methotrexate	Tablet	30 × 2.5 mg	20–25 mg weekly	$12.10
		50 × 10 mg		$30.70
Penicillamine	Tablet	100 × 125 mg	125–750 mg daily	$29.26
		100 × 250 mg		$41.00
Sulfasalazine	Tablet	200 × 500 mg	1–2 tabs twice daily	$55.77
Biologic DMARDs				
Adalimumab	Injection	2 × 40 mg	40 mg once every 2 weeks	$1,745.09
Anakinra	Injection	28 × 100 mg	100 mg daily	$1,351.36
Etanercept	Injection	2 × 25 mg	50 mg 1× weekly	$1,797.73
		1 × 50 mg		$1,745.10
Infliximab	Intravenous infusion	1 × 100 mg	1× every 6–8 weeks	$875.00

Notes

1. Based on maintenance does requirements.
2. The bDMARD rituximab was not included in the analysis as it was only added to the PBS late in the reporting period.

Source: Medicare Australia 2007; PBS data extract, Australian Rheumatology Association 2010.

The biologic DMARDs (bDMARDs) available between 2003 and 2007 were classified under the authority-required category on the PBS.

Some changes to the PBS restrictions for bDMARD supply were implemented in August 2010. The following information applies to bDMARD supply from 2003 to 2007.

To obtain bDMARDs through the PBS, a patient must have a medical practitioner submit an application to Medicare Australia. The prescriber must then be issued with pre-approval to supply the bDMARDs. This process requires supporting evidence that the use of these medications would benefit the patient, and needs to outline the expected progression of the disease. The practitioner must also supply baseline measurements for erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), and the number of active joints (more than 20 need to be affected). A patient may also be considered for bDMARD therapy if at least four major joints (elbows, wrists, knees, shoulders and/or hips) have severe, active disease.

This baseline is used to assess if the use of bDMARD has improved ESR or CRP levels, and has reduced the number of active joints. This assessment is normally completed after 12 weeks of therapy, and must be submitted to Medicare Australia no longer than 4 weeks after the therapy has concluded. (The initial therapy for adalimumab, etanercept and anakinra is 16 weeks, and for infliximab it is 22 weeks).

Apart from improvements in blood chemistry levels and reduction in the number of active joints, an additional four criteria must be met for a patient to qualify for further use of bDMARDs. These are:

- patient must have severe active rheumatoid arthritis
- only a rheumatologist or clinical immunologist can prescribe bDMARDs
- patients must have trialled at least three conventional DMARDs (one of which must be methotrexate) before a bDMARD is prescribed and
- people with rheumatoid arthritis who have qualified for the use of a bDMARD must show a response to the medicine within a treatment cycle (normally 3 months). Each person is entitled to trial up to two other bDMARDs if the first bDMARD fails to show remission. If one of the bDMARDs is successful in managing the rheumatoid arthritis and shows appropriate levels of response, the person can continue to use the bDMARD until they no longer respond to the medicine. On the other hand, if the person fails to show an adequate response to three different bDMARDs within the treatment cycle (3 months), they are not allowed to be prescribed any other bDMARD for a minimum period of 5 years.

Some restrictions are also placed on the use of specific bDMARDs. These include the previous treatment and severity of the disease. This past therapy will dictate which bDMARD should be prescribed next.

For further information on the use of bDMARDs and prescribing requirements and recent changes, see the Medicare Australia website, at <www.medicare.gov.au>.

Appendix C: PBS data and codes

Table C.1: Patient co-payments and safety net thresholds by year of supply, 2003–2007

	PBS subsidy status					
	Concessional beneficiaries			General beneficiaries		
Year	Co-payment	Safety net threshold	PBS safety net contribution	Co-payment	Safety net threshold	PBS safety net contribution
2003	$3.70	$192.40	free	$23.10	$708.40	$3.70
2004	$3.80	$197.60	free	$23.70	$726.80	$3.80
2005	$4.60	$239.20	free	$28.60	$874.90	$3.80
2006	$4.70	$253.80	free	$29.50	$960.10	$4.60
2007	$4.90	$274.40	free	$30.70	$1,059.00	$4.90

Table C.2: PBS codes for major specialities

Derived major specialty groupings	PBS code
General practitioner or other primary care medical practitioner (GP/OMP)	
General medicine	2, 82
Other non-specialist	104, 110
Vocationally registered GP	130
Family medicine program trainee	131
Fellow of College of GPs	132
Royal Australian College of General Practitioners (RACGP) trainee	133, 134
Intern	160
Queensland Country relieving program	177
Pre-vocational GP and special approved placement program	178, 179
Temporary resident doctor (various categories)	180–185, 505
Remote OMP, Outer metro OMP	186, 615
Medicare plus pre-1996 OMP (restricted and unrestricted)	188, 189
Local rural/remote relief	190
After hours	194
Workforce shortage	195
Rural and remote area placement program	196
Temporary resident and other medical practitioner program	198
Medical Deputising Service after hours OMP	199
Procedural GP (recognised and non-recognised)	201, 202
GP Trainee from March 2002	450
Specialists	
Rheumatology	13, 93
Immunology	3, 27, 83
Paediatrics	11, 91
Geriatrics	16, 96
Rehabilitation medicine	12, 58,92, 412
Orthopaedic surgery	35
Occupational medicine	41, 78, 405
Invalid provider	120
Overseas provider	121
Other	165, 475, 280, 408

Source: Medicare Australia specialty code information, 2007.

Appendix D: Detailed statistical tables

Table D.1: Demographic characteristics of people supplied with conventional DMARDs on the PBS, 2003–2007

	Year of supply				
Demographic characteristic	**2003**	**2004**	**2005**	**2006**	**2007**
			Number		
Sex					
Males	45,383	47,461	48,681	50,558	51,534
Females	77,391	81,712	84,242	88,113	90,674
Age group (in years)					
0–15	1,508	1,651	1,728	1,841	1,808
16–24	3,874	4,014	4,151	4,227	4,366
25–34	8,789	9,137	9,032	9,167	9,017
35–44	16,396	17,010	17,022	17,346	17,387
45–54	24,562	25,689	26,172	27,269	27,962
55–64	27,783	29,635	31,089	32,859	34,031
65–74	22,973	24,126	24,796	25,806	26,825
75–84	14,494	15,363	16,053	16,903	17,248
85+	2,395	2,548	2,880	3,253	3,564
Remoteness category					
Major cities	81,254	85,575	87,919	91,761	93,960
Inner regional	27,894	29,370	30,273	31,639	32,834
Outer regional	11,753	12,294	12,738	13,258	13,421
Remote	1,388	1,454	1,521	1,558	1,518
Very remote	403	431	438	422	444
Socioeconomic status (SES)					
SES 1 (lowest)	19,171	20,000	20,498	21,241	21,530
SES 2	23,840	24,919	25,636	26,621	27,237
SES 3	24,647	26,068	26,840	27,957	28,763
SES 4	24,731	26,048	26,972	28,163	29,001
SES 5 (highest)	29,487	31,215	32,050	33,689	34,591
PBS subsidy status					
General	48,325	52,224	54,717	58,861	61,619
Concession	74,449	76,949	78,206	79,810	80,589
Total	**122,774**	**129,173**	**132,923**	**138,671**	**142,208**

Notes
1. Remoteness category based on the Australian Standard Geographical Classification (ASGC); 102 people missing data.
2. SES category based on the Index of Relative Socioeconomic Disadvantage (IRSD): 1,778 people missing data.

Table D.2: Demographic characteristics of people supplied with at least one conventional DMARD through the PBS during the 5-year period, 2003 to 2007

Demographic characteristic	Number	Per cent
Sex		
Males	88,947	37.6
Females	147,509	62.4
Age group (in years)		
0–15	4,468	1.9
16–24	9,850	4.2
25–34	19,926	8.4
35–44	33,395	14.1
45–54	47,070	19.9
55–64	51,303	21.7
65–74	40,265	17.0
75–84	25,659	10.9
85+	4,520	1.9
Remoteness category		
Major cities	157,513	66.6
Inner regional	52,947	22.4
Outer regional	22,326	9.4
Remote	2,729	1.2
Very remote	839	0.4
Socioeconomic status (SES)		
SES 1 (lowest)	36,508	15.6
SES 2	45,011	19.2
SES 3	47,462	20.2
SES 4	47,758	20.4
SES 5 (highest)	57,939	24.7
PBS subsidy status		
General	102,939	43.5
Concessional	125,553	53.1
Repatriation (RPBS)	7,964	3.4
All persons	**236,456**	**100.0**

Notes
1. Remoteness category based on the Australian Standard Geographical Classification (ASGC); 102 people missing data.
2. SES category based on the Index of Relative Socioeconomic Disadvantage (IRSD): 1,778 people missing data.
3. Information is based on first DMARD record supplied to each individual from the PBS data extract.

Source: PBS data extract.

Table D.3: Demographic characteristics of people supplied with conventional DMARDs through the PBS, by drug, 2003–2007

Demographic characteristic	DMARD			
	Hydroxychloroquine	Leflunomide	Methotrexate	Sulfasalazine
	Per cent			
Sex				
Male	21.7	32.7	36.6	46.5
Female	78.3	67.3	63.4	53.5
Age group				
0–15	0.9	0.3	2.5	1.5
16–24	3.8	1.2	2.1	5.5
25–34	8.1	4.1	4.8	11.2
35–44	15.0	11.1	10.8	16.5
45–54	22.9	23.3	18.1	20.1
55–64	22.8	29.9	23.3	19.9
65–74	15.8	20.2	21.7	14.0
75–84	9.3	8.9	14.4	9.3
85+	1.5	1.0	2.2	2.0
Remoteness category				
Major cities	69.4	65.9	64.7	65.6
Inner regional	20.7	23.4	23.7	22.9
Outer regional	8.4	9.5	10.1	9.8
Remote	1.1	1.0	1.1	1.3
Very remote	0.4	0.3	0.3	0.4
Socioeconomic status (SES)				
SES 1 (lowest)	14.9	16.7	16.3	15.3
SES 2	19.0	19.2	19.6	19.3
SES 3	18.8	20.4	20.3	20.9
SES 4	20.5	19.2	20.4	20.5
SES 5 (highest)	26.8	24.5	23.4	24.0
PBS subsidy category				
General	46.5	39.3	34.8	50.6
Concessional	50.8	57.6	61.0	46.3
Repatriation (RPBS)	2.8	3.1	4.3	3.1
All persons	**21.0**	**4.7**	**27.7**	**31.7**

Notes
1. Remoteness category based on the Australian Standard Geographical Classification (ASGC); 102 people missing data.
2. SES category based on the Index of Relative Socioeconomic Disadvantage (IRSD); 1,778 people missing data.
3. Information is based on first DMARD record supplied to each individual from the PBS data extract.

Source: PBS data extract.

Table D.4: Demographic characteristics of people supplied with at least one biologic DMARD on the PBS, 2003–2007

Demographic characteristic	Number	Per cent
Sex		
Males	2,150	29.5
Females	5,148	70.5
Age group		
0–15	87	1.2
16–24	189	2.6
25–34	396	5.4
35–44	945	13.0
45–54	1,819	24.9
55–64	2,188	30.0
65–74	1,221	16.7
75–84	437	6.0
85+	16	0.2
Remoteness category		
Major cities	4,835	66.3
Inner regional	1,682	23.1
Outer regional	702	9.6
Remote	62	0.9
Very remote	17	0.2
Socioeconomic status (SES)		
SES 1 (lowest)	1,135	15.7
SES 2	1,401	19.3
SES 3	1,558	21.5
SES 4	1,413	19.5
SES 5 (highest)	1,744	24.1
PBS subsidy category		
General	3,115	42.7
Concessional	4,031	55.2
Repatriation (RPBS)	152	2.1
All persons	**7,298**	**100.0**

Notes
1. Remoteness category based on the Australian Standard Geographical Classification (ASGC).
2. SES category based on the Index of Relative Socioeconomic Disadvantage (IRSD); 47 people missing data.
3. Information is based on first DMARD record supplied to each individual from the PBS data extract.

Source: PBS data extract.

Table D.5: People supplied with biologic DMARDs through the PBS, 2003–2007

Demographic characteristic	Year of supply				
	2003	2004	2005	2006	2007
			Number		
Sex					
Males	193	530	965	1,383	1,768
Females	518	1,454	2,428	3,468	4,422
Age group (in years)					
0–15	13	41	40	30	24
16–24	25	49	88	107	130
25–34	28	85	171	246	291
35–44	71	225	422	632	761
45–54	174	476	815	1,169	1,504
55–64	236	645	1,043	1,496	1,921
65–74	120	327	582	862	1,150
75–84	42	130	225	297	385
85+	2	6	7	12	24
Remoteness category					
Major cities	472	1,335	2,248	3,229	4,125
Inner regional	165	451	781	1,108	1,399
Outer regional	69	180	334	464	591
Remote	4	12	25	41	59
Very remote	1	6	5	9	16
Socioeconomic status (SES)					
SES 1 (lowest)	116	300	540	761	936
SES 2	139	378	621	894	1,190
SES 3	129	417	732	1,023	1,321
SES 4	130	382	649	951	1,214
SES 5 (highest)	191	494	828	1,183	1,487
PBS subsidy status					
General	245	719	1,350	2,055	2,681
Concession	466	1,265	2,043	2,796	3,509
All persons	**711**	**1,984**	**3,393**	**4,851**	**6,190**

Notes
1. Remoteness category based on the Australian Standard Geographical Classification ASGC).
2. SES category based on the Index of Relative Socioeconomic Disadvantage (IRSD); 47 people missing data.

Source: PBS data extract.

Table D.6: Demographic characteristics of people who were supplied their first biologic DMARD between January 2004 and December 2006

Demographic characteristic	Number	Per cent
Sex		
Males	1,391	29.5
Females	3,321	70.5
Age group		
0–15	51	1.1
16–24	126	2.7
25–34	262	5.6
35–44	641	13.6
45–54	1,165	24.7
55–64	1,401	29.7
65–74	777	16.5
75–84	280	5.9
85+	9	0.2
Remoteness category		
Major cities	3,136	66.6
Inner regional	1,079	22.9
Outer regional	450	9.6
Remote	38	0.8
Very remote	9	0.2
Socioeconomic status (SES)		
SES 1 (lowest)	734	15.7
SES 2	873	18.7
SES 3	1,008	21.5
SES 4	940	20.1
SES 5 (highest)	1,124	24.0
PBS subsidy category		
General	2,001	42.5
Concessional	2,613	55.5
Repatriation (RPBS)	98	2.1
All persons	**4,712**	**100.0**

Notes

1. Remoteness category based on the Australian Standard Geographical Classification (ASGC).
2. SES category based on Index of Relative Socioeconomic Disadvantage (IRSD); 33 people missing data.
3. Information is based on first DMARD record supplied to each individual from the PBS data extract.

Source: PBS data extract.

Table D.7: Distribution of DMARDs supplied to people using a single conventional DMARD, 2003–2006

DMARD	Per cent	DMARD	Per cent
Leflunomide	38.1	Azathioprine	2.4
Methotrexate	37.1	Cyclosporine	2.3
Sulfasalazine	8.4	Penicillamine	0.3
Hydroxychloroquine	8.1	Cyclophosphamide	0.1
Sodium aurothiomalate	3.1	Auranofin	0.1

Notes

1. DMARD used in the 12 months before the supply of bDMARDs; covers only those people who were supplies only one DMARD in the period.
2. DMARDs not subsidised by the PBS are not included here.

Source: PBS data extract.

Table D.8: Conventional DMARD combinations supplied to people on biologic DMARD therapy, 2003–2006

DMARD combination		Per cent	DMARD combination		Per cent
DMARD type 1	DMARD type 2		DMARD type 1	DMARD type 2	
Methotrexate	Leflunomide	47.6	Leflunomide	Hydroxychloroquine	12.0
	Hydroxychloroquine	10.0		Sulfasalazine	8.0
	Sulfasalazine	6.0		Sodium aurothiomalate	2.0
	Cyclosporine	2.8		Azathioprine	1.0
	Sodium aurothiomalate	1.0		Cyclosporine	1.0
	Azathioprine	0.8			
Hydroxychloroquine	Sulfasalazine	2.0	Other combinations		4.8
	Azathioprine	1.0			
	Cyclosporine	1.0			

Notes

1. Combination DMARDs supplied in the 12 months before supply of the bDMARDs; 'other' includes all other combinations.
2. DMARDs not subsidised by the PBS are not included here.

Source: PBS data extract.

Table D.9: Supply of conventional DMARDs in the 12 months following biologic DMARD initiation, 2004–2007

	First bDMARD			
Conventional DMARD	**Etanercept**	**Adalimumab**	**Infliximab**	**Anakinra**
		Per cent		
Methotrexate	44.6	60.6	63.9	78.3
Leflunomide	32.0	35.8	20.7	26.1
Hydroxychloroquine	18.5	19.8	9.5	13.0
Sulfasalazine	12.4	13.4	9.2	17.4
Cyclosporine	2.1	1.7	1.7	0.0
Sodium aurothiomalate	1.3	1.8	1.1	0.0
Azathioprine	1.4	0.9	2.2	4.4
Penicillamine	0.5	0.5	0.0	0.0
Auranofin	0.1	0.1	0.6	0.0
Cyclophosphamide	0.1	0.1	0.0	0.0

Notes
1. The totals do not add up to 100% because of the supply of more than one conventional DMARD in conjunction with bDMARDs.
2. DMARDs supplied in the 12 months following the initiation of bDMARD therapy.
3. DMARDs not subsidised by the PBS are not included here.

Source: PBS data extract.

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