

1 Introduction

Arthritis and osteoporosis can have a major effect on a person's life. As with most chronic conditions, a variety of management strategies are used to reduce symptoms, control disease progression and enable people to live a normal life. One of the most common and frequently used strategies is medication.

Medicines are used in arthritis and osteoporosis to relieve symptoms, help to increase mobility, and prevent future complications, such as osteoporotic fractures. Although the use of non-drug therapies (such as exercise, physiotherapy and weight loss) is an important part of the management of these conditions, this report focuses on the use of medicines.

Box 1.1: What are arthritis and osteoporosis?

Arthritis

The term 'arthritis' refers to over 100 chronic conditions. Affecting any movable joint, arthritis causes damage to the joint structures, such as the articular cartilage and synovial lining (Martini 2004). The most common symptoms associated with arthritis are inflammation, pain, stiffness, decreased mobility and discomfort. This report looks at the two most common arthritic conditions, osteoarthritis and rheumatoid arthritis.

Osteoarthritis: a degenerative joint condition that mostly affects the hands, spine and weight-bearing joints, such as hips, knees and ankles (AIHW 2008a). Its main feature is the breakdown of the articular cartilage. This is a thin layer of hard tissue which lies across the ends of the bones, and acts as a defensive mechanism to reduce joint degeneration and bone erosion caused by the friction of movement (Martini 2004). When a person has osteoarthritis the articular cartilage is worn or eaten away, leaving bone exposed and causing pain and stiffness.

Rheumatoid arthritis: a chronic auto-immune disease marked by inflammation of the joints, most often affecting the hand joints in a symmetrical fashion. The immune system attacks the synovial tissues lining the joints, causing pain, swelling and stiffness (AIHW 2008a). Over time, the articular cartilage and surrounding muscles and tendons may also be damaged.

Osteoporosis

Osteoporosis is the thinning and weakening of bones, increasing the risk of fracture (AIHW 2008a). On a daily basis the skeletal system remodels bone, stripping away old bone and replacing it with new. Osteoporosis is a dysfunction in this bone remodelling process that causes bone to be broken down faster than it can be replaced, making it brittle and porous. Osteoporosis has no overt symptoms. Fractures from minimal trauma (for example, a trip and fall while walking) are often the first sign a person may have this condition.

Using medications to manage or prevent disease is referred to as *pharmacotherapy*. Not confined to prescription medicines, pharmacotherapy incorporates the use of over-the-counter (OTC) and complementary medicines. In the last decade, the variety of medicines available for managing arthritis and osteoporosis has expanded considerably. No longer focusing on just treating symptoms, several new medicines have evolved that can reduce the disease severity, slow its progression and in some cases prevent complications.

Subsequently, there has been a large growth in using medications to manage these conditions. This is reflected in expenditure figures. Between 2000–01 and 2004–05, overall expenditure on prescription medicines in Australia (adjusted for inflation) rose by 18% (AIHW 2009). In comparison, expenditure on prescription medicines for arthritis and musculoskeletal conditions rose by 25%.

The increase in expenditure and the ongoing and rapid advances in the medicines for these conditions indicate that there is a need to monitor changes in the pharmacotherapy of arthritis and osteoporosis. This report describes the types of medications used to manage these conditions and explores how this has changed over the last 10 years.

Management of arthritis and osteoporosis

Use of medications is often among the first actions to be taken when managing arthritis and osteoporosis. Incorporating both pharmaceutical and complementary medicines (Box 1.2), medications can provide quick and easy relief from pain and inflammation, and help to improve bone density and structure. According to self-reported information from the 2004–05 National Health Survey (NHS), using pharmaceuticals and complementary medicines is the most common management action taken by people with arthritis and osteoporosis (Figure 1.1).

Arthritis management centres around relieving pain and inflammation, and reducing the progression of the condition (Fleischmann et al. 2005; Hinton et al. 2002; Sambrook & Cooper 2006). Data from the 2004–05 NHS suggest that people with arthritis used complementary medicines more than they did pharmaceuticals (Figure 1.1). Apart from using medications, people with arthritis also managed their condition by doing physical exercise (21%), consulting a general practitioner (GP) or specialist (11%), or attending alternate therapy sessions, such as physiotherapy and hydrotherapy (9%).

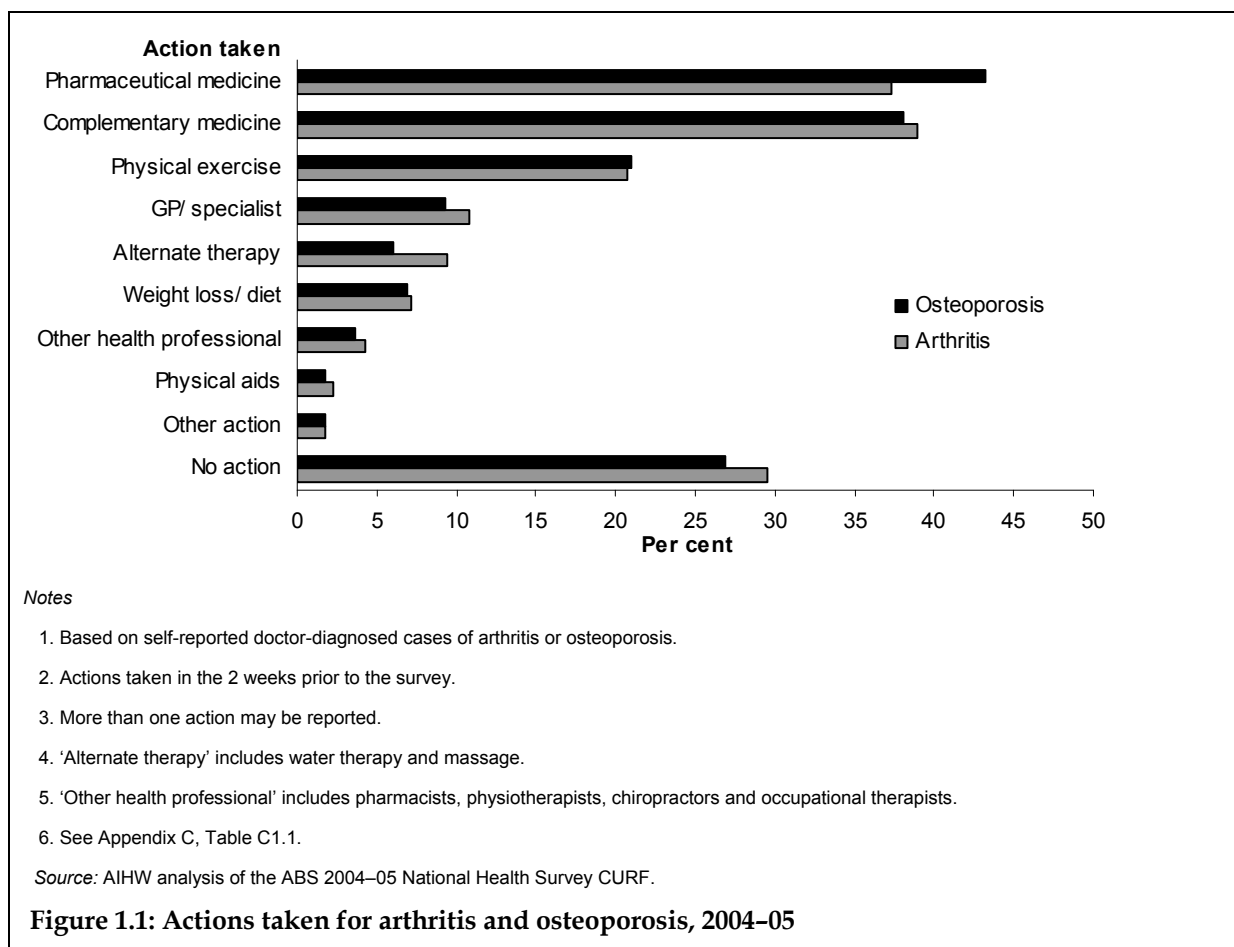
Box 1.2: Pharmaceuticals and complementary medicines

Pharmaceuticals are medications which require a script from a health professional, or can be purchased over the counter at pharmacies, supermarkets or related stores. Pharmaceuticals exclude natural supplements, vitamins and minerals. Examples are paracetamol, celecoxib, methotrexate, and alendronate.

Complementary or alternate medicines refer to the natural or herbal supplements, vitamins and minerals that can be purchased over the counter at pharmacies, supermarkets or related stores. Examples are glucosamine, fish oils and calcium.

Managing osteoporosis has a different focus, with the primary aim being to slow the loss of bone density and reduce the risk of fractures (RACGP 2008; Sambrook & Cooper 2006). Self-reported data indicate that over 40% of people with osteoporosis in 2004–05 used pharmaceuticals or complementary medicines to manage their condition, with pharmaceuticals used more commonly than complementary medicines (Figure 1.1). People with osteoporosis also undertook other management strategies, including physical exercise (21%) and seeking advice from GPs or specialists (9%).

Although arthritis and osteoporosis are conditions that generally require ongoing management, 27% of people with osteoporosis and 29% of people with arthritis reported that they took no action to manage their condition in the two weeks prior to the survey.



Structure of this report

This report describes the pharmacotherapy of three conditions: osteoarthritis, rheumatoid arthritis and osteoporosis. It is organised into five chapters. Chapter 1 provides background information about the conditions, briefly describing their management and the role of pharmacotherapy. A description of the data sources and methodology used in the report is also provided.

Chapter 2 provides information about the prevalence of arthritis and osteoporosis in Australia. It also includes an overview of the major types of medications used for these conditions, with a brief focus on medication use by area of residence.

Chapters 3 to 5 discuss the pharmacotherapy of the three conditions: osteoarthritis (Chapter 3), rheumatoid arthritis (Chapter 4) and osteoporosis (Chapter 5). Each of these chapters in turn describes the prevalence of the conditions and the most common pharmaceutical and complementary medicines used to manage them. These chapters also provide information about new medicines and specialised treatments, consider trends in GP recommendations about medications and give expenditure estimates for the three most common prescription medicines for each condition in 2007.

Data sources

The data presented in this report have been compiled using the 2004–05 NHS, the Bettering the Evaluation and Care of Health (BEACH) GP activity surveys from 1998–99 to 2007–08, and data from the 2007 Pharmaceutical Benefits Scheme (PBS). Although they cannot be compared to each other, each of these data sources offers a different perspective on how medications are used to manage these conditions. Data from the NHS offer the perspective of people with the conditions, whereas the BEACH data give the perspective of the GPs managing them. PBS data provide a national picture of subsidised medication use and costs.

The Australian Bureau of Statistics (ABS) conducts the NHS every 3 years and it is designed to obtain self-reported information on the health status of Australians, their use of facilities and services, and health-related aspects of people's lifestyles. In this report, data from the NHS are used to calculate the prevalence of each condition and identify the most common medications people use to manage them. As information from the NHS is self-reported, only cases where the person reported a doctor's diagnosis of the condition have been included.

The BEACH program has been running since 1998, and is the only continuous study of GP activity in Australia. It is an annual collection, gathering data from an ever-changing random sample of 1,000 GPs each year. Using paper forms, GPs who participate in this survey supply details about 100 consecutive patient encounters, as well as providing information about themselves and their practices (AIHW: Britt et al. 2008).

Data from the 2007–08 BEACH survey are used in this report to indicate the main medications GPs recommend when managing osteoarthritis, rheumatoid arthritis and osteoporosis. The report also uses BEACH data from 1998–99 to 2007–08 to examine trends in GP recommendation of medications for these conditions.

The PBS is a government-funded initiative to help with the cost of certain prescription medicines. The PBS Schedule lists all of the medicines available that can be dispensed to patients at a government-subsidised price, what co-payments need to be paid at the time of dispensing, and any restrictions defining who is eligible to receive these subsidies.

Pharmacies across Australia collect PBS data and the Department of Health and Ageing (DoHA) and Medicare Australia hold this information.

The data collected through the PBS include details of the medication that was dispensed and the subsidy it received, but do not indicate why the medication was prescribed (in terms of a diagnosis). This report uses the administrative PBS data from Medicare Australia's website in combination with BEACH data to estimate consumer and government expenditure for the three most common medicines that GPs recommended for osteoarthritis, rheumatoid arthritis and osteoporosis in 2007.

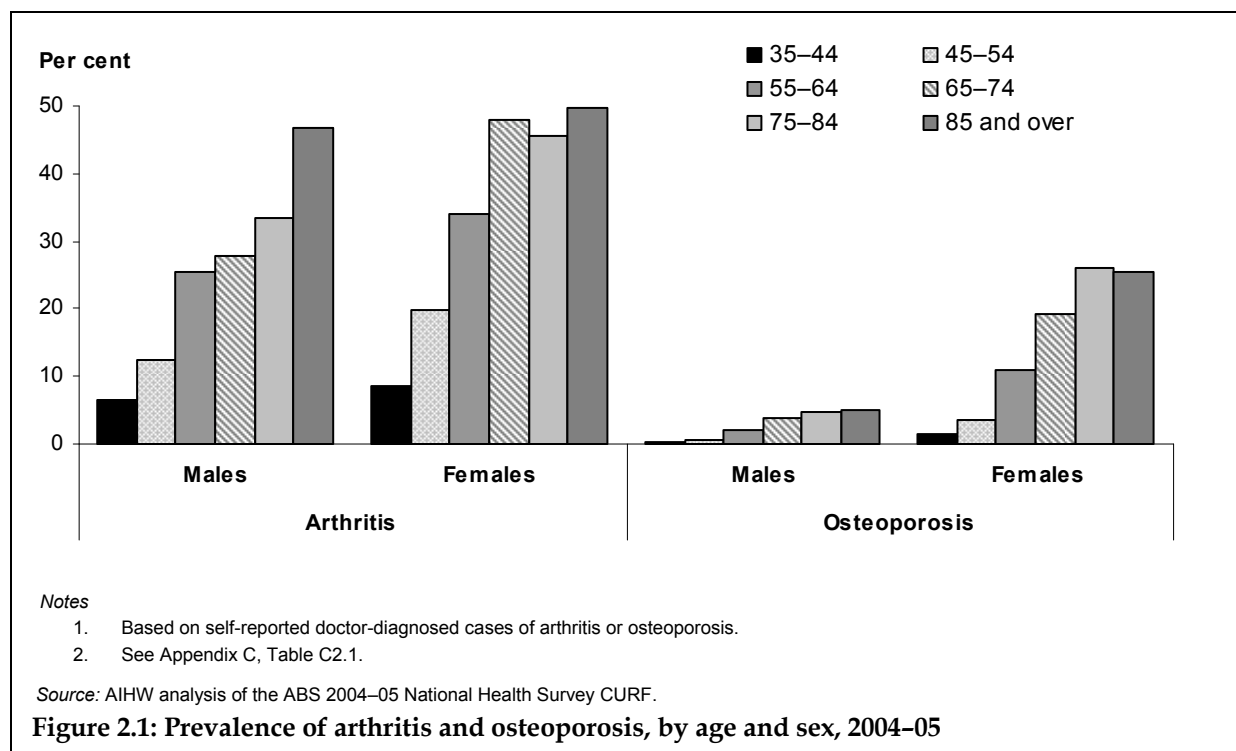
A more detailed description of the methodology and data sources for this report is in Appendix B.

2 Arthritis and osteoporosis in Australia

Musculoskeletal conditions affect over one-third of the Australian population and are some of the most common causes of pain and disability (ABS 2006; AIHW 2008a; AIHW: Rahman & Bhatia 2007). The most common musculoskeletal conditions affecting Australians are arthritis (estimated to affect 3.0 million people), back pain (2.1 million), disc disorders (1.1 million) and osteoporosis (0.6 million) (ABS 2006).

Over the last 10 years, arthritis and osteoporosis have become major areas of focus for health and wellbeing. Estimated to affect 15% and 3% of the population, respectively, arthritis and osteoporosis are considered to be some of the most prevalent and costly musculoskeletal conditions in Australia (ABS 2006).

The older age groups and females commonly reported these degenerative conditions (Figure 2.1). Information from the 2004–05 NHS suggests that 17% of the female population has one or both of these conditions, compared with 11% of males. Over 50% of the diagnosed cases of arthritis and osteoporosis are in people aged 65 years and over (Figure 2.1) (ABS 2006; AIHW 2008a). Although not common in the younger age groups, arthritis and osteoporosis can also affect children. In 2004–05, an estimated 38 per 10,000 and 5 per 10,000 people under the age of 25 had arthritis or osteoporosis, respectively.

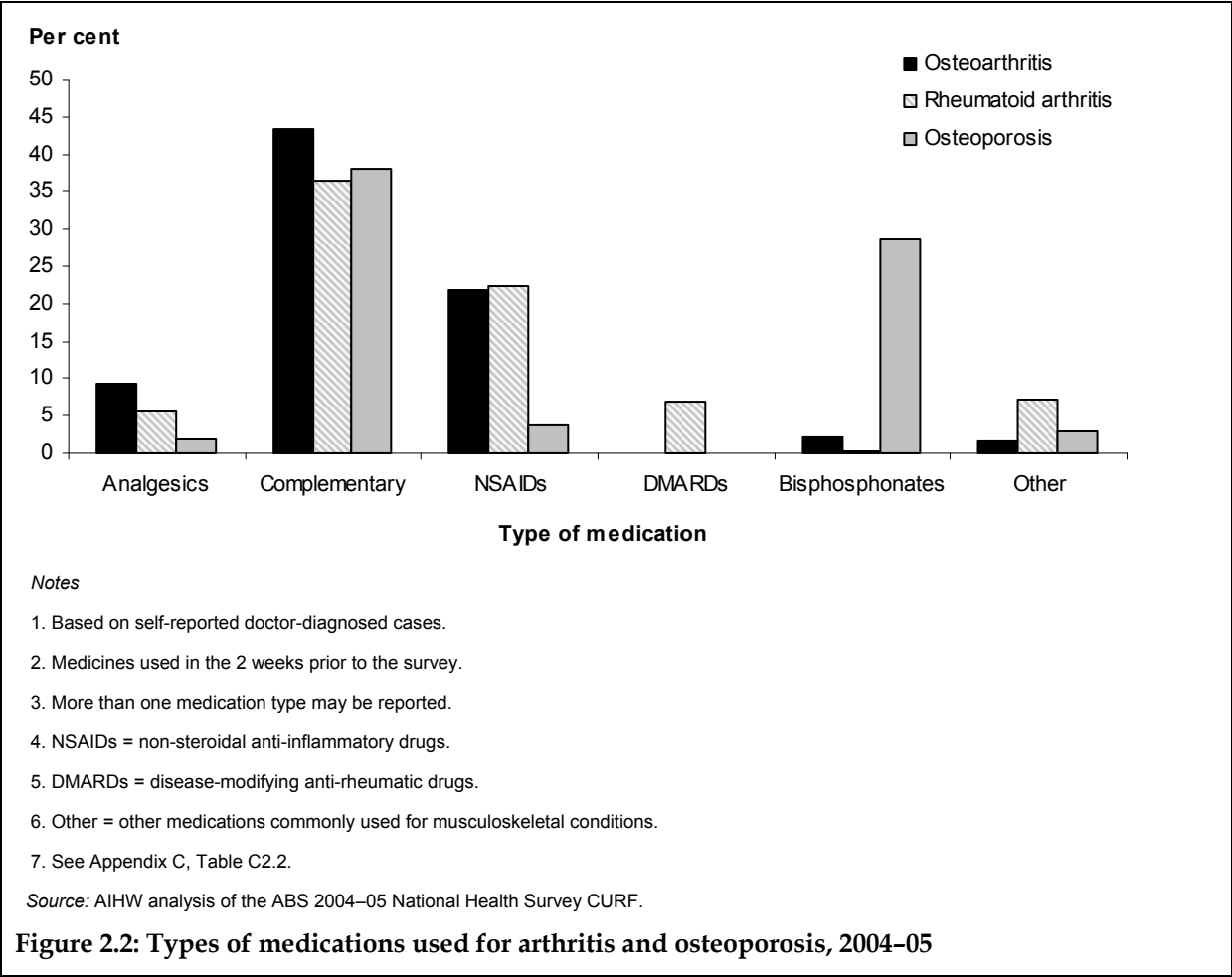


In July 2002, arthritis and musculoskeletal conditions were declared a National Health Priority Area (NHPA) and the *Better Arthritis Care* initiative was funded. The NHPA and the initiative were originally developed to monitor and support activities to reduce the burden of three musculoskeletal conditions: osteoarthritis, osteoporosis and rheumatoid arthritis (AIHW 2008a). In 2006, funding was extended through the *Better Arthritis and Osteoporosis Care* (BAOC) initiative, which now included juvenile idiopathic arthritis. The aims of this

initiative are to educate health professionals, raise awareness, provide education on self-management, prevent osteoporotic fractures and ensure medications are used appropriately. Although juvenile idiopathic arthritis is a focus area under the BAOC initiative, it has not been included in this report. As there are relatively small numbers of cases recorded in both the NHS and BEACH surveys, reliable estimates of medication use could not be calculated for this condition.

Major medication groups

Medicines used to manage arthritis and osteoporosis can be administered in many different shapes and forms. There are topical treatments and ointments used to alleviate inflammation and mild pain, tablets (often the most common) either to modify the symptoms (for example, analgesics) or the disease (for example, bisphosphonates), and injections which are administered directly into the affected joints to lubricate them or to slow disease progression. Although there are a wide variety of medications available for these conditions, the most common types reported are complementary medications, non-steroidal anti-inflammatory drugs (NSAIDs) and bisphosphonates (Figure 2.2).



Some of the most common and often the first types of medicines used to manage arthritis and osteoporosis are analgesics (Buys & Elliot 2009; RACGP 2009a). Pain-relieving, simple

analgesics, such as paracetamol, are commonly used in the early stages of arthritis and for osteoporotic fractures. Self-reported data indicate that people with osteoarthritis are more likely to use analgesics compared to people with rheumatoid arthritis or osteoporosis (Figure 2.2). But, in all three conditions, analgesics were less likely to be used than NSAIDs and complementary medicines.

Like analgesics, complementary medicines are commonly used as primary interventions for arthritis and osteoporosis. These types of medications are often used as first-line therapy for osteoarthritis and as combination therapy (with pharmaceuticals) for rheumatoid arthritis and osteoporosis (Little & Parsons 2000; Reginster et al. 2005; WHO 2003). People with osteoarthritis are more likely to report using complementary medicines than people with rheumatoid arthritis or osteoporosis (Figure 2.2).

As the most common pharmaceutical medications used to manage arthritis, NSAIDs offer relief from inflammation, reducing swelling and increasing mobility (Box 2.1). In people with osteoporosis, NSAIDs may be used to relieve pain after a fracture.

Box 2.1: Types of medications used for arthritis and osteoporosis

- *Non-steroidal anti-inflammatory drugs, or NSAIDs*, are used to relieve symptoms of pain, stiffness and inflammation in the muscles, joints and bones. NSAIDs can be selective or non-selective (see Box 2.1) and are commonly used to manage arthritis. Medications within this group include celecoxib, meloxicam, ibuprofen, diclofenac and naproxen.
- *Disease-modifying anti-rheumatic drugs or DMARDs* are immunosuppressant drugs used for rheumatoid arthritis. These types of medicines alter the disease progression, suppressing proteins of the immune system. Medications from this group include methotrexate, sulfasalazine, leflunomide and hydroxychloroquine*.
- *Biological disease-modifying anti-rheumatic drugs or bDMARDs* are specialised immunosuppressant medications used for rheumatoid arthritis. They alter disease progression by stopping cellular communication in the immune system. Medicines from this group include etanercept, adalimumab, infliximab, anakinra and rituximab.
- **Anti-resorptives** are a type of medication commonly used in osteoporosis. This group of medicines binds to bone to stop the removal of calcium, assisting in restoring bone density. Common medicines from this group include bisphosphonates such as alendronate, risedronate and other medications like strontium ranelate.
- **Analgesics** are medications that relieve pain. These types of medications are used to relieve the symptoms of mild, moderate and severe pain. Common medications used to manage arthritis and osteoporosis include paracetamol, tramadol and paracetamol combinations.
- **Complementary medicines** or alternate medications are vitamin, mineral or herbal supplements. This type of medication is commonly used in osteoporosis to increase levels of vitamin D and calcium. For arthritis, glucosamine and fish oils are commonly used to relieve pain and *swelling*.

*Hydroxychloroquine is also commonly referred to as an anti-malarial drug. This medication was commonly used as an anti-malarial to prevent and treat malaria and other parasitic infections. However due to the resistance of these parasites towards this medication, it is no longer routinely used for this purpose (ARA 2008a).

The loss of bone mineral density (BMD) is the major characteristic of osteoporosis. It has no overt symptoms and can progress undetected for many years (University of Melbourne 2007;

WHO 2003). The management of this condition requires specialised medications that help to reduce bone loss. People with osteoporosis most commonly use bisphosphonate medications as they slow the loss of bone and reduce the risk of fractures (Akesson 2003; Morello et al. 2009). Other medications such as strontium ranelate are also used for this purpose. As an autoimmune disease, rheumatoid arthritis requires pharmacological management which targets the immune system, controlling the disease's progression (NPS 2006). Disease-modifying anti-rheumatic drugs (DMARDs) and biological disease-modifying anti-rheumatic drugs (bDMARDs) are used predominantly for this purpose. These medications are designed to reduce or even stop disease activity (Box 1.3). About 7% of people with rheumatoid arthritis reported taking DMARDs in 2004–05 (Figure 2.2).

Medication use by area of residence

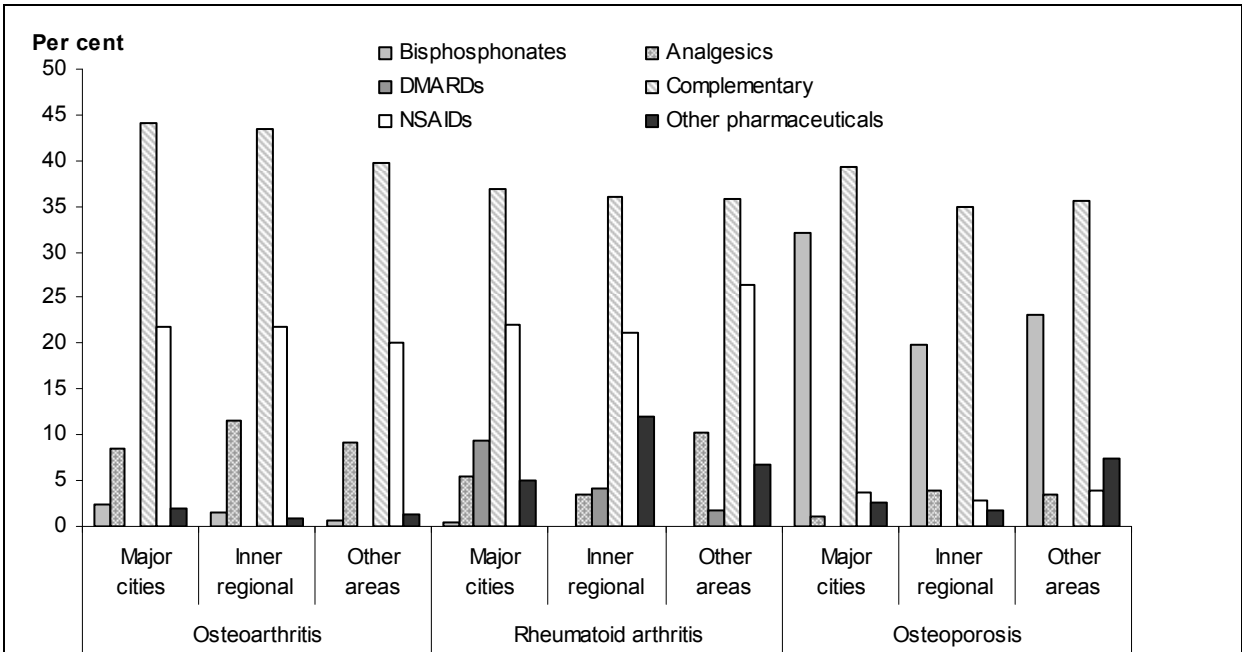
In general, people who live in *Remote areas* of Australia have poorer health than those living within the *Major cities* (AIHW 2008b). More likely to be disadvantaged with regard to education and employment opportunities, income, and access to health care and services, people from *Remote* locations are less likely to report having good or excellent health, and more likely to report having chronic conditions, such as arthritis and respiratory problems, compared with those in *Major cities* (AIHW 2008b).

The following three chapters of this report describe the use of specific medicines for managing osteoarthritis, rheumatoid arthritis and osteoporosis. However, NHS data on the use of specific medications cannot reliably be broken down by area of residence. Information about the use of broad medication groups by area of residence is provided below. This gives some insight into variations in arthritis and osteoporosis management by geographical location, which may indicate potential disparities in health care or access to treatment for these conditions that may need closer examination.

According to the 2004–05 NHS, in all three regions complementary medicines, NSAIDs and analgesics were the most common types of medicines used for osteoarthritis (Figure 2.3).

The distribution of some medication types for people with rheumatoid arthritis varied considerably between the three regions. People living in *Major cities* were more likely to report using DMARDs than those living in *Other areas*, who were more likely to be using analgesics. Complementary medicines were reported at similar rates across all three regions.

The most common pharmaceutical medicines used to manage osteoporosis are bisphosphonates. People living in major cities were more likely to report their use than people in *Inner regional* or *Other areas* (Figure 2.3).



Notes

1. Based on self-reported doctor-diagnosed cases.
2. Medicines used in the 2 weeks prior to the survey.
3. More than one medication type may be reported.
4. NSAIDs = non-steroidal anti-inflammatory drugs.
5. DMARDs = disease-modifying anti-rheumatic drugs.
6. Other pharmaceuticals = other medications commonly used for musculoskeletal conditions.
7. See Appendix E for a description of how area of residence is classified.
8. See Appendix C, Tables C2.3–C2.5.

Source: AIHW analysis of the ABS 2004–05 National Health Survey CURF.

Figure 2.3: Types of medication used for arthritis and osteoporosis, by area of residence, 2004–05

3 Pharmacotherapy of osteoarthritis

This chapter provides information on medications used to manage osteoarthritis. Using self-reported data and GP-patient encounter information, the most commonly reported pharmaceuticals and complementary medications are described. The chapter also examines trends in GP recommendation of medications over a 10-year period, and provides estimates of expenditure related to three of the most common prescription pharmaceuticals.

What is osteoarthritis?

Osteoarthritis is a degenerative condition caused by the loss of the articular cartilage within the movable joints. It mainly affects the weight-bearing joints of the knees and hips, as well as the hands, wrists and feet. It is the most common form of arthritis worldwide, and symptoms include low-grade inflammation, tenderness, crepitus (the sound or feeling of crunching or grating) and pain (AIHW 2008; Simpson 2004).

Osteoarthritis is a condition that requires consistent and ongoing management. Common actions taken to manage it include weight loss, increasing physical exercise, using alternate therapies, taking medications or having joints replaced. All these actions assist with reducing symptoms, increasing mobility and improving quality of life. The use of medications is often the quickest and easiest way to administer relief from symptoms, and is the most common action taken to manage this condition.

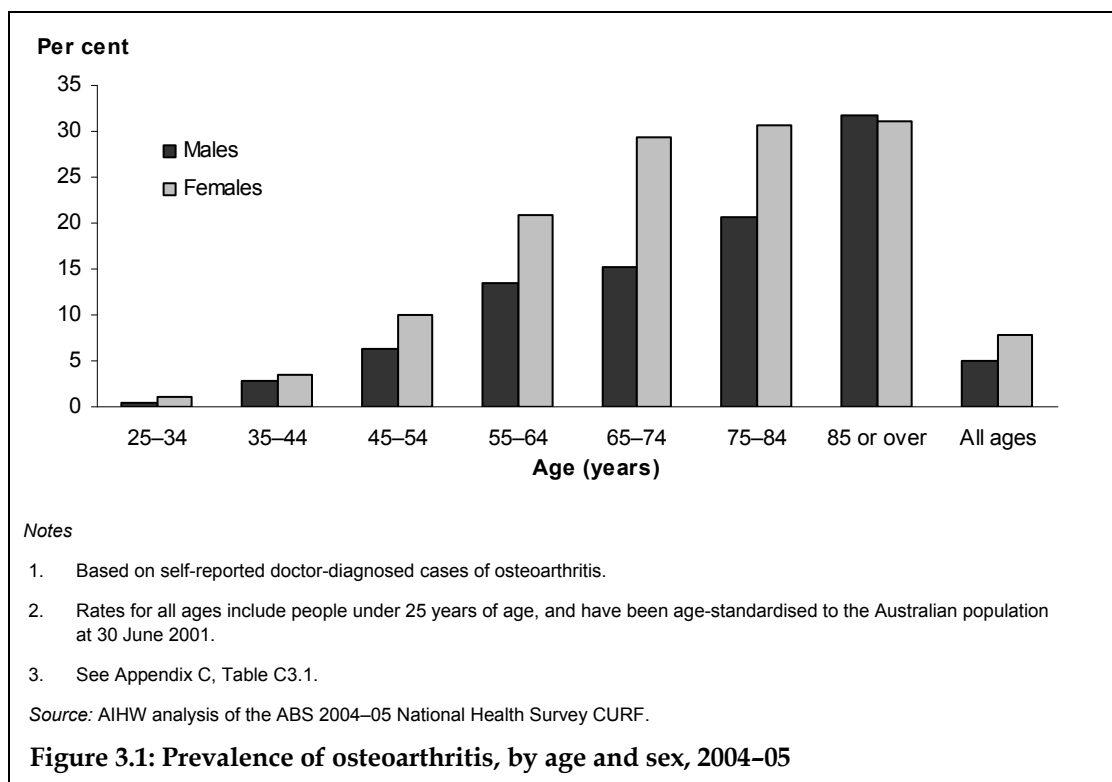
The extent of osteoarthritis in Australia

An estimated 1.5 million Australians (7.7%) had osteoarthritis in 2004–05. More likely to affect females (9%) than males (6%), the degenerative nature of this condition means it affects people as they age, with onset more likely to occur after the age of 55 years (Figure 3.1). Although commonly diagnosed within older age groups, this condition can also affect people in the younger age groups, with people under the age of 25 years reporting 1.5% of osteoarthritis cases.

Pharmacotherapy

The pharmacotherapy of osteoarthritis primarily centres on reducing symptoms (Buys & Elliot 2009). Medicines such as simple analgesics, complementary medicines and topical anti-inflammatory agents are frequently used to relieve pain and reduce inflammation. These medications are commonly used in the early stages of the condition, when symptoms are mild or moderate in nature.

When these medications fail to give adequate relief from pain or reduce inflammation, non-steroidal anti-inflammatory drugs (NSAIDs) are normally the next course of action (Buys & Elliot 2009; RACGP 2009A). Ranging in their strength and application, these medications are used to inhibit the inflammatory process without the use of steroids (hence the name 'non-steroidal').



When medication and other management strategies are no longer adequate, surgery is the next option (Felson et al. 2000). Osteotomies, arthroscopies and joint replacements are used in the more severe cases of osteoarthritis, where the damage to the bones and cartilage is so advanced that medications alone cannot help to manage the symptoms. Although a joint replacement may improve joint function and mobility, medication is often required to keep inflammation and pain to a minimum.

Common types of medicines

Simple analgesics, NSAIDs/COX-2 inhibitors (see Box 3.1) and complementary medicines are the most common medications used for osteoarthritis (Figure 3.2).

Box 3.1: The difference between selective and non-selective NSAIDs

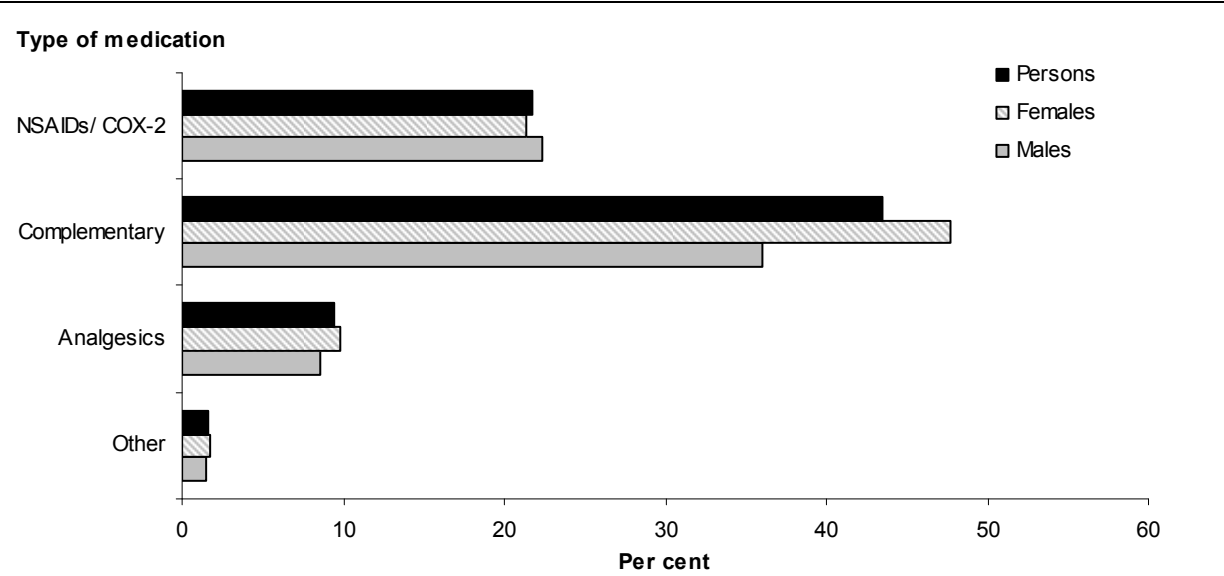
NSAIDs are medications that relieve inflammation and reduce pain and swelling in joints. Commonly used to manage osteoarthritis and rheumatoid arthritis, there are two different types of NSAIDs available: selective and non-selective. The difference relates to how these medications affect the COX enzymes.

The cyclo-oxygenase enzymes (COX for short) are enzymes linked to the inflammatory process and maintaining parts of the stomach lining. In the early 1990s, researchers discovered two different types of cyclo-oxygenase enzymes, COX-1 and COX-2 (Henry & Joyner 2006). The COX-1 enzyme maintains the stomach lining and the COX-2 enzyme is part of the inflammatory response.

Non-selective NSAIDs block both the COX-1 and COX-2 enzymes. These NSAIDs are effective in treating inflammation but can cause irritation in the stomach, producing gastric ulcers and reflux. In this report, non-selective NSAIDs are referred to as NSAIDs.

Selective NSAIDs block only the COX-2 enzyme, relieving inflammation without causing stomach irritations. In this report, selective NSAIDs are referred to as COX-2 inhibitors.

Specifically targeting the symptoms of pain and inflammation, analgesics and complementary medications are often the first types of medicines used to manage this condition (Buys & Elliot 2009; Felson et al. 2000; RACGP 2009a). Easily obtained, simple analgesics, such as paracetamol and paracetamol combinations (for example, paracetamol and codeine), offer immediate relief for mild to moderate pain and are usually the first types of medicines to be recommended (Cleland et al. 2000). Analgesics are the third most common type of medicine used in managing osteoarthritis, with females more likely to report their use than males (Figure 3.2). When simple analgesics can no longer provide adequate pain relief, stronger analgesics such as tramadol, oxycodone and buprenorphine are often used. Complementary medicines are commonly used in the early stages of osteoarthritis (Campbell & Ruddock 2007; Ebell 2006; Fox et al. 2006; Goldberg & Katz 2007) and offer people an alternative or supplement to the more traditional pharmaceutical treatments. These types of medicines do not only relieve pain, but may also reduce inflammation (Fox et al. 2006; McAlindon et al. 2000; Zochling et al. 2004). People with osteoarthritis are more likely to report using complementary medicines than analgesics or NSAIDs (Figure 3.2). When analgesics and complementary medicines fail to provide adequate pain relief or reduce inflammation, NSAIDs are used as second-line therapies (Cleland et al. 2000; Mikahil et al. 2007). Disrupting the inflammatory process, these medications reduce inflammation, which in turn reduces pain and swelling.



Notes

1. Based on self-reported doctor-diagnosed cases of osteoarthritis.
2. Medicines used in the 2 weeks prior to the survey.
3. More than one medication type may be reported.
4. NSAIDs = non-steroidal anti-inflammatory drugs.
5. COX-2 = selective non-steroidal anti-inflammatory drugs that inhibit the COX-2 enzyme.
6. Other = other medications commonly used for musculoskeletal conditions (excluding DMARDs and bisphosphonates).
7. See Appendix C, Table 3.2.

Source: AIHW analysis of the ABS 2004–05 National Health Survey CURF.

Figure 3.2: Medication types used for osteoarthritis, by sex, 2004–05

The discovery of the different COX enzymes saw the introduction of NSAIDs that were more effective in managing arthritis – the COX-2 inhibitors or selective NSAIDs (see Box 3.1). These medications control the inflammatory response and have less chance of causing stomach irritations and ulcers often associated with non-selective NSAIDs. In 2009, there was only one COX-2 inhibitor available in Australia, celecoxib. Over the last 10 years, there have been several other COX-2 inhibitors released onto the market but severe adverse side effects have seen them recalled (for further information, see pages 27 and 29).

Pharmaceutical medicines

The five most common pharmaceuticals reported in the 2004–05 NHS and 2007–08 BEACH survey are outlined below. The data have been broken into two sections: self-reported medication use (NHS data) and GP-recommended medications (BEACH data). Data presented in this chapter relate to persons aged 35 years and over. Although the two data sources did include people under the age of 35 with osteoarthritis, the number of cases was quite small and reliable estimates of medication use could not be calculated.

Self-reported pharmaceutical use

According to data from the 2004–05 NHS, people with diagnosed osteoarthritis most commonly used the pharmaceuticals celecoxib (8%), paracetamol (7%) and meloxicam (5%) (see Appendix C, Table C3.3).

Males were more likely to report use of celecoxib than females. The use of this pharmaceutical generally increased with age for both sexes (Table 3.1).

Paracetamol use was reported at similar rates in both sexes. In females its use increased with age, with those aged 75 and over the most common group reporting usage, whereas in males those aged 55–74 years were the most common users.

Apart from celecoxib, people with osteoarthritis commonly reported use of other NSAIDs, including meloxicam and diclofenac sodium. Females were more likely to report meloxicam use than males and usage rose with age for both sexes. People aged 75 years and over were the most likely group to report using this pharmaceutical.

Males reported diclofenac sodium use more commonly than females (Table 3.1). For males its use increased with age, whereas for females it remained relatively stable across age groups.

Pharmaceuticals recommended by GPs

During an encounter with a GP, patients may be prescribed a medication, given a sample or advised to purchase it over the counter. Within the BEACH reports, medications are recorded as *prescribed*, *supplied* or *advised*. In this report the term ‘recommended’ is used to refer to all medications that GPs prescribe, supply or advise.

In 2007–08, GPs mainly recommended the pharmaceuticals paracetamol (23 per 100 osteoarthritis contacts), meloxicam (13 per 100) and celecoxib (8 per 100) (see Appendix C, Table C3.4).

Table 3.1: Self-reported pharmaceutical use for osteoarthritis, by age and sex, 2004–05

Medicine name	Males							
	35–54 years		55–74 years		75 years & over		35 years & over	
	'000	Per cent	'000	Per cent	'000	Per cent	'000	Per cent
Celecoxib	3.5	*2.8	29.5	12.1	10.7	*10.3	43.8	9.2
Paracetamol	5.3	*4.3	16.5	6.7	6.4	*6.2	28.3	6.0
Meloxicam	5.9	*4.7	8.3	*3.4	5.5	*5.3	19.7	4.2
Diclofenac	2.4	**1.9	12.7	*5.2	6.3	*6.0	21.4	4.5
Paracetamol combinations	1.6	**1.3	4.9	*2.0	1.6	**1.5	8.1	*1.7

Medicine name	Females							
	35–54 years		55–74 years		75 years & over		35 years & over	
	'000	Per cent	'000	Per cent	'000	Per cent	'000	Per cent
Celecoxib	11.8	*6.2	32.4	7.6	16.8	8.8	60.9	7.6
Paracetamol	11.9	*6.3	31.6	7.4	15.2	7.9	58.7	7.3
Meloxicam	9.0	*4.7	26.1	6.2	14.2	*7.4	49.4	6.1
Diclofenac	6.9	*3.6	15.9	3.7	5.8	*3.0	28.6	3.5
Paracetamol combinations	4.3	*2.3	6.4	*1.5	1.7	**0.9	12.3	*1.5

* Subject to high standard errors and should be used with caution (i.e. relative standard error of 25–50%).

** Subject to sampling variability too high for practical purposes (i.e. relative standard error greater than 50%).

Notes

1. Based on self-reported doctor-diagnosed cases of osteoarthritis.
2. Medicines used in the 2 weeks prior to the survey.
3. More than one medication may be reported.
4. Five most frequently reported pharmaceuticals presented.
5. Paracetamol combinations may include paracetamol with codeine and paracetamol with dextropropoxyphene.
6. Data for all persons can be found in Appendix C, Table C3.3.
7. A description of all medicines can be found in Appendix A.

Source: AIHW analysis of the ABS 2004–05 National Health Survey CURF.

Paracetamol was more likely to be recommended to people in the older age groups (55 years and over) than to people in the younger groups (less than 55 years) (Table 3.2). GPs were generally more likely to recommend paracetamol to females than to males.

Of the NSAIDs, GPs most commonly recommended meloxicam (13 per 100 osteoarthritis contacts). This pharmaceutical was recommended at a similar rate to both sexes, and showed similar age-related patterns, generally decreasing with age (Table 3.2).

The COX-2 inhibitor celecoxib was the third most common medication to be recommended by GPs. It was recommended to males and females at similar rates overall (8 per 100 osteoarthritis contacts), but showed no clear age-related pattern.

Table 3.2: Pharmaceuticals recommended by GPs for osteoarthritis, by age and sex, 2007–08

Medicine name	Males				
	35–54 years (n=137)	55–74 years (n=490)	75–84 years (n=237)	85 years & over (n=75)	35 years & over (n=939)
Per 100 osteoarthritis contacts (95% confidence interval)					
Paracetamol	5.3 (1.5,9.0)	18.8 (14.7,22.8)	22.3 (15.5,29.2)	41.6 (27.5,54.9)	19.5 (16.4,22.6)
Meloxicam	18.5 (10.5,26.6)	13.0 (8.7,17.2)	9.8 (5.2,14.3)	10.8 (2.7,18.8)	12.8 (9.6,16.0)
Celecoxib	8.2 (2.8,13.5)	10.2 (6.2,14.2)	5.5 (2.2,8.7)	6.3 (0,13.7)	8.4 (5.6,11.2)
Paracetamol & codeine	10.3 (4.3,16.3)	7.2 (4.3,10.0)	7.7 (4.0,11.5)	6.1 (0,12.7)	7.7 (5.5,9.9)
Tramadol	6.0 (1.7,10.4)	4.0 (1.6,6.4)	5.1 (1.4,8.8)	2.4 (0,7.0)	4.5 (2.8,6.1)
Medicine name	Females				
	35–54 years (n=235)	55–74 years (n=740)	75–84 years (n=338)	85 years & over (n=150)	35 years & over (n=1,463)
Per 100 osteoarthritis contacts (95% confidence interval)					
Paracetamol	17.7 (12.2,23.2)	22.6 (18.7,26.4)	32.5 (26.0,39.0)	37.8 (28.9,46.7)	25.6 (22.7,28.5)
Meloxicam	13.4 (8.2,18.6)	14.6 (11.3,17.9)	9.7 (5.6,13.9)	9.4 (3.9,14.9)	12.8 (10.2,15.3)
Celecoxib	7.6 (3.9,11.3)	7.9 (5.3,10.4)	8.4 (5.1,11.7)	3.3 (0.2,6.4)	7.5 (5.9,9.1)
Paracetamol & codeine	6.2 (2.3,10.0)	6.2 (4.1,8.4)	4.5 (2.3,6.7)	4.8 (1.4,8.1)	5.7 (4.2,7.1)
Tramadol	2.7 (0.4,5.0)	4.3 (2.4,6.2)	3.9 (1.6,6.2)	7.2 (0,14.5)	4.3 (2.9,5.6)

Notes

1. Based on GP–patient encounter data.
2. More than one medication may be recommended.
3. The five most frequently reported pharmaceuticals are presented.
4. Sample sizes may not add to totals due to missing values.
5. Data for all persons can be found in Appendix C, Table C3.4.
6. A description of all medicines can be found in Appendix A.

Source: AIHW analysis of the 2007–08 BEACH survey.

Complementary medicines

Complementary medicines are often used in conjunction with pharmaceuticals or as an alternative to traditional medicines. In recent years, evidence-based research regarding the use of complementary medicines has gained more momentum.

Clinical trials for glucosamine and omega 3 for osteoarthritis have indicated that these medications may be effective in reducing pain, inflammation and stiffness (Goldberg & Katz 2007; McAlindon et al. 2000). However there are contradictions between research findings and methodologies that call into question whether these medications are truly effective in controlling the symptoms of osteoarthritis (McAlindon et al. 2000).

The four most frequently reported complementary medicines from the 2004–05 NHS and two most common from the 2007–08 BEACH survey are discussed below. As with pharmaceuticals, the data have been broken in two sections: self-reported use (NHS) and medications recommended by GPs (BEACH).

Self-reported complementary medicine use

Information from the 2004–05 NHS indicates that complementary medicines were the most common type of medication to be reported for osteoarthritis (see Figure 3.2). Females were more likely to be report usage than males overall (48% compared to 36%), with the most common complementary medicines used to manage osteoarthritis being glucosamine (25%) and fish oils/omega 3 (16%).

Table 3.3: Self-reported complementary medicine use for osteoarthritis, by age and sex, 2004–05

Medication name	Males							
	35–54 years		55–74 years		75 years & over		35 years & over	
	'000	Per cent	'000	Per cent	'000	Per cent	'000	Per cent
Glucosamine	31.1	24.9	51.7	21.1	19.3	18.5	102.1	21.5
Fish oils/omega 3	14.6	11.7	33.4	13.6	11.5	*11.0	59.6	12.6
Calcium	3.5	*2.8	8.7	*3.5	9.9	*9.5	22.1	4.7
Chondroitin	9.0	*7.2	9.6	*3.9	3.3	*3.2	21.9	4.6
Medication name	Females							
	35–54 years		55–74 years		75 years & over		35 years & over	
	'000	Per cent	'000	Per cent	'000	Per cent	'000	Per cent
Glucosamine	43.0	22.6	128.7	30.3	41.2	21.5	212.8	26.4
Fish oils/omega 3	34.7	18.3	81.8	19.3	25.4	13.2	141.8	17.6
Calcium	32.7	17.2	57.7	13.6	31.8	16.6	122.2	15.2
Chondroitin	12.0	*6.3	34.2	8.1	7.7	*4.0	53.9	6.7

* Subject to high standard errors and should be used with caution (i.e. relative standard error of 25–50%).

Notes

1. Based on self-reported doctor-diagnosed cases of osteoarthritis.
2. Medicines used in the 2 weeks prior to the survey.
3. More than one medication may be reported.
4. Four most frequently reported complementary medicines presented.
5. Data for all persons can be found in Appendix C, Table C3.5.
6. A description of all medicines can be found in Appendix A.

Source: AIHW analysis of the ABS 2004–05 National Health Survey CURF.

Both sexes most commonly reported using glucosamine, with females more likely to report usage than males (Table 3.3). The reported use of glucosamine by males decreased with age, with males 75 years and over the least likely group to report using it. For females the use of glucosamine was more varied, with females aged between 55–74 years the most likely group to report its use.

People aged 55–74 years most commonly reported the use of fish oils/omega 3 (Table 3.3). Females rather than males were more likely to report using this second most common complementary medicine, similar to glucosamine use. People over the age of 75 years were the least likely to report using this medication.

Complementary medicines recommended by GPs

In 2007–08, GPs most commonly recommended the complementary medicines glucosamine and fish oils/omega 3 to people with osteoarthritis.

Glucosamine was the only complementary medicine reported to be recommended to people aged 85 years and over with osteoarthritis in 2007–08 (Table 3.4). Overall, this medication was recommended to males and females at similar rates, around 4 per 100 osteoarthritis contacts. In comparison to glucosamine, recommendation of fish oils/omega 3 overall was relatively low at around 1 per 100 osteoarthritis contacts, and varied little with age.

Table 3.4: Complementary medicines recommended by GPs for osteoarthritis, by age and sex, 2007–08

Medicine name	Males				
	35–54 years (n=137)	55–74 years (n=490)	75–84 years (n=237)	85 years & over (n=75)	35 years & over (n=939)
Per 100 osteoarthritis contacts (95% confidence interval)					
Glucosamine	4.7 (0.0,9.4)	3.9 (1.8,6.0)	3.2 (0.6,5.8)	0.9 (0,2.6)	3.6 (2.0,5.2)
Fish oils/omega 3	0.8 (0.0,2.5)	1.1 (0.0,2.3)	0	0	0.7 (0.1,1.3)
Medicine name	Females				
	35–54 years (n=235)	55–74 years (n=740)	75–84 years (n=338)	85 years & over (n=150)	35 years & over (n=1,463)
Per 100 osteoarthritis contacts (95% confidence interval)					
Glucosamine	7.7 (3.6,11.9)	2.7 (1.5,3.9)	3.5 (1.4,5.7)	3.4 (0.4,6.3)	3.8 (2.4,5.1)
Fish oils/omega 3	1.1 (0.0,2.4)	1.1 (0.4,1.8)	1.3 (0.0,2.6)	0	1.0 (0.5,1.6)

Notes

1. Based on GP–patient encounter data.
2. More than one medication may be recommended.
3. The two most frequently reported complementary medicines are presented.
4. Sample sizes may not add to totals due to missing values.
5. Data for all persons can be found in Appendix C, Table C3.6.
6. A description of all medicines can be found in Appendix A.

Source: AIHW analysis of the 2007–08 BEACH survey.

Trends in medications recommended by GPs

The pharmacotherapy of osteoarthritis has changed since the late 1990s. The introduction of new medications and the recall of others has altered the way GPs manage the condition. Between 1998–99 and 2007–08 a number of new medicines became available that could help to reduce the symptoms of osteoarthritis, the most notable being the COX-2 inhibitors.

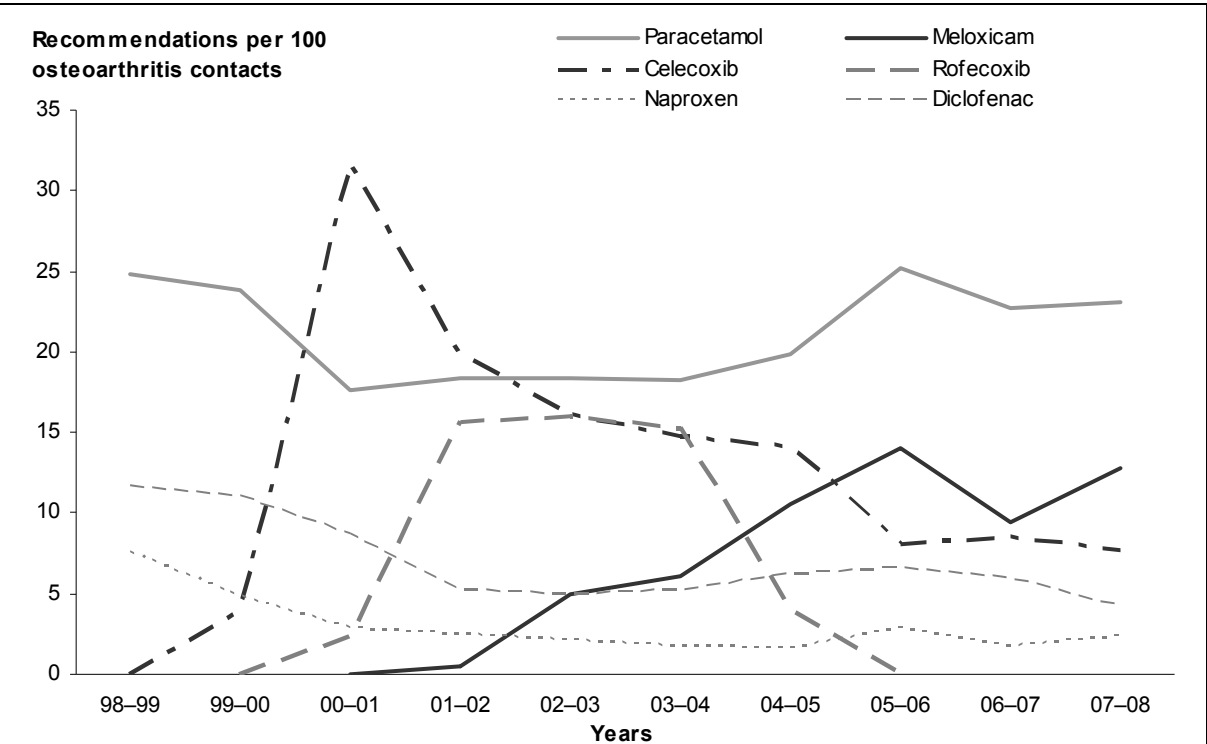
In 1999, celecoxib was released onto the market and was the first COX-2 inhibitor available in Australia for the management of arthritis. This medication became popular with GPs, as it offered relief from inflammation without the stomach irritation often associated with non-selective NSAIDs such as naproxen (Ausiello & Stafford 2002; Baker & Ferguson 2005). In July 2000, celecoxib became available for subsidy under the Pharmaceutical Benefits Scheme (PBS). The rapid uptake of this pharmaceutical by GPs is reflected in Figure 3.3, rising from 4 per 100 osteoarthritis contacts in 1999–00 to 32 per 100 in 2000–01. However, in 2001–02, the popularity of celecoxib with GPs diminished as a second COX-2 inhibitor, rofecoxib, was introduced onto the PBS schedule.

By 2001–02 the recommendation of rofecoxib had risen from 2 per 100 osteoarthritis contacts to 16 per 100, where it remained stable until 2003–04 (Figure 3.3). In late 2004 the Therapeutic Goods Administration (TGA) recalled rofecoxib from the market as clinical trials indicated

that using it for more than 18 months increased the risk of developing heart problems, such as cardiac arrest and stroke (TGA 2004). Between 2003–04 and 2004–05, GP recommendation of rofecoxib dropped from 15 to 4 per 100 osteoarthritis contacts.

The removal of rofecoxib adversely affected GPs’ recommendation of celecoxib. As another COX-2 inhibitor, celecoxib was classed in the same category as rofecoxib, causing a substantial reluctance by GPs to prescribe this medication (Hammett 2007; Mikahil et al. 2007; Zhang et al. 2007). Since 2005–06, recommendation of celecoxib has remained stable at around 8 per 100 osteoarthritis contacts (Figure 3.3). The apprehension in recommending celecoxib saw a rise in the use of naproxen, paracetamol and meloxicam.

Meloxicam was introduced to the Australian market in 2000–01, and became available on the PBS in February 2002. Its recommendation grew rapidly from 1 per 100 osteoarthritis contacts in 2001–02 to 14 in 2005–06, where it peaked for the ten-year period, possibly as a partial replacement for rofecoxib (Figure 3.3).



Notes

- 1. A description of all medicines can be found in Appendix A.
- 2. Based on GP–patient encounter data.
- 3. See Appendix C, Table C3.7.

Source: AIHW analysis of the 1998–99 to 2007–08 BEACH surveys.

Figure 3.3: Trends in pharmaceutical medicines recommended by GPs for osteoarthritis, 1998–99 to 2007–08

Overall the GP recommendation of paracetamol and naproxen did not vary greatly between 1998–99 and 2007–08. For most of this period, GPs most commonly recommended the pharmaceutical paracetamol for osteoarthritis. Its use decreased during the period when the COX-2 inhibitors became available, but increased to previous levels in 2005–06 after the withdrawal of rofecoxib. This pattern, on a smaller scale, is also seen in the recommendation of naproxen (Figure 3.3).

Expenditure

The allocated health expenditure for hospital-admitted patient services, out-of-hospital medical services (including GPs and specialists) and prescribed pharmaceuticals for osteoarthritis almost doubled (in constant prices) between 2000–01 and 2004–05 (AIHW 2009). Inflation-adjusted expenditure for osteoarthritis rose from \$842 million in 2000–01 to \$1.2 billion in 2004–05, a 42% increase, the majority of which was attributed to hospital-admitted patient services and out-of-hospital medical services. The expenditure for prescribed pharmaceuticals for osteoarthritis decreased by \$14 million, but still accounted for 9% of the health expenditure for osteoarthritis in 2004–05.

In 2007–08, the three most commonly recommended prescription pharmaceuticals for osteoarthritis were meloxicam, celecoxib and tramadol (Table 3.2). Use of these pharmaceuticals for osteoarthritis was estimated to cost consumers and government around \$13 million and \$71 million, respectively, in 2007 (Table 3.5).

Meloxicam was the most expensive prescription medication used for the management of osteoarthritis in 2007, at a total estimated cost of more than \$44 million. The cost of all three pharmaceuticals was significantly higher for government than for consumers, with costs to government for meloxicam and celecoxib estimated to be 5 to 6 times the costs to consumers.

Table 3.5: Estimated expenditure on selected pharmaceuticals for osteoarthritis, 2007

Medication name	Number of prescriptions	Estimated expenditure	
		Consumer expenditure	Government expenditure
Meloxicam	1,624,130	\$7,350,737	\$36,892,043
Celecoxib	1,206,609	\$5,168,631	\$32,154,274
Tramadol	105,241	\$534,430	\$1,586,084

Notes

1. Costs are estimated by allocating PBS prescriptions to disease, based on proportion of the prescriptions for specific diseases recorded in the BEACH survey. See Appendix B for details.
2. Only includes prescriptions where a subsidy was paid through PBS or RPBS.

Source: AIHW analysis of PBS administrative data 2007, and the 2007–08 BEACH survey.

New treatments and COX-2 inhibitor recall

As noted previously, medications for arthritis and musculoskeletal conditions have progressed considerably since the 1990s. New advancements in treatment and a better understanding of these conditions have seen an influx of new medications and treatments become available. The data presented in this report only reflect the medications that were available for osteoarthritis in 2004–05 and from April 2007 to March 2008, and do not consider more recent developments and changes to medications. Recent clinical trials for complementary medications and concerns regarding the use of a second COX-2 inhibitor have affected the way GPs and people with osteoarthritis now manage the condition. These changes are outlined below.

New treatments

Viscosupplementation (injection of fluid into a joint) is a relatively new treatment used to manage knee osteoarthritis. This treatment requires an injection of hyaluronic acid (HA) into the affected joints to improve the lubricating properties of synovial fluid, reducing pain and improving mobility (Baker & Ferguson 2005). HA occurs naturally in synovial joints, acting as a protective coating around cartilage cells. In people with osteoarthritis, HA becomes thinner, making the joint more susceptible to damage. A 2006 Cochrane Collaboration review (Bellamy et al. 2006) analysed 76 clinical trials for viscosupplementation of HA in the treatment of knee osteoarthritis. The report suggests that HA could improve mobility and reduce pain of knee osteoarthritis (Campbell & Ruddock 2007). However, there have been mixed reviews about the long-term effects and efficacy of this treatment (Campbell et al. 2004).

Current guidelines for osteoarthritis management state that viscosupplementation for hip osteoarthritis is not beneficial (RACGP 2009a).

COX-2 inhibitor recall

Separate to the recall of the COX-2 inhibitor rofecoxib in 2004 (see page 27), a second COX-2 inhibitor was also removed from the Australian market. Lumiracoxib was added to the PBS in 2006 but was removed from the market on 27 August 2007 amid concerns of liver complications. The TGA received eight reports, six submitted 6 weeks prior to the recall, indicating severe adverse liver effects due to the use of lumiracoxib. The most serious reactions resulted in two deaths and two liver transplants (Hammett 2007). Since the recall, lumiracoxib has not been available for purchase in Australia.

4 Pharmacotherapy of rheumatoid arthritis

This chapter provides information on medications used to manage rheumatoid arthritis. Based on self-reported data and general practitioner (GP)–patient encounter information, the most frequently used pharmaceuticals and most common complementary medicines are described. The chapter also provides trends in GP recommendation of medications and estimates of expenditure related to three of the most common prescription pharmaceuticals.

What is rheumatoid arthritis?

Rheumatoid arthritis is an autoimmune disease in which a person's immune system attacks and destroys its own cells, particularly those lining the joints. It is estimated to affect around 1% of the world's population (Fleischmann et al. 2005; Roberts et al. 2006). Normally affecting joints in a symmetrical fashion, its symptoms include low-grade inflammation, swelling, stiffness, severe pain, fatigue and general malaise. If left untreated, the disease can progress to the ligaments, tendon sheaths and bones (Gray 2003; Martini 2004). A systemic disease, rheumatoid arthritis also affects other areas of the body, including vital organs, and has been linked to premature mortality (Maiden et al. 1999; Peltomaa et al. 2002; Roberts et al. 2006).

The extent of rheumatoid arthritis in Australia

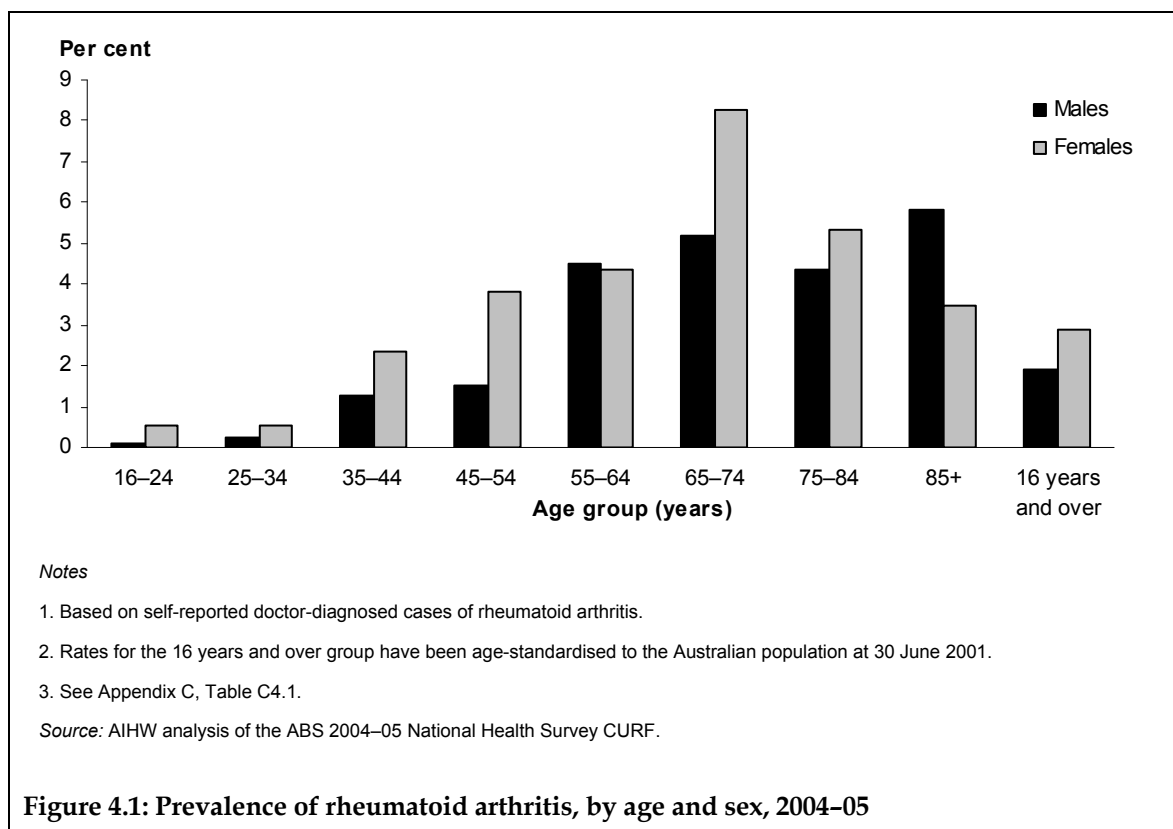
NHS self-reports suggest that approximately 2% of Australians (384,000 people) have rheumatoid arthritis. Around two-thirds of those affected are females. The disease is most likely to be diagnosed between the ages of 30–54 years (AIHW 2008a).

The prevalence of rheumatoid arthritis is highest in the age groups 65–74 years in females and 85 years or over in males (Figure 4.1). It is generally more common in females except among the oldest age group. Although more prominent in the older age groups, rheumatoid arthritis also affects 2% of females and 1% of males aged 35–44 years.

Although based on self-reports of a doctor's diagnosis, the NHS data for rheumatoid arthritis are believed to overestimate the prevalence of the condition. This may be due to confusion with the word 'rheumatism', a general term for musculoskeletal pain which older people often use.

Pharmacotherapy

The pharmacotherapy of rheumatoid arthritis has changed dramatically over the last 20 years. In the past, simple analgesics, complementary medicines and non-steroidal anti-inflammatory drugs (NSAIDs) were the most common medications used to manage this disease. These medicines targeted the symptoms of rheumatoid arthritis but did nothing to slow or alter disease progression (Kremers et al. 2004).



Rheumatoid arthritis progresses rapidly. Research over the last decade has shown that within the first few months of disease onset, a person can develop irreversible joint damage and deformities, and considerably decrease their life expectancy (Kremers et al. 2004; Vencovsky & Huizinga 2006). In order to reduce this risk, the early use of immunomodulating agents, such as disease-modifying anti-rheumatic drugs (DMARDs) is needed.

Early diagnosis and immediate use of DMARDs and biologics (bDMARDs) produces better clinical, radiological and functional outcomes, improving a person’s quality of life and reducing disability and impairment (Fleischmann et al. 2005; Symmons & Silman 2006). DMARDs and bDMARDs are medicines that target the cause of the disease, slowing or stopping immune cells from attacking the joints and reducing joint damage (NPS 2007; RACGP 2009b; Tonks 2008).

In the past, these types of medications were not used until there was sufficient radiological (X-ray) evidence indicating the affected joints had deteriorated significantly (Kremers et al. 2004). In the late 1990s, however, this practice changed, moving away from a symptom-based approach, and immunomodulating medications were recommended as one of the first medicines to be used when managing the disease. The use of NSAIDs, analgesics and complementary medicines took second place, used in conjunction with DMARDs and bDMARDs to help relieve symptoms (Emery & Kvien 2007; Goldberg & Katz 2007; RACGP 2009b; Scott 2007).

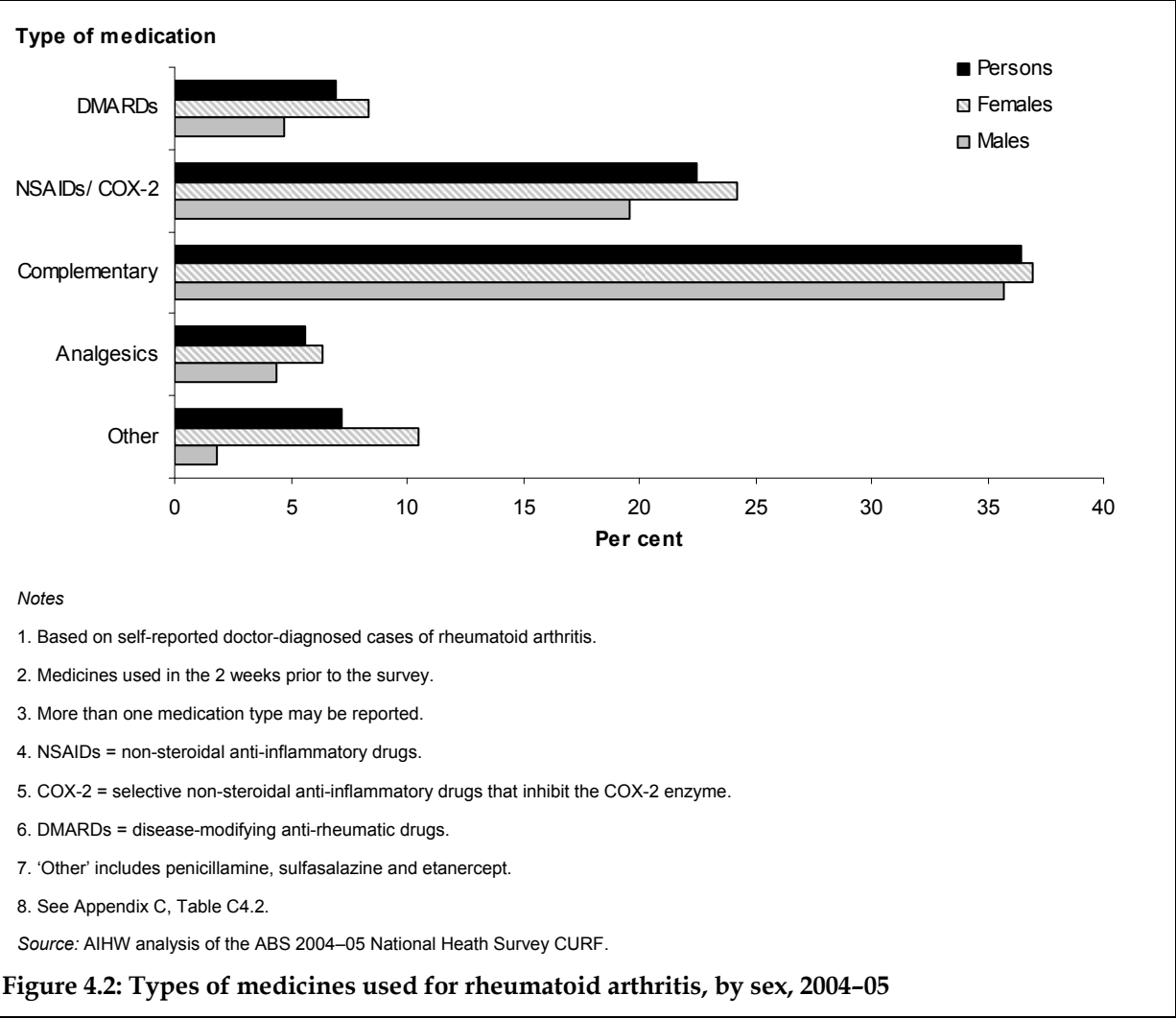
Common types of medicines

Medications used to manage rheumatoid arthritis focus on reducing the impact the disease has on an individual, controlling its progression and relieving symptoms. The main

medications used to achieve these objectives are DMARDs, NSAIDs, complementary medicines and analgesics.

The most common pharmaceutical medications used to manage rheumatoid arthritis are NSAIDs (Figure 4.2). Often used in conjunction with other medications, NSAIDs reduce symptoms of inflammation, swelling and pain.

Complementary medicines are also commonly used to manage rheumatoid arthritis (Figure 4.2). Primarily used to complement pharmaceuticals, these medicines help reduce the risk of pharmacologically induced conditions, such as osteoporosis, and may relieve pain and inflammation.



As outlined above, pharmacotherapy strategies used in rheumatoid arthritis have changed considerably over the last 20 years, and are still evolving. Because of this, the data presented in this report may not reflect the medications and strategies used to manage this disease in 2009 and 2010.

New medicines and PBS restrictions

As noted above, there has been a boom in the types of medications used to manage rheumatoid arthritis. Discoveries about how the disease progresses and what proteins are involved in its development have initiated rapid advances in medicines and changes to the way existing medicines are used. In order to give a clearer picture of how medications are currently used for rheumatoid arthritis, this section describes these relatively new types of medications, briefly explains how they help to manage the disease, and notes relevant PBS restrictions on their use.

Specialist prescriptions: the use of biological agents (bDMARDs)

Biological disease-modifying anti-rheumatic drugs (bDMARDs) are new types of medications that target the autoimmune response in rheumatoid arthritis, neutralising the proteins which the immune system makes. These medications reduce inflammation and pain as well as altering and slowing disease progression.

Currently in Australia there are six bDMARDs available to manage rheumatoid arthritis – etanercept, infliximab, adalimumab, anakinra, abatacept and rituximab. These six medications can be categorised into four subtypes: tumour necrosis factor (TNF) inhibitors, interleukin-1 (IL-1) antagonists, T-cell co-stimulators and anti-CD20 antibodies (Box 4.1).

Biological DMARDs are not given to all cases of rheumatoid arthritis. Only a rheumatologist or clinical immunologist can prescribe these medications to adults who have severe active rheumatoid arthritis and who meet the restriction criteria outlined by Medicare Australia. Information on these restrictions can be found in Appendix D.

Disease-modifying anti-rheumatic drugs (DMARDs)

Currently in Australia, there are nine DMARDs available on the PBS for managing rheumatoid arthritis. Methotrexate is the first line choice and is normally the first DMARD used (Christie et al. 2007; Cleland et al. 2000; Emery & Kvien 2007; Fleischmann et al. 2005; Horng 2007).

If the use of methotrexate is ineffective or a person is intolerant to it, leflunomide is often the next DMARD to be employed, managing the moderate to severe cases of the disease (RACGP 2009b; Simpson 2004). The remaining seven DMARDs (sulfasalazine, hydroxychloroquine, azathioprine, cyclosporin, aurothiomalate, auranofin and penicillamine) can be used individually or in conjunction with methotrexate to improve overall effectiveness.

DMARDs can be used as single-line therapy or in combination with other pharmaceuticals. How and when these types of medications are used to manage rheumatoid arthritis depends upon the person, their previous treatment and the current stage of the disease:

- Sulfasalazine is an immunosuppressant medicine that is often used in early rheumatoid arthritis or when the use of methotrexate is contraindicated. It is increasingly being used in combination with methotrexate and other DMARDs. Sulfasalazine contains an anti-inflammatory and an antibiotic, which helps to slow the progression of rheumatoid arthritis (Lee & Pile 2003).
- Hydroxychloroquine is normally given in conjunction with another DMARD, commonly methotrexate or sulfasalazine, for moderate to severe cases of rheumatoid arthritis. It can

also be used as the sole medication for people with mild cases of rheumatoid arthritis (Lee & Pile 2003; NPS 2006).

- Azathioprine, cyclosporine, sodium aurothiomalate, auranofin and penicillamine are infrequently used now in Australia but may be prescribed when methotrexate, leflunomide and sulfasalazine have failed or cannot be tolerated.

Box 4.1: Biological DMARDs

Biological DMARDs are medications that are used to slow or stop immune cell activation, by interrupting cellular communication. There are four subcategories of bDMARDs, each of which act upon a different component of the immune system response:

- **Tumour necrosis factor (TNF)** is a stimulator of the immune response. The overproduction of TNF proteins by immune cells causes inflammation, bone erosion and synovial damage (Nash & Florin 2005). The bDMARDs etanercept, infliximab and adalimumab inhibit TNF production.
- **Interleukin-1 (IL-1)** is a protein produced in a variety of cells, including specialised cells of the synovial lining (Bryant & Knights 2007). This protein stimulates responses involved in the immune defences against infections, but also causes joint damage in rheumatoid arthritis. Anakinra is an antagonist that prevents IL-1 from binding to its receptor, blocking the inflammatory process and slowing the destruction of the joints.
- T-cells belong to a group of white blood cells called lymphocytes, which play a pivotal role in the immune response. **T-cell co-stimulation** is an advanced process of the immune system response, which involves the stimulation of T-cells in conjunction with antigens (Sharpe & Abbas 2006). Abatacept blocks this co-stimulation, altering the immune responses and suppressing the overproduction of T-cells.
- B-cells are white blood cells that produce antibodies, which are an important component of the immune response. Rituximab is an **anti-CD20 antibody** that acts to deplete B-cells and the antibodies they produce (Mack 2008). Rituximab temporarily removes the antibodies that attack the synovial joints, reducing inflammation and joint damage (TGA 2007). Originally used for people with non-Hodgkin lymphoma, rituximab became available to adults with severe active rheumatoid arthritis in 2006.

New insights: some new evidence for complementary medicines

Recent clinical research into complementary medicines has identified two polyunsaturated fatty acids that may assist in reducing the pain of rheumatoid arthritis. Omega 3 and gamma-linolenic acid (GLA) have recently shown some analgesic qualities, reducing tenderness in joints, pain and morning stiffness (Fortin et al. 1995; Goldberg & Katz 2007; Little & Parsons 2000).

Although there are some positive indications for the use of omega 3 and GLA, studies are inconclusive due to varied methodological procedures and outcomes.

Pharmaceutical medicines

As well as offering relief from the symptoms of pain, inflammation and stiffness, pharmaceuticals such as DMARDs play an important role in altering the disease's progression (Horng 2007; Reginster et al. 2002; Vencovsky & Huizinga 2006). The main types

of pharmaceuticals used to manage rheumatoid arthritis are NSAIDs, DMARDs, analgesics and other medications, such as corticosteroids.

As rheumatoid arthritis affects around 2% of the Australian population it is not often well represented in population surveys. In both the NHS and BEACH surveys the sample of people with this disease is relatively small, meaning that the statistics calculated from these surveys are less precise than those for more common diseases, such as osteoarthritis. For the majority of medicines represented in Tables 4.2 and 4.3 the estimates have a high relative standard error (more than 25%) and should be interpreted with caution. Differences between age and sex groups are not statistically significant in many cases, but do provide a general indication of variations in pharmacotherapy.

The five most frequently reported pharmaceuticals identified in the 2004–05 NHS and 2007–08 BEACH survey are outlined below. The data have been broken into two sections: self-reported medication use (NHS) and pharmaceuticals recommended by GPs (BEACH).

The data presented in this section have been restricted to people aged 35 years and over. Although both data sources did include people under the age of 35 with rheumatoid arthritis, the number of cases was quite small and reliable estimates of medication use could not be calculated.

Self-reported pharmaceutical use

Information from the 2004–05 NHS suggests that the most common pharmaceuticals people with rheumatoid arthritis used were celecoxib (8%) methotrexate (6%) and diclofenac sodium (6%) (see Appendix C, Table C4.3).

Females were more likely to report celecoxib use than males (10% compared to 5%), and the most likely group to report using it was females aged 55–74 years (Table 4.1). The number of males using celecoxib decreased with age.

People with rheumatoid arthritis reported methotrexate as the second most common pharmaceutical, and this was often the first DMARD used to manage their condition. Females used it more commonly than males (Table 4.1). Its use increased with age in males, but was more varied in females.

Other pharmaceuticals reported for rheumatoid arthritis treatment included the NSAIDs diclofenac sodium, naproxen and meloxicam. Diclofenac sodium is the only pharmaceutical in Table 4.1 that males were more likely to use than females. Females were more likely to report use of meloxicam, with usage increasing with age. Among males the use of meloxicam and naproxen decreased with age, with no males in the 75 years and over age group reporting these medications.

Table 4.1: Self-reported pharmaceutical use for rheumatoid arthritis, by age and sex, 2004–05

Medicine name	Males							
	35–54 years		55–74 years		75 years & over		35 years & over	
	'000	Per cent	'000	Per cent	'000	Per cent	'000	Per cent
Celecoxib	3.3	*8.3	2.9	**3.5	0.4	**2.0	6.6	*4.6
Methotrexate	1.3	**3.4	3.3	**4.0	1.0	**4.8	5.6	*3.9
Diclofenac sodium	2.6	**6.6	5.5	*6.7	1.6	**7.5	9.7	*6.8
Naproxen	1.6	**4.0	0.9	**1.1	0	0	2.4	**1.7
Meloxicam	0.7	**1.9	0	0	0	0	0.7	**0.5
Medicine name	Females							
	35–54 years		55–74 years		75 years & over		35 years & over	
	'000	Per cent	'000	Per cent	'000	Per cent	'000	Per cent
Celecoxib	9.9	*11.3	11.7	*11.4	0.6	**2.0	22.3	10.0
Methotrexate	7.2	*8.2	9.9	*9.6	0	0	17.0	7.7
Diclofenac sodium	6.1	*7.0	3.8	*3.6	1.0	*3.1	10.9	*4.9
Naproxen	5.6	*6.4	1.0	**1.0	1.0	**3.1	7.6	*3.4
Meloxicam	2.1	**2.4	4.3	*4.1	1.8	**5.6	8.1	*3.7

* Subject to high standard errors and should be used with caution (i.e. relative standard error of 25–50%).

** Subject to sampling variability too high for practical purposes (i.e. relative standard error greater than 50%).

Notes

1. Based on self-reported doctor-diagnosed cases of rheumatoid arthritis.
2. Medicines taken in the 2 weeks prior to the survey.
3. More than one medication may be reported.
4. Five most frequently reported pharmaceutical medicines presented.
5. Data for all persons can be found in Appendix C, Table C4.3.
6. A description of all medicines is in Appendix A.

Source: AIHW analysis of the ABS 2004–05 National Health Survey CURF.

Pharmaceuticals recommended by GPs

During an encounter with a GP, the GP may prescribe medications to the patient, supply medications to them or advise over-the-counter purchase. Within the BEACH survey, when a GP recommends a medication it is recorded as *supplied, prescribed or advised*. In this report the term ‘recommended’ is used to refer to medications that were prescribed, supplied or advised by GPs.

In the 2007–08 BEACH survey GPs most commonly recommended the following pharmaceuticals for rheumatoid arthritis: methotrexate (19 per 100 rheumatoid arthritis contacts), paracetamol (8 per 100), hydroxychloroquine (7 per 100) and prednisolone (7 per 100) (see Appendix C, Table C4.4).

Methotrexate is often the first pharmaceutical to be recommended in managing rheumatoid arthritis (Lee & Pile 2003; RACGP 2009b; Roberts et al. 2006). It was more likely to be recommended to females than to males, and was the most common medicine in both sexes (Table 4.2).

GPs most commonly recommended the analgesic paracetamol for this disease, and it was more likely to be recommended to females than to males. For females, the recommendation

of paracetamol generally increased with age, countering the decrease in other pharmaceuticals.

Although there were encounters for rheumatoid arthritis in males aged 85 years and over recorded in the 2007–08 BEACH survey, GPs did not recommend any of the pharmaceuticals listed in Table 4.2 to manage their disease.

Table 4.2: Pharmaceuticals recommended by GPs for rheumatoid arthritis, by age and sex, 2007–08

Medicine name	Males				
	35–54 years (n=26)	55–74 years (n=64)	75–84 years (n=27)	85 years & over (n=4)	35 years & over (n=121)
	Per 100 rheumatoid arthritis contacts (95% confidence interval)				
Methotrexate	2.5 (0,7.8)	24.1 (8.5,39.7)	12.3 (0,26.7)	0	16.1 (7.4,24.7)
Paracetamol	0	5.1 (0,10.8)	7.4 (0,22.2)	0	4.4 (0.1,8.6)
Hydroxychloroquine	3.6 (0,8.9)	2.8 (0,6.1)	5.5 (0,11.6)	0	3.1 (0.3,5.9)
Prednisolone	5.6 (0,14.5)	5.9 (0,13.0)	12.3 (0,26.1)	0	7.1 (2,12.2)
Meloxicam	8.1 (0,20.9)	4.9 (0,10.7)	7.2 (0,22.3)	0	6.0 (1.3,10.7)
	Females				
	35–54 years (n=77)	55–74 years (n=147)	75–84 years (n=51)	85 years & over (n=9)	35 years & over (n=284)
	Per 100 rheumatoid arthritis contacts (95% confidence interval)				
Methotrexate	20.0 (9.5,30.6)	20.4 (12.1,28.7)	22.4 (8.8,36.1)	12.9 (0,35.1)	20.4 (14.3,26.6)
Paracetamol	5.8 (0,11.8)	8.4 (2.9,13.9)	13.1 (2.6,23.7)	15.7 (0,38.6)	8.8 (5.0,12.6)
Hydroxychloroquine	3.5 (0,8.1)	10.4 (4.5,16.4)	9.9 (0,20.4)	0	8.3 (4.4,11.8)
Prednisolone	4.3 (0,9.3)	4.8 (0.5,9.0)	12.8 (1.0,26.6)	11.8 (0,32.8)	6.3 (2.8,9.9)
Meloxicam	13.1 (3.9,22.3)	5.9 (1.4,10.4)	0	0	6.6 (3.1,10.0)

Notes

1. Based on GP–patient encounter information.
 2. More than one medication may have been recommended.
 3. Five most frequently reported pharmaceutical medicines presented.
 4. Sample sizes may not add to totals due to missing values.
 5. Data for all persons can be found in Appendix C, Table C4.4.
 6. A description of all medicines can be found in Appendix A.
- Source: AIHW analysis of the 2007–08 BEACH survey.

Complementary medicines

Often taken in conjunction with pharmaceuticals, complementary medicines are used to reduce the risk of other conditions (such as osteoporosis) and help to relieve inflammation and pain (Cleland et al. 2000; Goldberg & Katz 2007). The most common complementary medicines used to manage rheumatoid arthritis include omega 3, glucosamine and folic acid. Similar to that for pharmaceutical medicines, the data presented in Table 4.3 need to be interpreted with caution as some estimates have a relative standard error above 50%.

Self-reported complementary medicine use

Data from the 2004–05 NHS suggest that males and females with rheumatoid arthritis use complementary medicines at a similar rate (37% and 36%, respectively). The most commonly reported medicines were fish oils/omega 3 (16%), glucosamine (15%) and calcium (8%).

Table 4.3: Self-reported complementary medicine use for rheumatoid arthritis, by age and sex, 2004–05

Medicine name	Males							
	35–54 years		55–74 years		75 years & over		35 years & over	
	'000	Per cent	'000	Per cent	'000	Per cent	'000	Per cent
Fish oils/omega 3	8.3	*21.3	8.2	*10.0	4.1	*19.3	20.6	14.5
Glucosamine	4.1	*10.5	7.0	*8.5	6.7	*31.6	17.8	12.5
Calcium	0	0	8.0	*9.8	0.4	**1.8	8.4	*5.9
Chondroitin	0.3	**0.8	0.2	**0.3	0.5	**2.3	1.0	**0.7
Medicine name	Females							
	35–54 years		55–74 years		75 years & over		35 years & over	
	'000	Per cent	'000	Per cent	'000	Per cent	'000	Per cent
Fish oils/omega 3	13.5	*15.4	20.5	19.8	4.8	*15.1	38.7	17.4
Glucosamine	12.7	*14.5	18.2	17.6	4.5	*14.5	35.5	16.0
Calcium	3.9	*4.4	12.4	*12.0	2.9	**9.3	19.2	8.7
Chondroitin	3.5	*4.0	4.9	*4.8	0.5	**1.7	9.0	*4.1

* Subject to high standard errors and should be used with caution (i.e. relative standard error of 25–50%).

** Subject to sampling variability too high for practical purposes (i.e. relative standard error greater than 50%).

Notes

1. Based on self-reported doctor-diagnosed cases of rheumatoid arthritis.

2. Medicines taken in the 2 weeks prior to the survey.

3. More than one medication may be reported.

4. Four most frequently reported pharmaceutical medicines presented.

5. Data for all persons can be found in Appendix C, Table C4.5.

6. A description of all medicines can be found in Appendix A.

Source: AIHW analysis of the ABS 2004–05 National Health Survey CURF.

Females were more likely to use fish oils/omega 3 than males (Table 4.3). The groups most likely to report using this medicine were females aged 55–74 years and males aged 35–54 years.

People with rheumatoid arthritis reported glucosamine as the second most common complementary medicine. As with fish oils/omega 3, females were more likely to use glucosamine than males.

Complementary medicines recommended by GPs

In the BEACH survey of 2007–08 GPs recommended only five complementary medicines to people with rheumatoid arthritis. Because of the low frequencies, detailed estimates are not presented here.

The majority of GP recommendations for complementary medicines for rheumatoid arthritis were to patients in the older age groups (55 years and over) with folic acid the most common (3 per 100 contacts).

Trends in medications recommended by GPs

Data from the BEACH surveys from 1998–99 to 2007–08 illustrate the changes in the way pharmaceuticals are used to manage rheumatoid arthritis, with the focus shifting from relieving symptoms to targeting disease progression.

Over this period GPs most commonly recommended the medications methotrexate, paracetamol, sodium aurothiomalate, hydroxychloroquine, and the corticosteroids prednisolone and prednisone (Figure 4.3).

Methotrexate is the first line choice when managing all but the mildest cases of rheumatoid arthritis (Cleland et al. 2000; RACGP 2009b; Roberts et al. 2006). Between 1999–98 and 2007–08 GPs most commonly recommended methotrexate for the disease (Figure 4.3). GP recommendation of methotrexate remained constant between 1998–99 and 2003–04 at around 19 per 100 rheumatoid arthritis contacts, but in 2004–05 it fell to 16 per 100. At this time there was an increase in the recommendation of paracetamol and prednisone. In 2005–06, GP recommendation of methotrexate rose to 25 per 100 rheumatoid arthritis contacts, before falling again in 2007–08 to 19 per 100 contacts.

Hydroxychloroquine is another common DMARD that GPs recommend. This medication is often used as a single-line therapy for mild rheumatoid arthritis, or in conjunction with other DMARDs. Between 1998–99 and 2006–07 the recommendation of this pharmaceutical remained relatively low at around 3 per 100 rheumatoid arthritis contacts. But in 2007–08 it more than doubled to become one of the main pharmaceuticals that GPs recommended to people for rheumatoid arthritis (see Table 4.2).

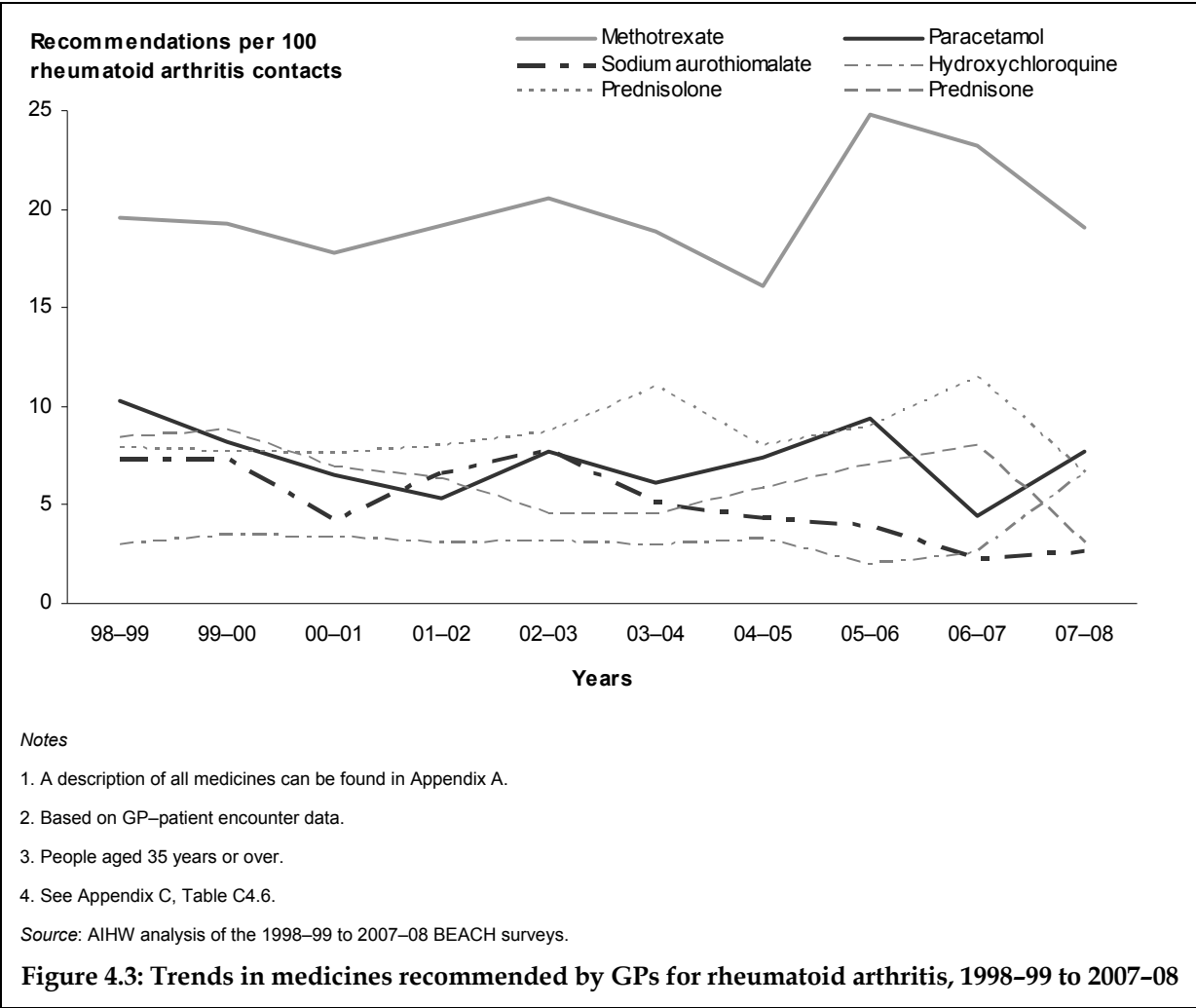
The use of medications containing gold compounds has been associated with the management of rheumatoid arthritis for the last 70 years (ARA 2008b). Thought to help suppress some of the autoimmune response, these types of medications were used to reduce swelling, inflammation and pain (ARA 2008b). Gold medications have declined in popularity as more effective treatments have become available (Kremers et al. 2004; Schuna 2009).

Sodium aurothiomalate was the sole gold medication that GPs reported for management of rheumatoid arthritis. Its use was relatively stable from 1998–99 to 2002–03 at around 7 per 100 rheumatoid arthritis contacts, but gradually decreased to 3 per 100 in 2007–08 (Figure 4.3).

Corticosteroids are often used for rheumatoid arthritis as short-term or low-dose therapy, as long-term use can induce other conditions such as osteoporosis, increased blood pressure and psychological effects (Henry & Joyner 2006). Offering relief from pain, stiffness and inflammation, corticosteroids are also used to suppress the immune system and are commonly used in conjunction with methotrexate and other medications (Henry & Joyner 2006). Prednisone and prednisolone were the two most common corticosteroids that GPs recommended to manage rheumatoid arthritis. The use of prednisolone remained relatively

steady between 1998-99 and 2007-08, but GP recommendation of prednisone showed a general decrease overall.

The most common analgesic GPs recommended for rheumatoid arthritis was paracetamol. It declined in recommendation from 1998-99 to 2001-02 (from 10 to 5 per 100 rheumatoid arthritis contacts), but no clear trend in its use was seen between 2001-02 and 2007-08 (Figure 4.3).

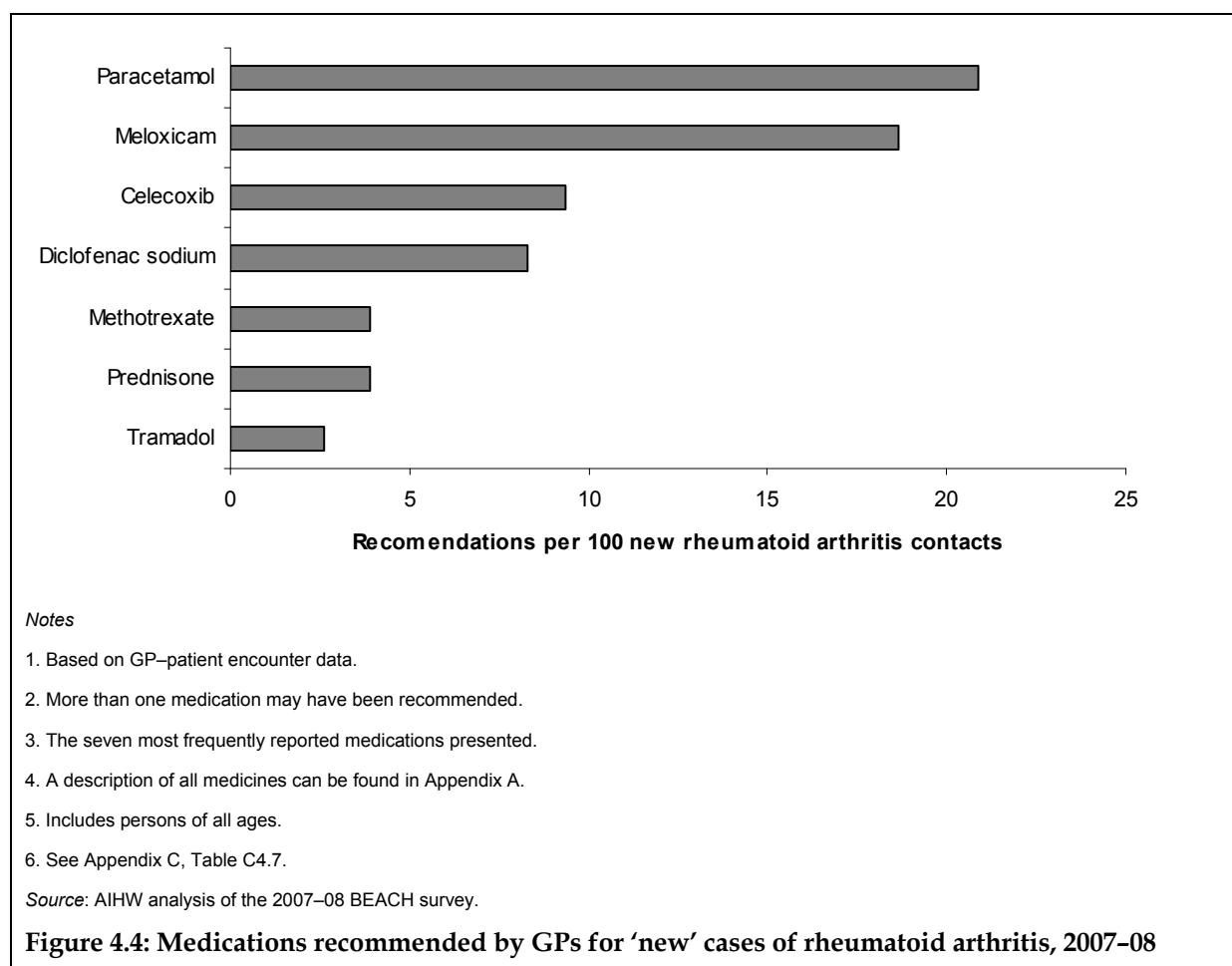


Management of new cases

Rheumatoid arthritis requires swift, early intervention. Clinical research has indicated that within the first 3 months of onset, this disease can cause irreversible deformities, considerably limit movement and reduce a person’s life expectancy (Hornig 2007). The early diagnosis and immediate use of pharmacological agents such as DMARDs has been shown to reduce the impact rheumatoid arthritis has on a person’s life (Hornig 2007; NPS 2006; RACGP 2009b).

The diagnosis of rheumatoid arthritis is often complicated as its symptoms can be non-specific. There is no definitive test that can indicate if a person has the disease, with diagnoses relying on radiological evidence and laboratory results (Schuna 2009). Patterns of joint pain and swelling can indicate that rheumatoid arthritis is developing and for this

reason most cases initially present to primary care services, meaning GPs play a key part in early management of the disease (RACGP 2009b). The main objectives of GPs when managing a new case of rheumatoid arthritis are to provide primary medication strategies to relieve pain and slow disease progression, refer patients to specialists (ideally for assessment within 6 weeks) and relevant support services, and offer advice on how people can effectively self-manage their disease (RACGP 2009b).



In the 2007–08 BEACH survey, there were 429 GP–patient contacts (in people of all ages) where rheumatoid arthritis was managed, 52 of which (12%) were recorded as being ‘new’ cases (that is, the patient had not previously sought medical care for the condition). The majority of these new cases were females (56%) and people aged 35–54 years (47%). The most common medications GPs recommended to newly diagnosed cases were paracetamol (21 per 100 contacts), meloxicam (19 per 100) and celecoxib (9 per 100) (Figure 4.4).

GP recommendations for new cases of rheumatoid arthritis were solely the DMARDs methotrexate (4 per 100 contacts) and hydroxychloroquine (1 per 100).

Expenditure

The allocated direct health expenditure on hospital-admitted patient services, out-of-hospital medical services (including GPs and specialists) and prescribed pharmaceuticals for

rheumatoid arthritis increased (in constant prices) from \$102 million to \$171 million between 2000–01 and 2004–05 (AIHW 2009). Prescription medications accounted for the majority of this increase, rising by \$64 million.

In the 2007–08 BEACH survey, the three most common GP-recommended prescription medications to manage rheumatoid arthritis were methotrexate, hydroxychloroquine sulphate and prednisolone (Table 4.2). Combined, these three medications cost an estimated \$2.3 million to consumers and \$4.4 million in government subsidies through the PBS and RPBS (Table 4.4).

As the recommended first-line medication, methotrexate is estimated to account for the majority of this expenditure, costing consumers and the government \$1.1 million and \$2.5 million, respectively. The consumer cost of the DMARD hydroxychloroquine sulphate was similar to that for methotrexate, at just over \$1 million, but the government cost was comparatively less at \$1.7 million.

The estimated expenditure on prednisolone was considerably less compared to methotrexate and hydroxychloroquine sulphate. As a corticosteroid, prednisolone is more likely to be prescribed as short-term or low-dose therapy (see page 42).

Table 4.4: Estimated expenditure on selected pharmaceuticals for rheumatoid arthritis, 2007

Medicine name	Number of prescriptions	Estimated expenditure	
		Consumer expenditure	Government expenditure
Methotrexate	109,075	\$1,105,266	\$2,533,255
Hydroxychloroquine sulphate	77,999	\$1,052,193	\$1,687,740
Prednisolone	51,029	\$183,088	\$254,299

Notes

1. Costs are estimated by allocating PBS prescriptions to disease, based on proportion of the prescriptions for specific diseases recorded in the BEACH survey. See Appendix B for details.
2. Only includes prescriptions where a subsidy was paid through PBS or RPBS.

Source: AIHW analysis of PBS administrative data 2007, and the 2007–08 BEACH survey.

5 Pharmacotherapy of osteoporosis

This chapter provides information on medications used to manage osteoporosis. Using self-reported data and GP-patient encounter information, the most commonly used pharmaceuticals and complementary medications are described. The chapter also provides a ten-year trend in GP recommendation of medications for osteoporosis, and examines expenditure related to three of the most common prescription pharmaceuticals.

What is osteoporosis?

Osteoporosis is characterised by the excess thinning of bone, which leads to an increased risk of fracture and disability (Akesson 2003; Heany 2003). Worldwide it is estimated that osteoporosis affects one in every three females and one in every five males over the age of 50 (University of Melbourne 2007; WHO 2003).

Bone is remodelled and reconstructed on a regular basis in order to maintain strength and durability (Martini 2004). Two different cells perform this remodelling – the osteoclasts (cells that break down and strip away old bone) and the osteoblasts (cells that construct new bone). When a person is diagnosed with osteoporosis, it means that the osteoclasts have been breaking bone down faster than the osteoblasts can replace it. When this occurs, the spongy bone tissue (the inner most part of the bone) is destroyed and the density of the bones is reduced, making them weak and brittle (Sambrook & Cooper 2006). The clinical definition of osteoporosis is when a person has a bone mineral density (BMD) T-score that is less than -2.5 (RACGP 2008) (Box 5.1).

Box 5.1: Measuring bone mineral density

A test called dual-energy X-ray absorptiometry, commonly referred to as DXA or DEXA, is used to determine bone mineral density. This test is considered the 'gold standard' for diagnosing osteoporosis (Ewald et al. 2009; RACGP 2008; Sambrook & Cooper 2006). Using an enhanced form of X-ray, low-energy beams are aimed at the bones and the degree of bone X-ray absorption determines the BMD T-score. The most common measurements are taken from the hips and/or spine.

BMD T-scores are divided into three sub-groups:

- **Normal (T-score greater than -1):** BMD less than 1 standard deviation below the average BMD in young adults of the same sex.
- **Osteopenia (T-score between -1 and -2.5):** BMD between 1 and 2.5 standard deviations below the average BMD in young adults of the same sex.
- **Osteoporosis (T-score less than -2.5):** BMD more than 2.5 standard deviations below the average BMD in young adults of the same sex.

Source: WHO 1994.

Osteoporosis develops over many years and is often referred to as a 'silent disease' because it has no overt symptoms (University of Melbourne 2007; WHO 2003). Its development usually goes undetected, and a large proportion of cases are diagnosed after a fracture from a minimal trauma has occurred (AIHW 2008a). The weak and brittle nature of osteoporotic

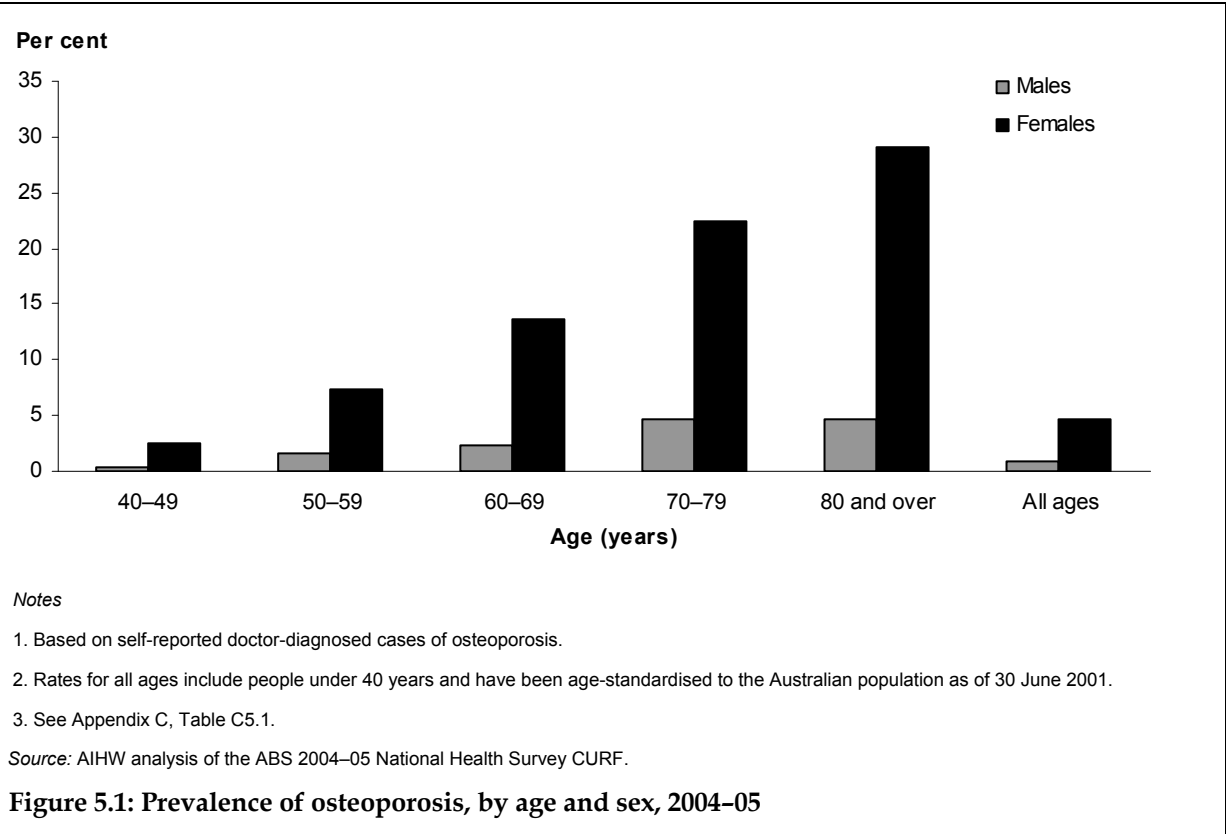
bones means a fracture is more likely to occur from day-to-day occurrences such as a fall while walking or getting out of bed, incidents that would not normally cause healthy bones to break.

Osteoporosis can be managed using a number of different actions. Changing diet, increasing physical exercise and taking medications are among the most common actions, and these can help to prevent osteoporosis, as well as slowing bone loss in people who already have it. Exercises like Tai Chi, and having regular medication reviews, have also been found to be particularly effective in reducing the number of falls and fractures in people with the condition (AIHW 2008a).

The extent of osteoporosis in Australia

Data from the 2004–05 NHS indicate that 581,000 Australians (3%) have osteoporosis. Females (4%) are more likely to report osteoporosis than males (1%), and the majority of those affected are over the age of 55 years (Figure 5.1).

Osteoporosis is more likely to affect people as they age, with males aged 70–79 years and females aged 80 years or over the most likely groups to report its occurrence (Figure 5.1). As osteoporosis usually goes undetected as it develops, it is thought that self-reported data underestimate the actual prevalence of the condition (AIHW 2008a).



Pharmacotherapy

Osteoporosis is a preventable condition (NPS 2007a). As described above, bone is made of minerals and proteins that require consistent maintenance. Increasing the intake of minerals

such as vitamin D and calcium can help to prevent this condition from developing. In addition, the use of these minerals and other pharmaceutical agents can help to stop or slow further bone loss in people who already have osteoporosis. The pharmacotherapy of osteoporosis therefore has two aspects: prevention and management. The data presented in this report, however, only refer to diagnosed cases of osteoporosis and so do not include pharmacotherapy for prevention.

Since 1995 there have been a number of advancements in the medications used to manage osteoporosis. The introduction of oral bisphosphonate medication has changed the pharmacotherapy of this condition, offering a more targeted pharmaceutical approach to improving bone mass and reducing the risk of fractures (Akesson 2003; Cardarett et al. 2008).

Common types of medicines

There are three main objectives of managing osteoporosis with medications. Bone mass needs to be maximised, fractures should be prevented, and pain should be minimised for those with fractures and in the advanced stages of the condition (Akesson 2003).

The two main types of pharmaceuticals used are the anti-resorptives (such as bisphosphonates) and the anabolic agents (Akesson 2003; Henry & Joyner 2006). The anti-resorptives focus on reducing the absorption of minerals from the bones whereas the anabolic agents promote bone formation. Other medications used in the pharmacotherapy of osteoporosis include non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics, which aid in the reduction of inflammation and pain, normally associated with fractures.

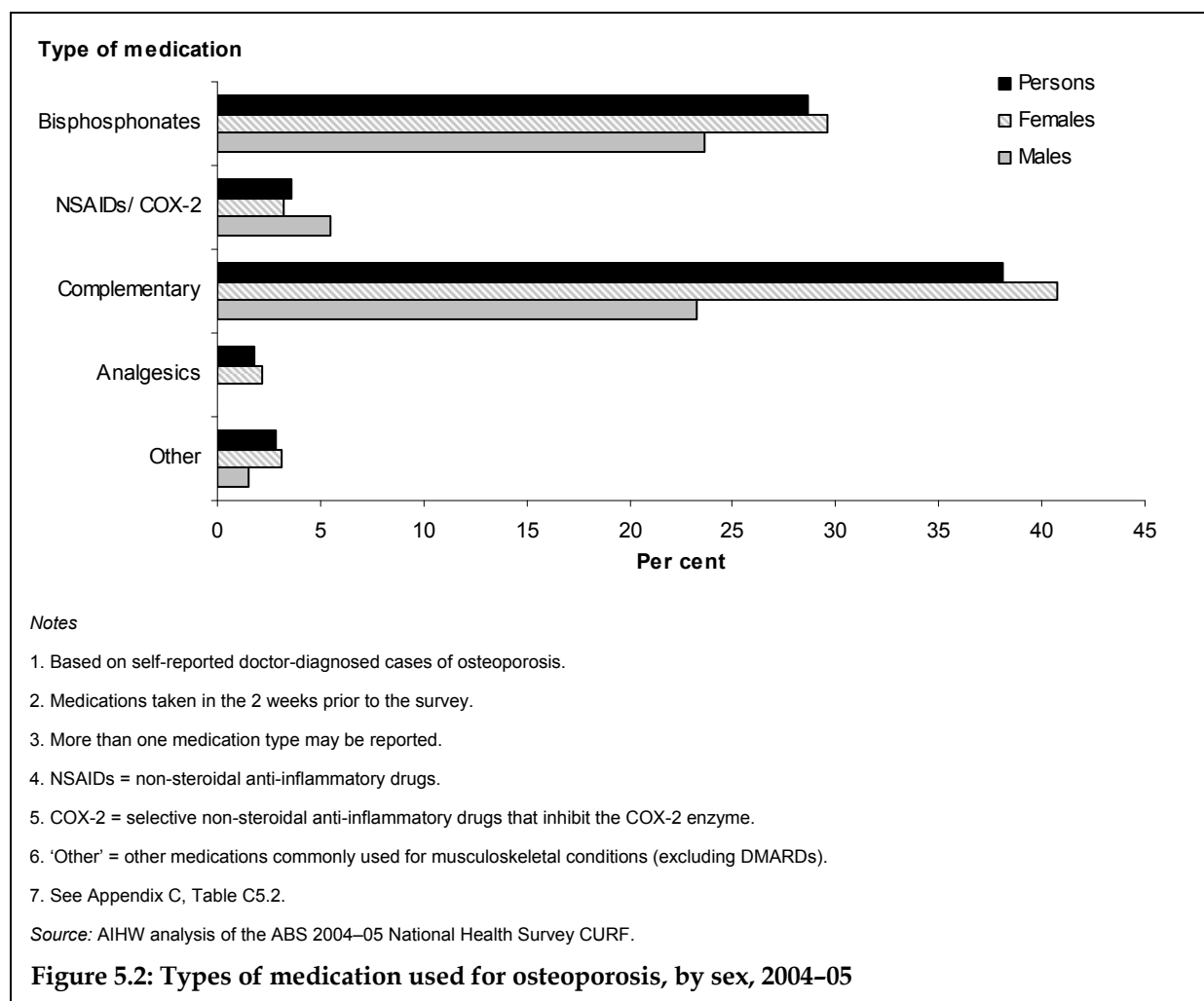
The most common types of pharmaceutical medicines used to manage osteoporosis are bisphosphonates (Figure 5.2). As anti-resorptives, bisphosphonates inhibit the osteoclasts breaking down old bone, reducing the risk of fracture and slowing the degeneration of bone structure (Ravn et al. 2000).

Complementary medicines are the most common type of medication used to manage osteoporosis. Some of these, such as calcium and vitamin D, are important components in the remodelling of bones, aiding in the reconstruction of bone tissue and the absorption of calcium from the liver (Akesson 2003; Henry & Joyner 2006; NPS 2007a). Complementary medicines are often used in conjunction with anti-resorptives, as the latter provide a mechanism to slow bone destruction but generally do not help bone formation. In the 2004–05 NHS, females with osteoporosis were almost twice as likely as males to report using complementary medicines to manage their condition (Figure 5.2).

Pharmaceutical medicines

Pharmaceutical medicines are normally used in the management of osteoporosis to increase bone mineral density, manage symptoms such as pain and inflammation, and reduce the risk of fractures. The most common pharmaceuticals used for this condition are bisphosphonates, analgesics and synthetic hormones.

The most frequently reported pharmaceuticals from the 2004–05 NHS and 2007–08 BEACH survey are outlined below. The data have been broken in two sections: self-reported information (NHS) and pharmaceuticals recommended by GPs (BEACH). The data presented in this section have been restricted to people aged 40 years and over. Although both data sources did include people under the age of 40 with osteoporosis, the number of cases was quite small and reliable estimates of medication use could not be calculated.



Self-reported pharmaceutical use

In 2004–05, people with osteoporosis most commonly use the pharmaceuticals bisphosphonates alendronate (23%) and risedronate (6%) (see Appendix C, Table C5.3).

Used to reduce the risk of fracture, bisphosphonates reduce bone loss and can relieve pain associated with osteoporotic symptoms (Akesson 2003; Seeman & Eisman 2004). Both sexes reported bisphosphonates as the most common types of pharmaceuticals used (Figure 5.3). Alendronate and risedronate are considered first-line bisphosphonates for the management of osteoporosis (RACGP 2008). Alendronate was more commonly used than risedronate in both sexes, and its use generally increased with age (Table 5.1). Female use of risedronate was stable across the age groups at around 6%, but usage was more varied for males (Table 5.1).

In the 2004–05 NHS, only females reported the use of analgesics for osteoporosis in the 2 weeks prior to the survey (Table 5.1 and Figure 5.2). Paracetamol was the most common analgesic used and it was more common in those aged 75 years or over (Table 5.1). Females also used other analgesics including paracetamol combinations, tramadol and other opioids.

Table 5.1: Self-reported pharmaceutical use for osteoporosis, by age and sex, 2004–05

Medicine name	Males							
	40–59 years		60–74 years		75 years & over		40 years & over	
	'000	Per cent	'000	Per cent	'000	Per cent	'000	Per cent
Alendronate	1.8	**6.8	9.5	*29.2	6.1	*28.1	17.4	21.7
Risedronate	1.4	**5.5	0.5	**1.5	0.4	**1.8	2.3	**2.9
Paracetamol	0	0	0	0	0	0	0	0
Other bisphosphonates	0	0	0	0	0.6	**2.8	0.6	**0.8
Medicine name	Females							
	40–59 years		60–74 years		75 years & over		40 years & over	
	'000	Per cent	'000	Per cent	'000	Per cent	'000	Per cent
Alendronate	13.6	*10.5	48.9	26.4	47.6	29.3	110.1	23.0
Risedronate	7.6	*5.8	11.3	*6.1	11.6	*7.1	30.5	6.4
Paracetamol	1.6	**1.2	2.3	**1.2	4.2	*2.6	8.1	*1.7
Other bisphosphonates	0	0	3.0	**1.6	0.8	**0.5	3.8	*0.8

* Subject to high standard errors and should be used with caution (i.e. relative standard error of 25–50%).

** Subject to sampling variability too high for practical purposes (i.e. relative standard error greater than 50%).

Notes

1. Based on self-reported doctor-diagnosed cases of osteoporosis.
2. Medications taken in the 2 weeks prior to the survey.
3. More than one medication may be reported.
4. The four most frequently reported pharmaceuticals presented.
5. 'Other bisphosphonates' include etidronate, etidronate plus calcium pamidronate and zoledronic acid.
6. Data for all persons can be found in Appendix C, Table C5.3.
7. A description of all medicines can be found in Appendix A.

Source: AIHW analysis of the ABS 2004–05 National Health Survey CURF.

Pharmaceuticals recommended by GPs

During an encounter with a GP, medications may be prescribed to the patient, be supplied by the GP or be advised for over-the-counter purchase. Within the BEACH survey, when a GP recommends a medication it is recorded as being *supplied, prescribed or advised*. In this report the term 'recommended' is used to refer to medications that were prescribed, supplied or advised by GPs.

Overall, the most common GP-recommended pharmaceuticals for osteoporosis in 2007–08 were alendronate (24 per 100 osteoporosis contacts), alendronate with cholecalciferol (12 per 100) and risedronate with calcium carbonate (11 per 100) (see Appendix C, Table C5.4).

Alendronate and alendronate with cholecalciferol were the most common pharmaceuticals recommended to both sexes (Table 5.2). The recommendation of alendronate decreased with age for males and was countered by the use of its combination, alendronate with cholecalciferol. For females the recommendation of alendronate increased with age, with the highest prevalence in the group aged 85 years and over.

Risedronate and its combination, risedronate with calcium carbonate, were recommended to males and females at similar rates. No clear age-related patterns in these medications were seen.

Table 5.2: Pharmaceuticals recommended by GPs for osteoporosis, by age and sex, 2007–08

Medicine name	Males			
	40–64 years (n=34)	65–84 years (n=124)	85 years & over (n=24)	40 years & over (n=182)
	Per 100 osteoporosis contacts (95% confidence interval)			
Alendronate	32.7 (11.3,54.2)	18.2 (9.8,26.6)	12.6 (0,27.2)	20.2 (13.1,27.3)
Alendronate with cholecalciferol*	9.3 (0,23.4)	15.0 (2.8,27.3)	20.4 (0,47.0)	14.7 (3.7,25.7)
Risedronate sodium with calcium carbonate	3.8 (0,11.7)	11.7 (4.7,18.7)	15.1 (0,35.6)	10.7 (4.9,16.5)
Risedronate sodium	6.1 (0,18.3)	5.6 (1.2,10.0)	10.6 (0,22.2)	6.3 (2.3,10.3)
Medicine name	Females			
	40–64 years (n=179)	65–84 years (n=460)	85 years & over (n=90)	40 years & over (n=729)
	Per 100 osteoporosis contacts (95% confidence interval)			
Alendronate	22.6 (15.6,29.6)	24.3 (19.3,29.3)	28.0 (17.1,39.0)	24.3 (20.2,28.5)
Alendronate with cholecalciferol*	5.8 (1.8,9.9)	14.4 (8.3,20.4)	10.2 (2.4,18.1)	11.8 (6.7,16.8)
Risedronate sodium with calcium carbonate	10.6 (5.6,15.6)	11.6 (8.0,15.2)	11.3 (3.5,19.1)	11.3 (8.3,14.4)
Risedronate sodium	7.5 (3.4,11.7)	5.8 (3.4,8.3)	13.4 (5.6,21.1)	7.2 (5.0,9.4)
Raloxifene	3.9 (1.1,6.8)	4.6 (2.3,6.9)	1.9 (0,4.7)	4.1 (2.5,5.7)

* Cholecalciferol is a form of vitamin D3.

Notes

1. Based on GP–patient encounter data.
2. More than one medication may be recommended.
3. The four most recommended pharmaceuticals for males and five for females are presented.
4. Sample sizes may not add to totals due to missing values.
5. Data for all persons can be found in Appendix C, Table C5.4.
6. A description of all medicines can be found in Appendix A.

Source: AIHW analysis of the 2007–08 BEACH survey.

Complementary medicines

Complementary medicines are very common in the pharmacotherapy of osteoporosis. Often used to reduce bone reabsorption, these types of medications are normally used in conjunction with pharmaceuticals, or for primary prevention. In the 2004–05 NHS, 38% of people with osteoporosis reported using complementary medicines to manage their condition (see Figure 5.2).

The most frequently reported complementary medicines from the 2004–05 NHS and 2007–08 BEACH survey are outlined below. The data have been broken in two sections: self-reported information (NHS) and pharmaceuticals recommended by GPs (BEACH). As for pharmaceuticals, data in this section relate to people aged 40 years or over.

Self-reported complementary medicine use

Data from the 2004–05 NHS indicate that females were more likely than males to use complementary medicines for osteoporosis (41% compared to 23%). The most common were calcium (26%), glucosamine (9%) and fish oils/omega 3 (8%) (see Table 5.3).

Table 5.3: Self-reported complementary medicine use for osteoporosis, by age and sex, 2004–05

Medicine name	Males							
	40–59 years		60–74 years		75 years & over		40 years & over	
	'000	Per cent	'000	Per cent	'000	Per cent	'000	Per cent
Calcium	4.6	*18.0	4.3	*13.1	2.6	**11.9	11.5	*14.3
Glucosamine	2.8	**10.7	2.3	**7.1	0.2	**0.9	5.3	*6.6
Fish oils/omega 3	2.4	**9.3	2.0	**6.0	0	0	4.3	*5.4
Vitamin D	1.5	**5.9	1.7	**5.3	1.9	**8.7	5.1	*6.4

Medicine name	Females							
	40–59 years		60–74 years		75 years & over		40 years & over	
	'000	Per cent	'000	Per cent	'000	Per cent	'000	Per cent
Calcium	41.9	32.3	53.9	29.1	35.5	21.9	131.3	27.5
Glucosamine	10.3	*7.9	21.6	11.7	14.1	*8.7	46.0	9.6
Fish oils/omega 3	14.6	11.3	12.4	*6.7	15.0	9.2	42.0	8.8
Vitamin D	9.3	*7.1	9.2	*5.0	4.9	*3.0	23.4	4.9

* Subject to high standard errors and should be used with caution (i.e. relative standard error of 25–50%).

** Subject to sampling variability too high for practical purposes (i.e. relative standard error greater than 50%).

Notes

1. Based on self-reported doctor-diagnosed cases of osteoporosis.
2. Medications taken in the 2 weeks prior to the survey.
3. More than one medication may be reported.
4. Four most frequently reported complementary medicines presented.
5. Data for all persons can be found in Appendix C, Table C5.5.
6. A description of all medicines can be found in Appendix A.

Source: AIHW analysis of the ABS 2004–05 National Health Survey CURF.

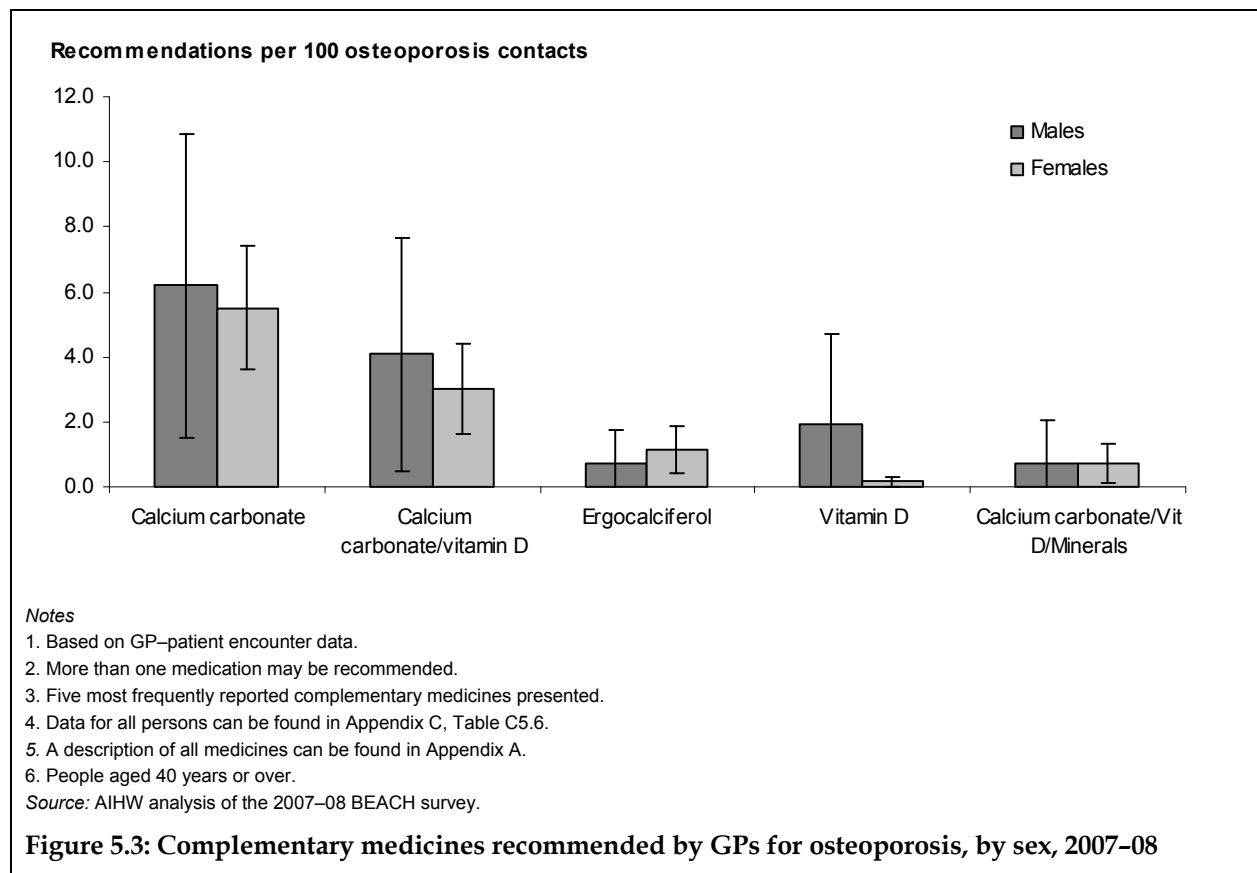
Females were more likely to report calcium use than males, and its use in both sexes decreased with age (Table 5.3). The use of glucosamine decreased rapidly with age in males, but was more varied in females.

Females were more likely than males to report using fish oils/omega 3. Among males the use of fish oil/omega 3 decreased with age, with no men aged 75 years or over reporting it. Overall both males and females reported using vitamin D at a similar rate, around 5%. In males the use of vitamin D tended to increase with age whereas for females the opposite trend was seen.

Complementary medicines recommended by GPs

Although females are more likely than males to report using complementary medicines for osteoporosis (see Figure 5.1), GP–patient encounter data suggest that, overall, complementary medicines are recommended to both sexes at similar rates. In 2007–08, GPs

most frequently recommended the following complementary medicines for osteoporosis: calcium carbonate (6 per 100 osteoporosis contacts), calcium carbonate with vitamin D (3 per 100) and ergocalciferol (1 per 100) (Figure 5.3).

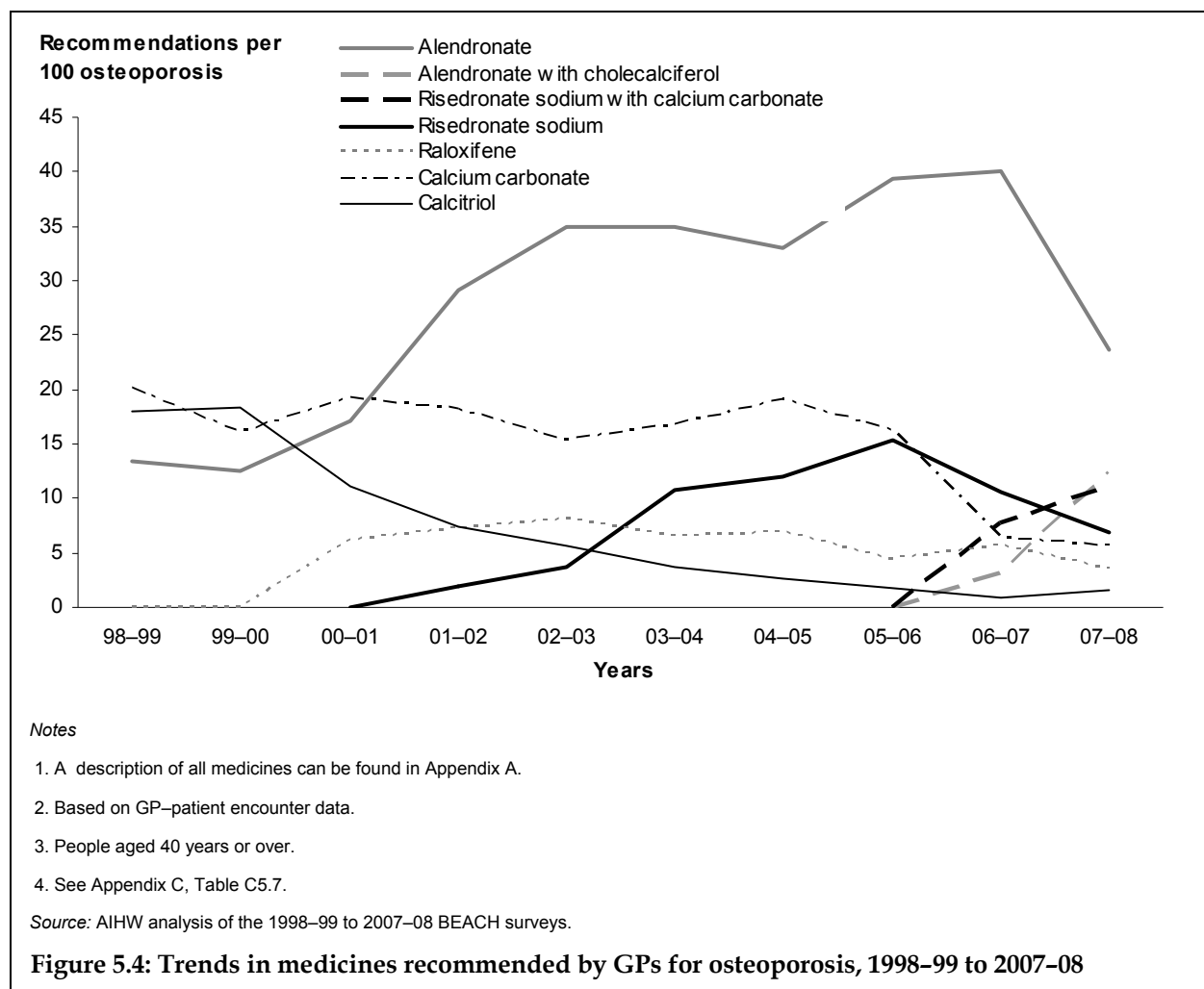


Trends in medications recommended by GPs

The pharmacotherapy of osteoporosis has changed considerably since the late 1990s. The way GPs manage the condition has altered, due to the introduction of bisphosphonates and combination bisphosphonates and also changes to PBS subsidy restrictions.

In 1998-99, the most common GP-recommended medications for osteoporosis were calcium carbonate (20 per 100 osteoporosis contacts), calcitriol (18 per 100) and alendronate (13 per 100) (Figure 5.4). Recommendations of the new bisphosphonate drugs replaced those for calcitriol and calcium carbonate, which declined considerably between 1998-99 and 2007-08.

Calcitriol is a vitamin D analog which regulates calcium and phosphate levels in the blood and re-mineralises bone (Sambrook & Eisman 2000). Prescribed to postmenopausal females and subsidised on the PBS for people with established osteoporosis with a minimal trauma fracture, GP use of this medication declined from 18 per 100 osteoporosis contacts in 1998-99 to 2 per 100 in 2007-08 (Figure 5.4). This decline may be due to several factors, including changes to general practice guidelines, the availability of new medications and the Therapeutic Goods Administration (TGA) releasing an adverse reaction bulletin in 1997. The TGA advised of a fatality and 51 adverse event reports that were linked to the use of calcitriol and the development of hypercalcaemia (high levels of calcium in the blood) (TGA 1997).



GPs commonly recommended calcium carbonate as a complementary medication to increase the level of calcium in the blood. Recommendation of this medication was relatively steady from 1998-99 to 2004-05, but then fell to 6 per 100 osteoporosis contacts in 2007-08 (Figure 5.4). This decline may be related to the introduction of combination bisphosphonates in 2006.

As one of the first oral bisphosphonates to become available to people with osteoporosis, alendronate was initially listed on the PBS in 1997. In 1998-99, GPs recommended bisphosphonates at 13 per 100 osteoporosis contacts, and this continued to increase until 2006-07, peaking at 40 per 100 contacts (Figure 5.4). In 2007-08, the recommendation of alendronate dropped to 24 per 100 contacts. The introduction and uptake of alendronate with cholecalciferol countered this decline, with a fourfold increase between 2006-07 and 2007-08 (Figure 5.4).

The introduction of combination bisphosphonates in 2006 also affected the GP use of risedronate sodium. Listed on the PBS in 2001, GPs recommended this pharmaceutical at 2 per 100 osteoporosis contacts in 2001-02 (Figure 5.4). Between 2002-03 and 2005-06, GP recommendation increased sevenfold to 15 per 100 contacts. However, the recommendations for risedronate sodium fell to 10 per 100 in 2006-07 and then to 7 per 100 in 2007-08. The use of risedronate with calcium carbonate countered this decline, similar to alendronate.

Raloxifene is a selective oestrogen receptor modulator (SERM) that was introduced onto the Australian market in the mid 1990s. GP recommendation of this pharmaceutical was

relatively steady at around 7 per 100 osteoporosis contacts between 2000–01 and 2004–05, but after this decreased to 4 per 100 osteoporosis contacts in 2007–08.

Expenditure

Allocated health expenditure on hospital-admitted patient services, out-of-hospital medical services (including GPs and specialists) and prescribed pharmaceuticals for osteoporosis rose (in constant prices) from \$160 million in 2000–01 to \$297 million in 2004–05 (AIHW 2009). This rise can be largely attributed to expenditure on prescribed pharmaceuticals, which more than doubled, from \$88 million to \$215 million.

In 2007, the three most common GP-recommended prescription medicines for osteoporosis were alendronate, risedronate with calcium carbonate and alendronate with cholecalciferol (see Table 5.2). As all three medications are only subsidised on the PBS and RPBS for managing osteoporosis, government expenditure figures are the actual cost and not estimated costs, as presented in the osteoarthritis and rheumatoid arthritis expenditure sections. The expenditure figures for consumers are estimates, as the price for filling a prescription may vary, depending on the premiums that apply to particular brands.

Table 5.4: Estimated expenditure on selected pharmaceuticals for osteoporosis, 2007

Medicine name	Number of prescriptions	Consumer expenditure	Government expenditure
Alendronate	1,673,808	\$11,635,663	\$75,779,080
Risedronate with calcium carbonate	576,219	\$3,971,895	\$26,362,703
Alendronate with cholecalciferol	586,810	\$3,816,523	\$26,890,072

Note: Only includes prescriptions where a subsidy was paid through PBS or RPBS.

Source: AIHW analysis of PBS administrative data 2007 and the 2007–08 BEACH survey.

Overall the cost of these prescription medications was considerably higher for government than for consumers (Table 5.4). Alendronate was the most expensive, costing consumers and government around three times as much as the combination bisphosphonates risedronate with calcium carbonate and alendronate with cholecalciferol.

Changes to the PBS and other medications

The data presented in this chapter relate only to the most common medications reported for managing osteoporosis up to March 2008. The information presented below discusses recent changes to PBS subsidises that may affect osteoporosis pharmacotherapy, and describes other medications used to manage osteoporosis that are not presented in this report. This section also provides information on how combination bisphosphonates differ from their single-line equivalents.

Changes to the PBS

In 2007 three significant changes to subsidies on the PBS affected the pharmacotherapy of osteoporosis. These changes expanded the subsidy restrictions to include other patient categories and introduced new medications into the scheme.

1. In April 2007 the bisphosphonate strontium ranelate was added to the PBS. This medication was initially subsidised to reduce the risk of spinal, non-spinal and hip fractures in postmenopausal females who have had a minimal trauma fracture. On 1 November 2007, PBS eligibility was extended to include females aged over 70 years whose bone mineral density (BMD) T-score was -3.0 or less (see Box 5.1 page 42). Strontium ranelate is now a first-line medication (similar to alendronate and risedronate) commonly used for postmenopausal osteoporosis (NPS 2007b).
2. In April 2007, PBS eligibility for alendronate was extended. Originally only subsidised for people with osteoporosis who had had a fracture due to minimal trauma or were receiving ongoing treatment for a fracture, alendronate is now also subsidised for people aged 70 years and over whose BMD T-score is -3.0 or less.
3. In August 2007, the risedronate subsidy was also extended to include people aged 70 years or over whose BMD T-score is -3.0 or less.

Other medications for osteoporosis

Apart from the first-line medications (such as alendronate, risedronate and strontium ranelate) the pharmacotherapy of osteoporosis may also include second-line bisphosphonates, combination bisphosphonates, hormones, and anabolic agents.

Second-line bisphosphonates

Etidronate reduces the risk of vertebral fractures and is a second-line bisphosphonate in managing osteoporosis (NPS 2007a). This medication is generally used when people show an intolerance to alendronate and risedronate (NPS 2007a; Sambrook et al. 2002).

Intravenous bisphosphonates

Zoledronic acid is given as a yearly injection, and has been shown to reduce the risk of spinal, non-spinal and hip fractures in post-menopausal females (Lambrinouadaki et al. 2008; Reid et al. 2002). Clinical fractures and mortality have also been reduced when zoledronic acid is given after a hip fracture in elderly males and females (Pharmaceutical Benefits Advisory Committee 2008). This medication was listed on the PBS in December 2008.

Ibandronic acid reduces the risk of vertebral fractures and is an alternate option for postmenopausal females who have had adverse reactions to other bisphosphonates (NPS 2007a). From 1 March 2008 this pharmaceutical has been available on the PBS, but was only subsidised for use in breast cancer and not osteoporosis.

Hormones

Hormone replacement therapy (HRT) is sometimes given to post-menopausal females with severe menopausal symptoms or to males who have low testosterone levels (Boonen et al. 2005; Sambrook et al. 2002). HRT, including oestrogen for females, offers fracture prevention but has been linked to an increased risk of breast cancer and cardiovascular events in females aged 70 and over. The effects of testosterone on fracture prevention in males are less clear.

Anabolic agents

Parathyroid hormone (PTH) was listed on the PBS in May 2009. It is an anabolic agent used to stimulate bone formation, increasing bone strength (Akesson 2003; Sambrook & Cooper 2006). In Australia, teriparatide or human PTH (1-34), is the only PTH available to manage osteoporosis. It is used for people with established osteoporosis when other forms of

medications (including bisphosphonates) are unsuitable or ineffective (NPS 2007a). In order to receive this medication on the PBS, a person must have established severe osteoporosis, with a very high risk of fracture and a BMD score less than -3.0 . The person also must have had two or more fractures due to minimal trauma, including at least one within the previous 12 months.

Combination bisphosphonates

In recent years, innovations and advancements in osteoporosis medication has seen the introduction of new bisphosphonates, often referred to as combination bisphosphonates. In Australia, there are currently three combination bisphosphonates available: risedronate with calcium carbonate, risedronate with calcium carbonate and cholecalciferol, and alendronate with cholecalciferol.

Combination bisphosphonates have a supplement of calcium and/or vitamin D, employed to help people with significant deficiencies in either vitamin D or calcium manage their osteoporosis. These combination medicines have the benefit of a bisphosphonate, coupled with an increase in calcium intake and vitamin D levels.

The introduction of combination bisphosphonates to the PBS began in 2006, with risedronate with calcium carbonate being listed in April and alendronate with cholecalciferol (vitamin D3) listed in August. The effect this had on osteoporosis pharmacotherapy is shown in the GP-patient encounter information (see Figure 5.4), with uptake of combination bisphosphonates and a consequent decrease in recommendations of single-line bisphosphonates. Risedronate with calcium carbonate and cholecalciferol was listed on the PBS in May 2008, and therefore is not included within the data presented in this chapter.

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