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Use of antiresorptive agents for osteoporosis management

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Australian Institute of Health and Welfare

Board Chair

Dr Andrew Refshauge

Director

David Kalisch

Any enquiries about or comments on this publication should be directed to:

Communications, Media and Marketing Unit

Australian Institute of Health and Welfare

GPO Box 570

Canberra ACT 2601

Tel: (02) 6244 1032

Email: info@aihw.gov.au

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Summary

Antiresorptive agents are bone preserving medications which can slow down the bone loss associated with osteoporosis (O'Neil et al. 2004). These reduce bone loss by inhibiting bone degeneration activity and/or promoting bone formation. This report examines the supply pattern of antiresorptives for management of osteoporosis in Australia during 2003–07.

Who received antiresorptive drugs?

- A total of 562,597 Australians were supplied with at least one antiresorptive medication for the management of osteoporosis in the 5-year period from 1 January 2003 to 31 December 2007.
- Of the above total, 297,795 people received their first antiresorptive medication during the 5-year period between 1 July 2003 and 30 June 2007. They are referred to as 'the initiating cohort', as they were considered to have commenced antiresorptive therapy in this time period.
- Three quarters of the initiating cohort were females and aged 65 years and over.

What antiresorptive drugs were supplied?

- Alendronate and risedronate were typically the first drugs supplied for treatment of osteoporosis (or first-prescribed medicine) during the study period, and the majority of the initiating cohort (96%) was supplied with one of these.
- Combination bisphosphonates overtook single formulation of bisphosphonate as the first-prescribed antiresorptive in the year between July 2006 and June 2007.

Who prescribed antiresorptive drugs?

- General practitioners (GPs) and other primary care medical practitioners (OMPs) played a major role in prescribing antiresorptives and managing osteoporosis. The majority of the initiating cohort (88%) was prescribed with antiresorptives by their GPs/OMPs.
- During the first 12 months of antiresorptive therapy, the majority of the patients received their prescriptions from one or two prescribers (71% and 24%, respectively).

Were enough antiresorptives supplied during the first 12 months of treatment?

- Two in 5 patients (40%) did not receive the quantity of antiresorptives required to maintain sufficient regular intake of this medication during the first 12 months of therapy to receive the adequate benefits.

Did patients continue to receive antiresorptives after their first supply?

- During the first 12 months of antiresorptive therapy, one quarter (25%) of the patients had stopped receiving antiresorptives by 6 months; one in 10 (10%) only received the first supply.
- There appears to be a clear need to monitor the use of antiresorptive therapy, particularly in the first 6 to 7 months to ensure appropriate health benefits are obtained at both individual and population levels.

1 Introduction

Pharmaceutical interventions play an important role in treating osteoporosis (meaning 'porous bones'). Antiresorptive medicines, in particular, reduce the adverse outcomes of osteoporosis such as fragility fractures and associated morbidity, disability and mortality (National Osteoporosis Foundation 2009). Antiresorptives are pharmacological agents that reduce bone loss by inhibiting bone degradation activity and promoting bone formation.

This report provides an overview of the use of antiresorptives in the management of osteoporosis in Australia. The focus is on whether enough doses of antiresorptives are supplied to patients during the first 12 months of antiresorptive therapy. The report explores the administrative dataset of the Australian Government's Pharmaceuticals Benefits Scheme (PBS).

What is osteoporosis?

Osteoporosis is a systemic skeletal disease that causes the bones to become thin and weak to the extent that they break easily even after a minor incident. The bone loss generally occurs over a long period of time (albeit at a much faster rate among post-menopausal females). Consequently, osteoporosis is more common in older people, particularly post-menopausal women (AIHW 2008, 2010).

The extent of bone loss can be measured through bone mineral density (BMD) scans of the hip or spine (WHO Study Group 1994). The results are expressed as T-scores (or standard deviations) comparing a person's BMD with the average BMD of a 30-year-old person of the same sex (Box 1.1). Three broad categories are identified: normal bone density, osteopenia (low bone density) and osteoporosis (severe bone loss).

Every year, a large number of elderly Australians, particularly females, suffer from osteoporotic fractures and consequent deformity, disability, and mobility limitations (AIHW 2008). Hip fractures are costly to treat, with hospital episodes for procedures such as partial joint replacement costing on average \$15,500 to \$19,500 (AIHW 2010).

Hip fractures often also incur other costs for rehabilitation, outpatient visits for follow-up treatment if required, and assistance with activities of daily living at home during the recovery period. In some cases, permanent residential care is required.

While osteoporosis is rarely a direct cause of death, osteoporotic hip fractures are linked to premature deaths in the years following the event (Haentjens et al. 2010).

Box 1.1: Diagnosing osteoporosis using bone mineral density testing

The 'gold standard' method for measuring bone mineral density (BMD) is dual-energy X-ray absorptiometry, also known as DXA or DEXA. Low-dose X-ray beams are aimed at the bones, and bone density can be determined from the amount of X-rays that are absorbed. Measurements are usually taken at the hip and/or spine.

BMD results can be divided into three categories:

Normal: BMD less than 1 standard deviation below the average BMD in young adults of the same sex.

Osteopenia (literally 'poor bones'): BMD between 1 and 2.5 standard deviations below the average BMD in young adults of the same sex.

Osteoporosis: BMD more than 2.5 standard deviations below the average BMD in young adults of the same sex.

Other methods used for measuring BMD include quantitative computed tomography and quantitative ultrasound (QUS). QUS is a screening test that is offered at pharmacies or shopping centres, where the measurement is taken at the heel. This test can help to identify persons who might need further investigation, but is not used alone for diagnosis or monitoring as its responsiveness to therapy or change over time is uncertain.

Source: WHO Study Group (1994).

The extent of the problem

Estimating the prevalence of osteoporosis in a population can be difficult. Osteoporosis is a 'silent' condition with no overt symptoms, and often remains undiagnosed. Many people with osteoporosis may be unaware of the condition until they experience a fracture following minimal trauma.

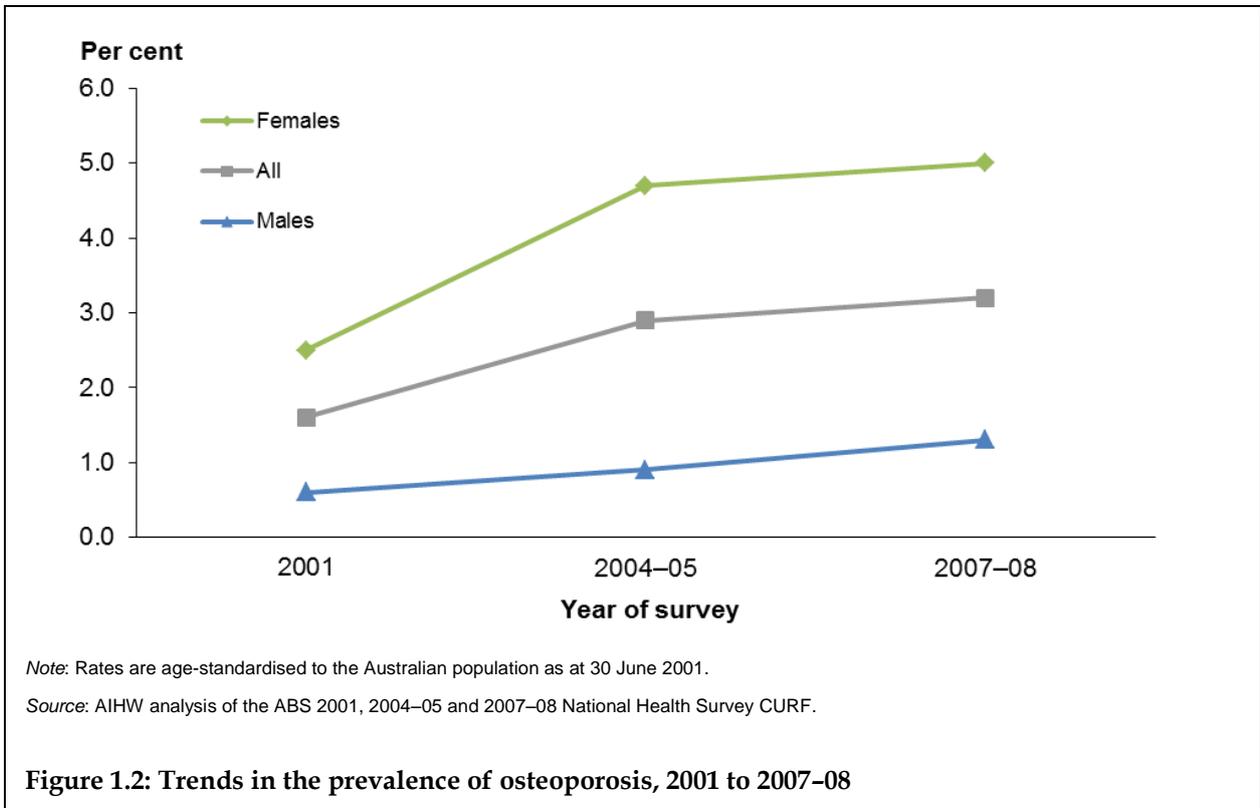
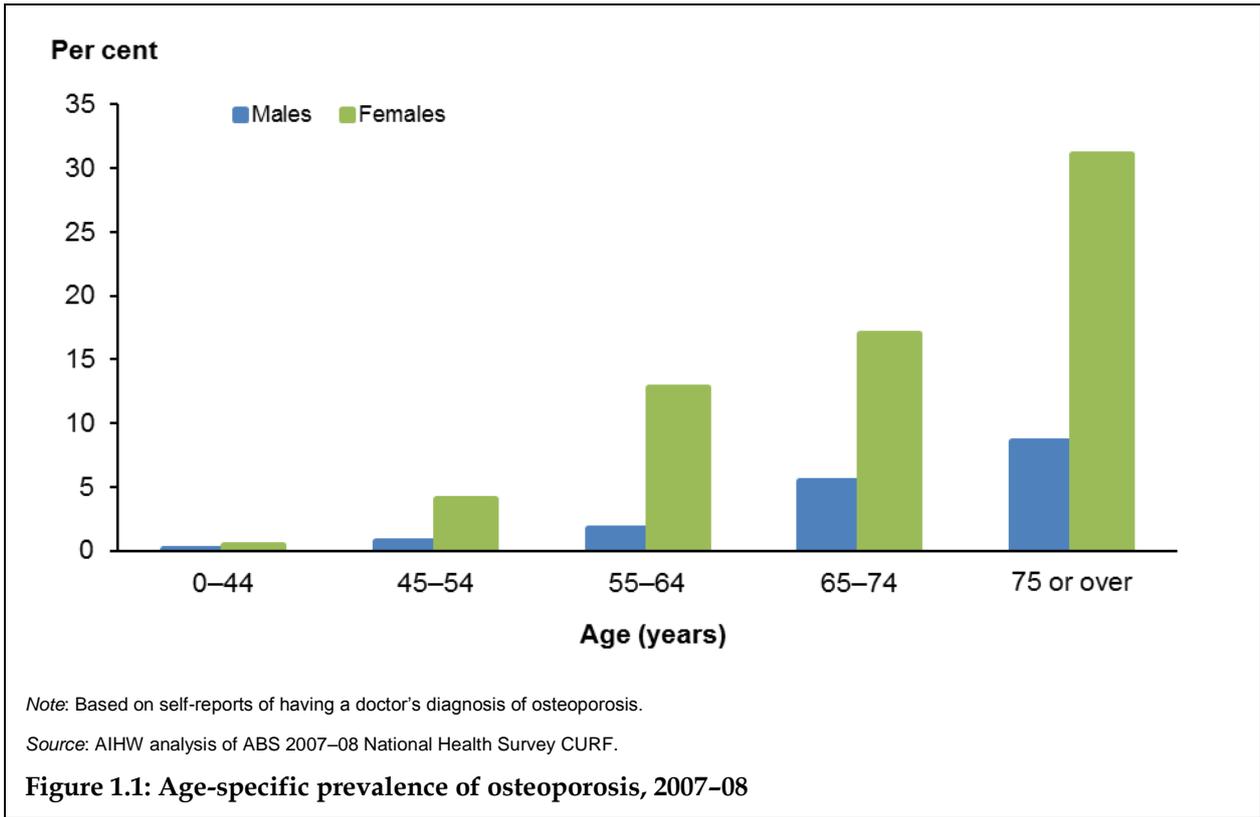
Even after experiencing minimal trauma fracture(s), some cases of osteoporosis go undiagnosed and/or untreated. This may occur where fractures, particularly spinal fractures, are undetected (Delmas et al. 2005). In other cases underlying osteoporosis may not be investigated following minimal trauma fractures (Elliot-Gibson et al. 2004).

In the absence of population studies using biomedical criteria to diagnose osteoporosis, the extent of this underestimation is not fully known.

An estimated 692,000 Australians (3.4% of the total population) have doctor-diagnosed osteoporosis based on the 2007–08 National Health Survey (NHS) (ABS 2009). This is likely to be an underestimate.

Women account for the majority of cases (81.9%), and the disease mostly affects people aged 55 years and over (Figure 1.1).

NHS data suggest there was a considerable increase in the prevalence of osteoporosis, almost double, between 2001 and 2004–05. The prevalence remained similar between 2004–05 and 2007–08 (Figure 1.2).



General practitioner (GP) consultations

The prevention and management of osteoporosis in Australia occurs in a variety of settings. In most cases, general practitioners (GPs) are the first port of call, and they are the main prescribers of required pharmaceuticals. Endocrinologists, orthopaedic surgeons, geriatricians and other medical specialists also provide health care for osteoporosis.

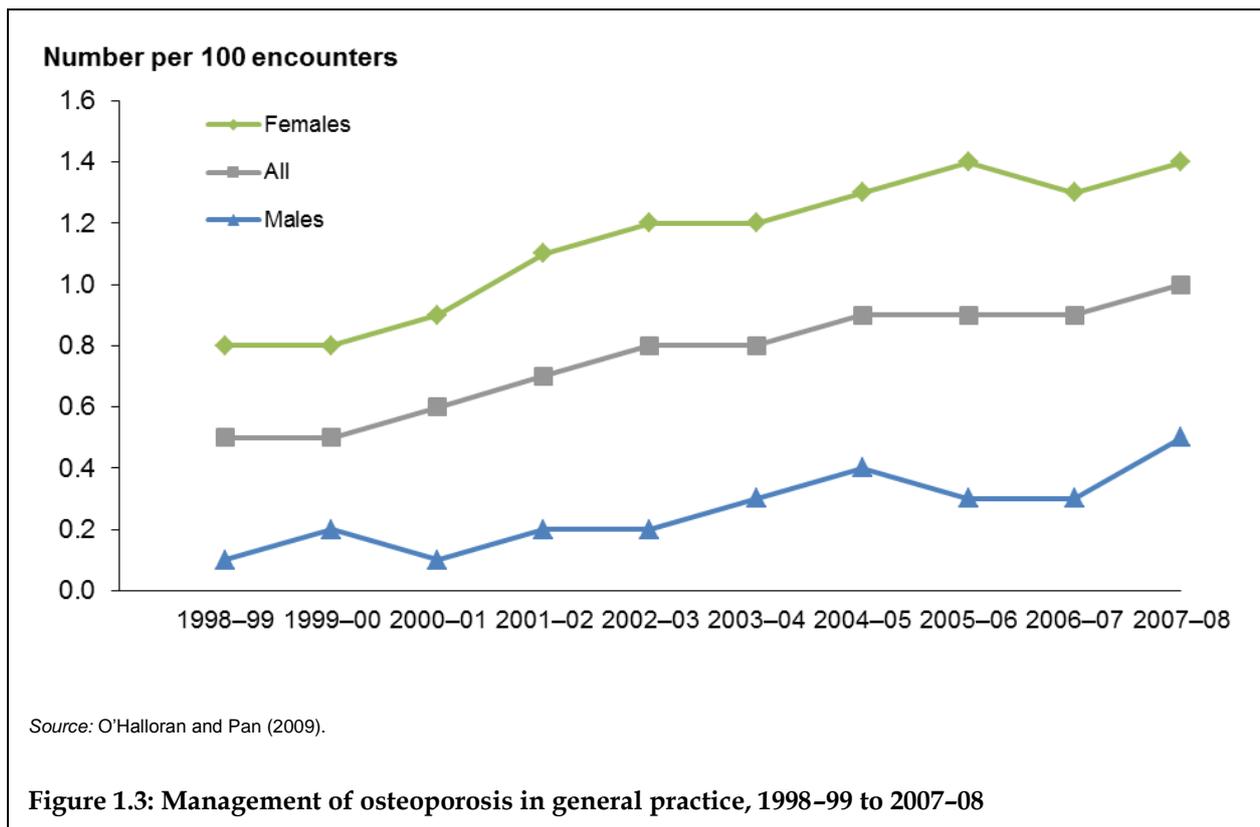
Information about the management of osteoporosis by GPs is collected through the Bettering the Evaluation and Care of Health (BEACH) survey (Britt 2009). The BEACH program is a continuous national study of general practice activity, based on a new sample each year of about 1,000 GPs, each of whom provides details for 100 consecutive GP-patient encounters. The BEACH program began in 1998, and is ongoing. Data collected in the survey include reasons for GP-patient encounter, problems managed, and details of pharmacological and non-pharmacological management options. With regards to recommendation of pharmacological management, the survey records whether the GP provided the prescription for the medicine, supplied the medicine, or advised to purchase over-the-counter medicine.

In 2007-08, osteoporosis was managed at a rate of 1.0 per 100 GP-patient encounters (O'Halloran & Pan 2009), and made up 0.6% of all problems managed (Britt et al. 2008). The most commonly reported reason for encounters was requests for prescriptions (37.9 per 100 encounters for osteoporosis) (O'Halloran & Pan 2009). Medications were prescribed, advised, or supplied in the management of more than four out of five osteoporosis problems managed.

There was a noticeable change in the management of osteoporosis by GPs over the decade between 1998-99 and 2007-08 (O'Halloran & Pan 2009). The management rate of osteoporosis doubled from 0.5 per 100 encounters to 1.0 per 100 encounters (Figure 1.3) in this time period. The increase is noteworthy in view of virtually no change in the GP-patient encounter rate for all other musculoskeletal conditions during that decade.

While osteoporosis managed in GP-patient encounters centred on medications in 2007-08, the rate of supply of prescriptions decreased from 91.9 per 100 osteoporosis problems managed in 1998-99 to 72.9 per 100 osteoporosis problems managed in 2007-08.

Partly counteracting this was a substantial increase in the rate of GPs advising purchase of over-the-counter medicine. The rate of advice for over-the-counter medicines increased from 1.0 per 100 osteoporosis problems managed to 9.6 per 100 osteoporosis problems managed. The increased availability of combination products such as vitamin D and calcium over the counter is likely to have influenced this (O'Halloran & Pan 2009).



Osteoporosis and bone remodelling

Bone is a dynamic tissue that constantly undergoes remodelling even once growth and modelling of the skeleton have been completed (Hill & Orth 1998). Bone remodelling is a process in which there is localised removal of old bone (resorption) and replacement with newly formed bone (formation).

- In healthy adults, there is a balance between the amount of bone formed and the amount of bone resorbed. The balance between bone formation and bone resorption, however, may be upset by factors such as:
- low calcium intake or absorption
- genetic susceptibility
- glucocorticosteroid use
- low levels of the hormone estrogen
- local growth factors or stimuli
- physical stress
- ageing (Eastell & Hart 2002).

In osteoporosis, more bone is removed than formed, resulting in loss of bone density.

Antiresorptives available in 2003–07

The antiresorptives operate through a variety of mechanisms to reduce or stop net bone loss (Henderson & Goltzman 2000). The emphasis generally is on minimising bone loss by reducing bone resorption rather than increasing bone formation.

A variety of antiresorptive medications were prescribed in Australia to manage osteoporosis between 2003 and 2007. The major categories of these were bisphosphonate monotherapy, combination bisphosphonates, a selective estrogen receptor modulator (SERM) and strontium ranelate. Of these, bisphosphonates (single formulation or combination) were the most widely used antiresorptives.

Between 2003 and 2007, three subtypes of bisphosphonates were available in Australia; alendronate, risedronate, and etidronate. Alendronate and risedronate are typically the first pharmaceutical medicine supplied to manage osteoporosis (NPS 2007a) (see Box 1.2 for distinction between first-line and second-line treatment for osteoporosis). The third subtype, etidronate, is supplied if alendronate or risedronate is not tolerated or otherwise contraindicated.

The use of combination bisphosphonates became widespread in mid-2006. These combination medications have a supplement of calcium and/or vitamin D to help people with significant deficiencies in calcium or vitamin D to better manage their osteoporosis. These combination medicines have the benefit of bisphosphonate coupled with an increase in calcium intake and vitamin D levels (see Box 1.3 for the effects of calcium and vitamin D in bone resorption).

While the action of bisphosphonates is limited to reduction in bone resorption, the SERM and strontium ranelate are said to stimulate bone formation as well (NPS 2007a). Both of these antiresorptives are recommended for women only, and used when bisphosphonates are not tolerated or otherwise contraindicated (NPS 2007a).

Box 1.2: First-line therapy and second-line therapy for osteoporosis

Bisphosphonates alendronate and risedronate are recommended for the initial treatment of osteoporosis (Sambrook et al. 2002), and they may be referred to as osteoporosis' first-line therapy. First-line treatment for a condition is usually determined on the basis of evidence for drugs' efficacy, safety, and cost.

When the first-line therapy does not work for reasons of intolerance, low compliance, adverse side effect and other events, alternative therapies are trialled (second-line therapy). During the 5-year study period, disodium etidronate and calcium carbonate, raloxifene hydrochloride, and strontium ranelate were considered second-line therapy for osteoporosis (NPS 2007a; NPS 2007b; Sambrook et al. 2002).

Box 1.3: Function of calcium and vitamin D supplements in antiresorptives

As well as providing strength to bones, calcium plays critical roles in muscular, nervous, and hormonal systems. Many physiological functions depend on calcium being available in the blood. When adequate serum calcium level cannot be maintained by dietary intake, calcium stored in bones is 'withdrawn', resulting in bones becoming porous and osteoporotic. Calcium in the combination bisphosphonates is designed to add to the bisphosphonates' antiresorptive action.

Vitamin D promotes calcium absorption from the gastrointestinal system, and thus adds to antiresorptive action.

Source: Osteoporosis Australia (2010).

Compliance with antiresorptive therapy

Medication compliance refers to the extent to which patients take medications as prescribed by their health care providers. Rates of compliance for individual patients are usually reported as the ratio of the prescribed doses of the medication actually taken by the patient over a specified period expressed in percentage. Compliance can vary from 0 to more than 100 per cent as patients sometimes take more than the prescribed amount of medication (Osterberg & Blaschke 2005).

Low compliance with prescribed medicine is very common and is not specific to any disease, disease severity or treatment (Haynes et al. 2002). An American study found that 20% of patients given medication prescriptions never filled their prescriptions, and of those who did fill their prescriptions, 50% did not take the medication as directed (Ellickson et al. 2000). Typical compliance rates for prescribed medications are said to be around 50% (Haynes et al. 2002).

Various reasons for noncompliance with drug therapy have been suggested (Table 1.1), and these are said to apply across many conditions including osteoporosis (Sambrook 2006).

A compliance level of 75–80% or better is often considered the level that is required to obtain the therapeutic benefits of bisphosphonates (Clowes et al. 2004; Siris et al. 2006; Reginster et al. 2006). The average figure reported in a recent review of compliance with bisphosphonate treatment ranged from 58% to 81%, mostly below the criterion figure (Cramer et al. 2003).

The administrative records of the Pharmaceutical Benefits Scheme and Repatriation Pharmaceutical Benefits Scheme (collectively referred to as PBS dataset) have been used as an indirect measure of compliance in Australia (Roughead et al. 2009; Simons et al. 2008).

The PBS claims data are unable to show precise levels of compliance because not all medications supplied are necessarily taken. These data can however, give an indication of the maximum possible compliance level.

Table 1.1: Factors that affect compliance with medication

Disease	Drug related	Patient	Follow-up	Others
Absence of symptoms	Prevention vs. treatment	Lack of social support	Time	Patient–doctor relationship
Long-term therapy required	Adverse effects	Lack of disease knowledge	Cost	
No immediate advantage from therapy	Duration of treatment	Denial of illness	Difficulties of follow-up	
Multiple morbidities	Complexity of regimen	Patient's own view about how they are best treated		
	Greater number of drugs	Patient's concerns about the value or appropriateness of taking medicines		
	Frequency of administration	Confusion or physical difficulties associated with taking medicine		
	Costs	Disruption to lifestyle or inconvenience		
	Access to medication			

Source: Sambrook (2006).

Questions addressed in this study

This report used the PBS data extract to explore the following questions:

- who is starting on what antiresorptive drug?
- what medical specialists are involved in prescribing antiresorptives?
- how has antiresorptive supply changed over time?
- is enough antiresorptive supplied to individual patients to enable compliance with the therapy?

Calcium and vitamin D supplements are used to manage osteoporosis. These are supplied over-the-counter at pharmacies as well as through other outlets (e.g. supermarkets and health food shops). The supply of these supplements is not captured in the PBS data and thus will not be covered in this report.

Structure and aims of the report

This report examines the supply of antiresorptives from 2003 to 2007. This brief introductory chapter has provided background to the study and the questions it seeks to answer.

Chapter 2 describes the study design, the PBS data extract, and the antiresorptives monitored. The approach used for constructing data cohorts, namely the initiating cohort and follow-up cohort, is also described.

Chapter 3 focuses on the initiating cohort, describing their demographic characteristics, antiresorptives prescribed to them, and specialist category of medical practitioners who prescribed these medicines.

Chapter 4 focuses on a subset of the initiating cohort, or follow-up cohort, concerning their first 12 months of antiresorptive therapy. Specifically, whether enough antiresorptives were supplied is explored.

Chapter 5 discusses the key findings in light of some methodological issues with using the administrative data in monitoring medicine supply.

Two appendixes include more information about the PBS data extract and the composition of the patient cohorts.

2 The study design

This chapter provides a brief outline of the PBS and key information concerning the PBS-subsidised antiresorptives which were available from 2003 to 2007.

Pharmaceutical Benefits Scheme

The Australian Government subsidises the cost of medicines through the Pharmaceutical Benefits Scheme (PBS) and the Repatriation Pharmaceutical Benefits Scheme (RPBS). Medicare Australia administers the PBS on behalf of the Department of Health and Ageing, and the RPBS on behalf of the Department of Veterans' Affairs (DVA). The purpose of the PBS and RPBS is to ensure all Australians have affordable and reliable access to a wide range of necessary medicines. The PBS and RPBS are collectively referred to as the PBS in this report.

PBS payment category and safety net

The government subsidy is applied when the cost of a drug dispensed at a pharmacy exceeds the patient co-payment threshold. Two broad categories of patient co-payments, general and concessional, are briefly explained in Box 2.1.

Box 2.1: Patient co-payment on the PBS

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

Holders of a health care card, pensioner concession card, or Commonwealth Seniors Health Card are entitled to concessional status and pay less for their medication than those in the general category.

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

The PBS safety net provisions apply once a family's co-payments exceed a set amount within a calendar year. General category patients are then entitled to the PBS medications at the concession price for the remainder of the calendar year, while concession patients are entitled to the PBS medications at no cost.

In 2007, the safety net threshold was \$1,059.00 for the general category and \$274.40 for the concessional category (see Appendix A Table A.1 for the safety net threshold for general and concessional categories between 2003 and 2007).

PBS benefits category

Medications listed on the PBS fall into four broad categories of benefits:

- unrestricted benefits which have no restrictions on their therapeutic uses
- restricted benefits which can only be prescribed for specific therapeutic uses
- authority required benefits which require prescribers to record an authority code issued by Medicare Australia or DVA obtained over the phone or in writing
- streamlined authority required benefits which require prescribers to include a 'streamlined authority code' listed with the listing of each medicine for which this category of benefits apply.

Streamlined authority required benefits were introduced on 1 July 2007. All antiresorptive medicines supplied during the study period were in the authority required benefits category until 30 June 2007, and were prescribed under streamlined authority benefits after this type of benefit was introduced.

A brief overview of the eligibility criteria for the PBS subsidy for antiresorptives is provided in Box 2.2.

Box 2.2: PBS eligibility criteria for antiresorptive subsidy

Prior to April 2007, Australians were eligible for osteoporosis therapy through the PBS only if they had sustained a fracture following minimal trauma, and it was confirmed by X-ray, computed tomography, or magnetic resonance imaging scans. Testing for low BMD was not required. By these criteria, these medicines were restricted to people with 'established' osteoporosis.

The eligibility criteria for alendronate, risedronate and strontium ranelate changed in 2007 (April, August and November respectively). The new criteria cover all persons over the age of 70 years with significant bone loss (BMD T-score of -3.0 or less). Those on long-term corticosteroid therapy with intermediate to high bone loss (T-score of -1.5 or less) have also become eligible to receive risedronate. These changes in eligibility criteria are aimed at preventing osteoporotic fractures. The focus of the use of antiresorptives has thus changed from one of treatment to that of prevention and treatment.

Source: Department of Health and Ageing (2007).

Records in the PBS data

Around 80 per cent of medicines prescribed in Australia are subsidised through the PBS (Department of Health and Ageing 2011a). Supply of PBS-subsidised medicine was recorded in the PBS data when the drugs were listed on the PBS and their full cost was above the patient co-payment threshold.

All supplies of antiresorptives that were supplied to manage osteoporosis through the PBS from 2003 to 2007 were captured in the PBS data as these were above the general patient co-payment threshold.

PBS Data items

The PBS data were obtained from the Department of Health and Ageing, covering all records of antiresorptives processed from 1 January 2003 to 31 December 2007.

The prescription supply records were linked to person-based records using a personal information number to track all antiresorptive prescriptions supplied to an individual over the study period. Each record (de-identified) in the PBS data extract included demographic and pharmaceutical information as well as pharmacy and prescriber details (Table 2.1).

Table 2.1: Data items for the PBS data extract

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

Antiresorptives monitored

Three major categories of antiresorptives available in Australia between 2003 and 2007 were:

- bisphosphonates (single formulation and combination)
- a selective estrogen receptor modulator (SERM)
- strontium ranelate.

Some subtypes of bisphosphonates (namely, alendronate, risedronate and etidronate) were supplied to manage Paget's disease of bone and to preserve bone mineral density in patients on long-term glucocorticoid therapy aside from osteoporosis.

The PBS item numbers were used to identify the supply of these bisphosphonates for specific conditions (Table 2.2). Only the supply of antiresorptives for management of osteoporosis was included in the analysis.

Table 2.2: PBS-subsidised antiresorptives supplied for multiple conditions

Antiresorptive	Form and strength	PBS item number	Condition managed	Inclusion in this study
Alendronate sodium	Tablet equivalent to 10 mg alendronic acid	8102K	Osteoporosis	Include
	Tablet equivalent to 70 mg alendronic acid	8511Y	Osteoporosis	Include
	Tablet equivalent to 40 mg alendronic acid	8090T	Paget's disease of bone	x
Risedronate sodium	Tablet 5 mg	8481J	Osteoporosis	Include
		4443W	Long-term glucocorticoid use	x
	Tablet 35 mg	8621R	Osteoporosis	Include
		4444X	Long-term glucocorticoid use	x
	Tablet 30 mg	8482K	Paget's disease of bone	x
Disodium etidronate and calcium carbonate	Pack containing 28 tablets disodium etidronate 200 mg and 76 tablets calcium carbonate 1.25 g	8056B	Osteoporosis	Include
Disodium etidronate	Tablet 200 mg	2920Q	Paget's disease of bone	x

Source: Department of Health and Ageing 2003, 2006, 2007.

Table 2.3 summarises the antiresorptive types included in the analysis, brands, the PBS item number, dosage, regimen and defined daily dosage (DDD). The DDD is the amount necessary to treat one adult for one day (Miller & Draper 2001). One pack supply of all antiresorptives covered 28 or 30 days, except for disodium etidronate and calcium carbonate which covered 90 days.

Out of seven subtypes of antiresorptives, five were bisphosphonates.

Table 2.3: PBS-subsidised antiresorptive drugs supplied to manage osteoporosis, 2003–07

Type	Subtype	PBS item number	Brands	PBS listing	Dosage regimen	Maximum quantity	DDD per pack
Single formulation bisphosphonate	Alendronate sodium	8102K	Fosamax 10 mg ^(a)	Jan 2003 ^(b)	Daily	30 tablets	30
		8511Y	Fosamax Once Weekly	Jan 2003 ^(b)	Weekly	4 tablets	28
			Alendro Once Weekly ^(c)	Dec 2005			
			Chem mart Alendronate ^{(c)(d)}	Dec 2006			
			GenRx Alendronate ^{(c)(d)}	Dec 2006			
	Terry White Chemists Alendronate ^{(c)(d)}	Dec 2006					
Risedronate sodium	8481J	Actonel	Jan 2003 ^(b)	Daily	28 tablets	28	
	8621R	Actonel Once Weekly	Jan 2003 ^(b)	Weekly	4 tablets	28	
Combination bisphosphonates	Disodium etidronate and calcium carbonate	8056B	Didrocal	Jan 2003 ^(b)	Daily	90 tablets	90
		9012H	Fosamax Plus	Aug 2006	Weekly	4 tablets	28
		8899J	Actonel Combi	Apr 2006	Weekly for risedronate sodium and daily for calcium carbonate	4 tablets of risedronate sodium, 24 tablets of calcium carbonate	28
SERM	Raloxifene hydrochloride	8363E	Evista	Jan 2003 ^(b)	Daily	28 tablets	28
Other	Strontium ranelate	3036T	Protos 2 g	Apr 2007	Daily	28 tablets	28

(a) Fosamax 10 mg was deleted from the PBS schedule in August 2004.

(b) PBS listing for these drugs was before January 2003.

(c) Alendro Once Weekly, Chem mart Alendronate, GenRx Alendronate and Terry White Chemists Alendronate are generic alendronate sodium.

(d) Chem mart Alendronate, GenRx Alendronate and Terry White Chemists Alendronate were deleted from the PBS schedule in February 2007.

(e) Cholecalciferol is a form of vitamin D (vitamin D₃).

Source: Department of Health and Ageing 2003, 2006, 2007.

Cohort selection

Two cohorts, the initiating cohort and follow-up cohort, were identified to study the supply pattern of antiresorptives in Australia. The initiating cohort was established to examine:

- the demographic characteristics of those who started on antiresorptive therapy
- the medical specialty categories of prescribers involved in initiating antiresorptive therapy
- the time taken for the first antiresorptive prescriptions to be filled.

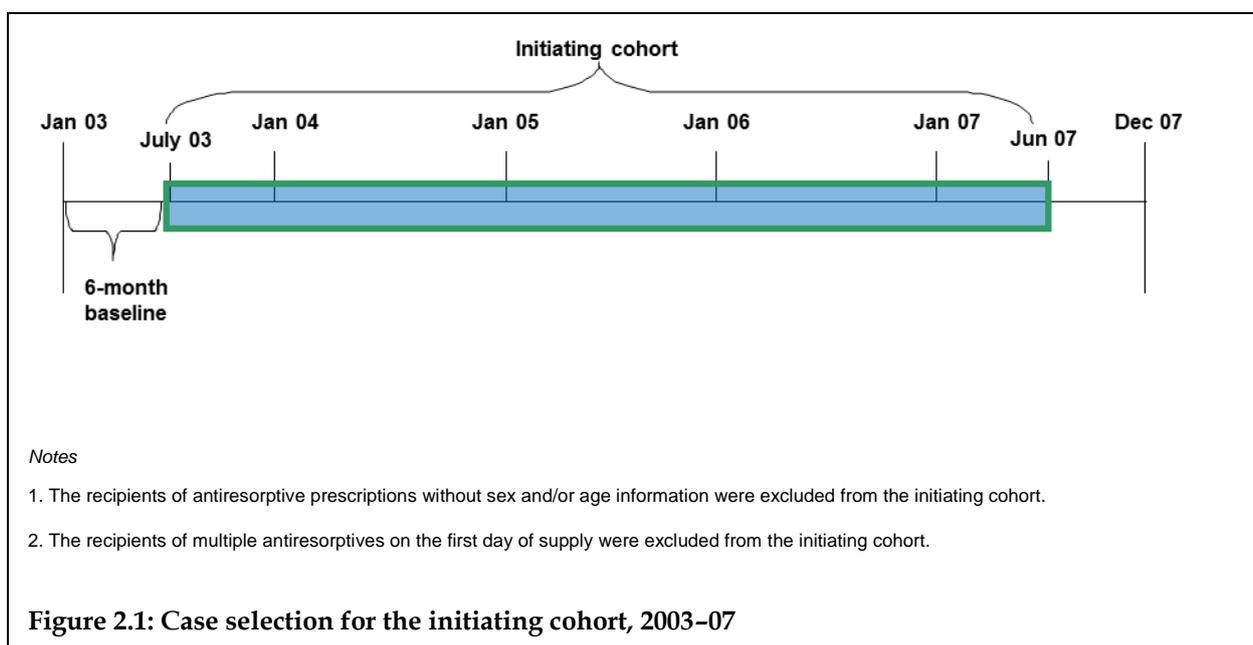
The follow-up cohort, a subset of the initiating cohort, was used to monitor whether enough antiresorptives were supplied over the first 12 months.

A brief outline of the sample selection process for the two cohorts is provided in the following.

Initiating cohort

A subset of the PBS data for a defined time period does not include sufficient information to be certain whether an individual had received a class of medicine previously.

‘The initiating cohort’ was created by selecting a subset of patients out of those who received at least one antiresorptive supply from 1 January 2003 to 31 December 2007. Figure 2.1 depicts case selection for the initiating cohort, and the selection criteria applied are noted below.



The following case selection steps were taken:

- the recipients of at least one antiresorptive supply from 1 January 2003 to 31 December 2007 were identified
- the date of their first antiresorptive supply during the 5-year period was noted
- the records without age and/or sex information were excluded

- the records of individuals with multiple antiresorptive records on the first day of supply were excluded because dispensing multiple supplies of antiresorptives as a first supply is unlikely
- those whose first date of antiresorptive supply during the 5-year period occurred before 1 July 2003 were excluded as they might be continuing with antiresorptive therapy initiated prior to January 2003
- those whose first date of supply during the study period occurred after 1 July 2007 were excluded because the data from the last few months in 2007 were likely to be incomplete due to the lag between supply of PBS-subsidised medicine and processing of records.

Except for disodium etidronate and calcium carbonate, one supply of all antiresorptives available during the study period covered 28 to 30 days of therapy (Table 2.3). A supply of disodium etidronate covered 90 days of therapy. Thus, 6 months without supply suggests that these patients have not previously been supplied with antiresorptives or that they have missed two or six scripts.

For this reason, the patients included in the initiating cohort had at least a 6-month period where they were apparently not taking antiresorptives.

While some uncertainty remains regarding whether the initiating cohort inadvertently included people returning to antiresorptive therapy after 6 months, the baseline period of 6 months was deemed appropriate in the light of pack sizes of the majority of antiresorptives available at the time. For more details on the selection process, see Appendix B.

Follow-up cohort

Among those in the initiating cohort, those whose first antiresorptive supply occurred from 1 July 2003 to 30 June 2006 were selected to form the follow-up cohort as it was possible to examine the following 12 months of antiresorptive supply.

Figure 2.2 depicts case selection for the follow-up cohort. For more details on the selection process see Appendix B.

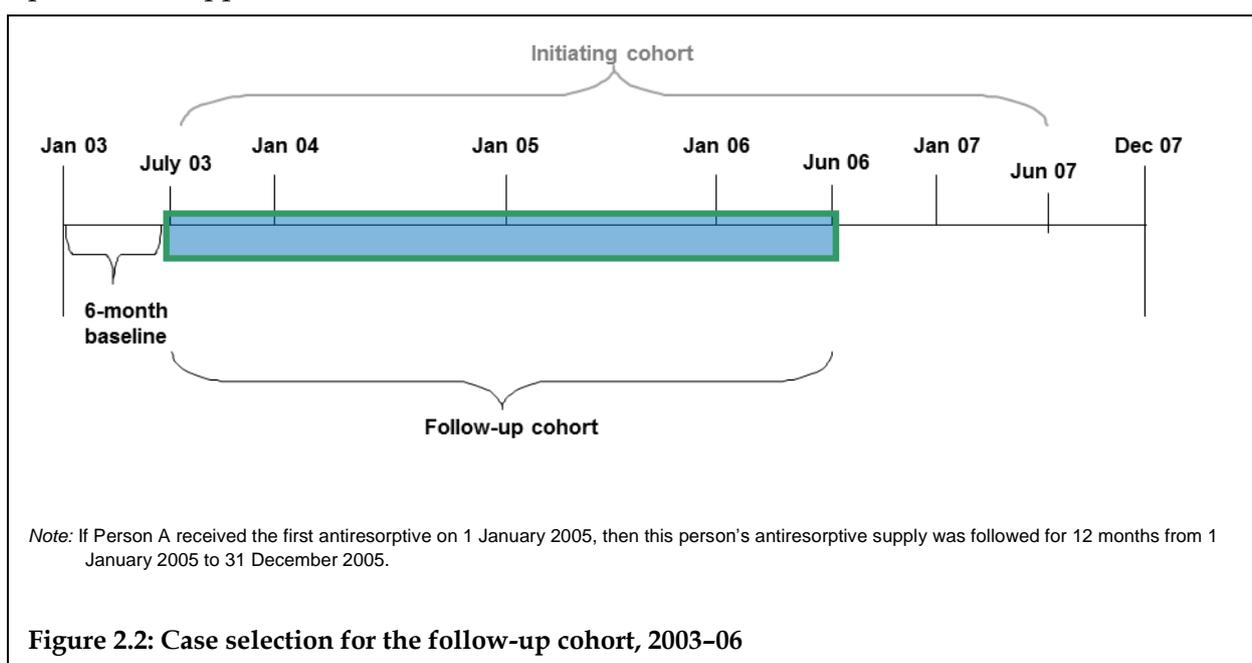


Figure 2.2: Case selection for the follow-up cohort, 2003-06

3 Initiation of antiresorptive therapy

This chapter provides an overview of the first antiresorptives supplied to individuals in the 4-year period from 1 July 2003 to 30 June 2007. This chapter also reports on the relative supply of various antiresorptives, the prescribers of the first antiresorptive drug and how long it took for the first prescriptions to be filled.

Demographic characteristics of initiating cohort

There were 562,597 Australians who received at least one antiresorptive medication between 1 January 2003 and 31 December 2007.

Out of the above total, 297,795 people met the selection criteria for the initiating cohort outlined in Chapter 2. About three quarters of the initiating cohort were females (Table 3.1).

Table 3.1: Antiresorptives initiating cohort, July 2003 to June 2007

Demographic characteristic	Number	Per cent
<i>Sex</i>		
Males	69,214	23.2
Females	228,581	76.8
<i>Age group</i>		
0–34	1818	0.6
35–44	4076	1.4
45–54	19,119	6.4
55–64	54,198	18.2
65–74	81,869	27.5
75–84	99,101	33.3
85+	37,614	12.6
<i>Remoteness</i>		
Major cities	212,899	71.5
Inner regional	82,525	27.7
Other	2,290	0.8
<i>PBS subsidy category</i>		
General	48,470	16.3
Concessional	249,325	83.7
Total	297,795	100.0

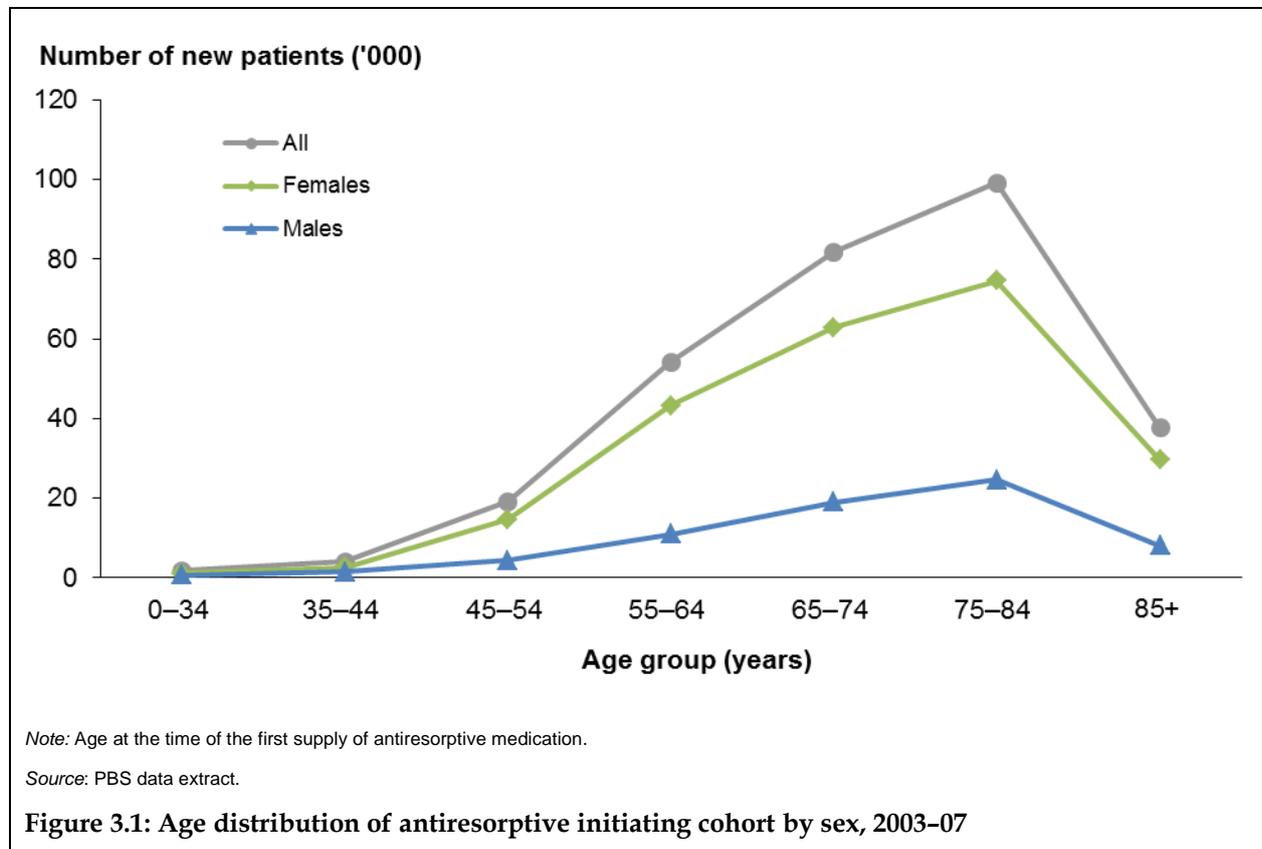
Notes

1. Remoteness category based on the Australian Standard Geographical Classification (ASGC) (ABS 2008). The remoteness category is based on how distant a place is by road from urban centres of different sizes, and thus provides a relative indication of how difficult it might be for residents to access services including health care and education. 'Other' includes Outer regional, Remote, and Very remote areas.

2. The PBS data extract included 81 people with missing remoteness data.

Source: PBS data extract.

The average age of starting antiresorptive therapy was 71.7 years for females and 71.4 years for males. The majority of the initiating cohort was 65 years and over in both males and females (Figure 3.1), with only 2% of the initiating cohort being younger than 45 years of age (Table 3.1).



The first prescribed antiresorptive

Alendronate and risedronate are recommended as the first-line therapy for management of osteoporosis (Sambrook et al. 2002). The PBS data indicate this recommendation was widely practised between July 2003 and June 2007.

From 1 July 2003 to 30 June 2007, almost all patients commencing antiresorptive therapy (94.6%) were started on a bisphosphonate (Table 3.2). Alendronate compound (single formulation or combination therapy) was the most commonly supplied antiresorptive, with more than 60% of the initiating cohort being prescribed this particular bisphosphonate.

Risedronate compound (single formulation or combination therapy) was the second most widely prescribed antiresorptive, being prescribed to 1 in 3 new starters (34.0%).

Raloxifene hydrochloride and strontium ranelate were not recommended for males, and the PBS authority restricted their use to females with post-menopausal osteoporosis. Virtually all prescriptions of these two antiresorptives were supplied to females (95.5% and 95.2% respectively).

Table 3.2: The first antiresorptives used for the management of osteoporosis, 2003–07

Antiresorptive subtype	Males		Females		All	
	Number	Per cent	Number	Per cent	Number	Per cent
Alendronate compound ^(a)	45,124	65.2	135,331	59.2	180,455	60.6
Risedronate compound ^(b)	22,901	33.1	78,444	34.3	101,345	34.0
Disodium etidronate and calcium carbonate	550	0.8	1,279	0.6	1,829	0.6
Raloxifene hydrochloride	576	0.8	12,290	5.4	12,866	4.3
Strontium ranelate	63	0.1	1,237	0.5	1,300	0.4
Total	69,214	100.0	228,581	100.0	297,795	100.0

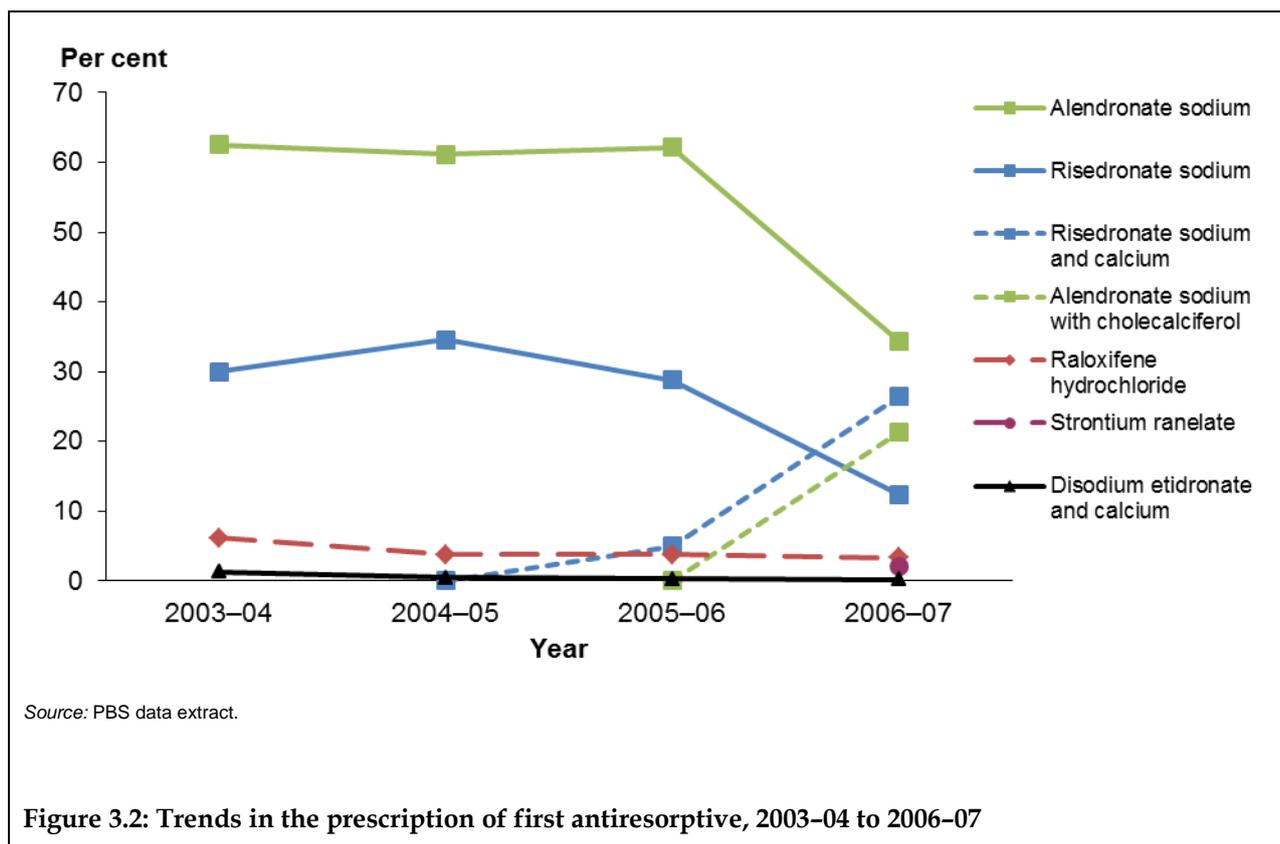
(a) Includes alendronate sodium and alendronate sodium with cholecalciferol.

(b) Includes risedronate sodium and risedronate sodium and calcium carbonate.

Source: PBS data extract.

Combination alendronate and risedronate bisphosphonates became available through the PBS in 2006, and this markedly changed the antiresorptives supply through the PBS (see Figure 3.2). Since mid-2006, the first-prescribed treatment for osteoporosis shifted from single formulation of alendronate and risedronate to combination therapy.

The supply of second-line antiresorptives remained relatively unchanged during the study period for the initiating cohort. Raloxifene hydrochloride and disodium etidronate and calcium were available before January 2003, and their supply was low and steady during the 4-year study period. Strontium ranelate was listed on the PBS in April 2007, and this accounts for it being supplied to a few people only in 2006–07.



Prescribers

A total of 25,787 medical practitioners initiated antiresorptive therapy for 297,795 patients in the initiating cohort in the 4-year period.

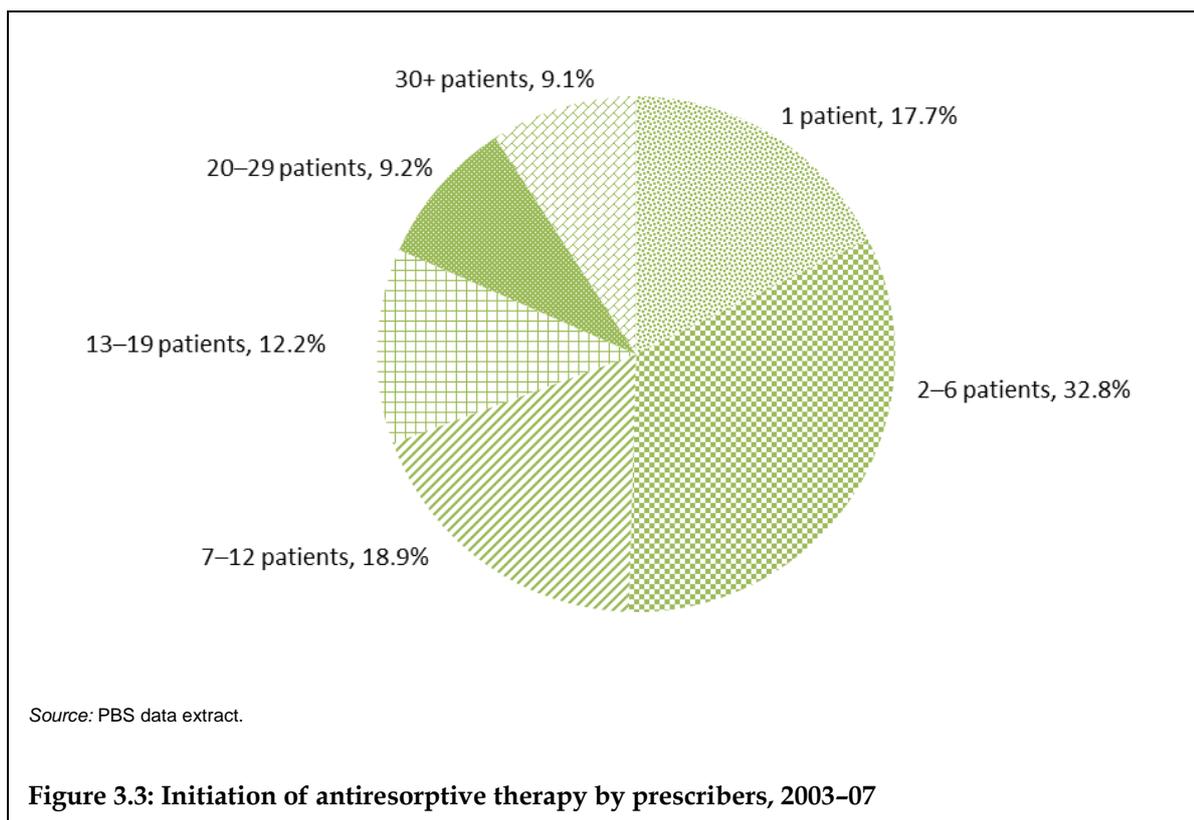
Over half (50.4%) of medical practitioners have a small caseload of patients on antiresorptive therapy. They supplied the first antiresorptive medicine to six or fewer patients in the initiating cohort in the 4-year period. One in 6 (17.7%) prescribers initiated therapy for one patient.

Some medical practitioners, however, manage considerable caseloads of patients on antiresorptive therapy. Approximately one in 10 (9.1%) initiated therapy for more than 30 patients in this period. Thus, there appears to be a wide range of patient caseloads among doctors.

Four different groups of prescribers were identified:

- general practitioners (GPs) along with other primary care medical practitioners (OMPs)
- endocrinologists
- rheumatologists
- other.

The medical specialties of physicians included in the GPs/OMPs are listed in Appendix A Table A.2.



During the 4-year period, the majority (87.5%) of the patients in the initiating cohort received their first antiresorptive prescription from GPs/OMPs (Table 3.3). Only 2.0% received their first antiresorptive prescription from endocrinologists, 2.5% from rheumatologists and 8.0% from prescribers in other major specialty categories.

Table 3.3: Prescribers of first antiresorptives, 2003-07

Prescriber major specialty	Initiating cohort	
	Number	Per cent
GPs/OMPs	260,500	87.5
Rheumatologists	7,493	2.5
Endocrinologists	5,878	2.0
Other	23,810	8.0
Total	297,681	100.0

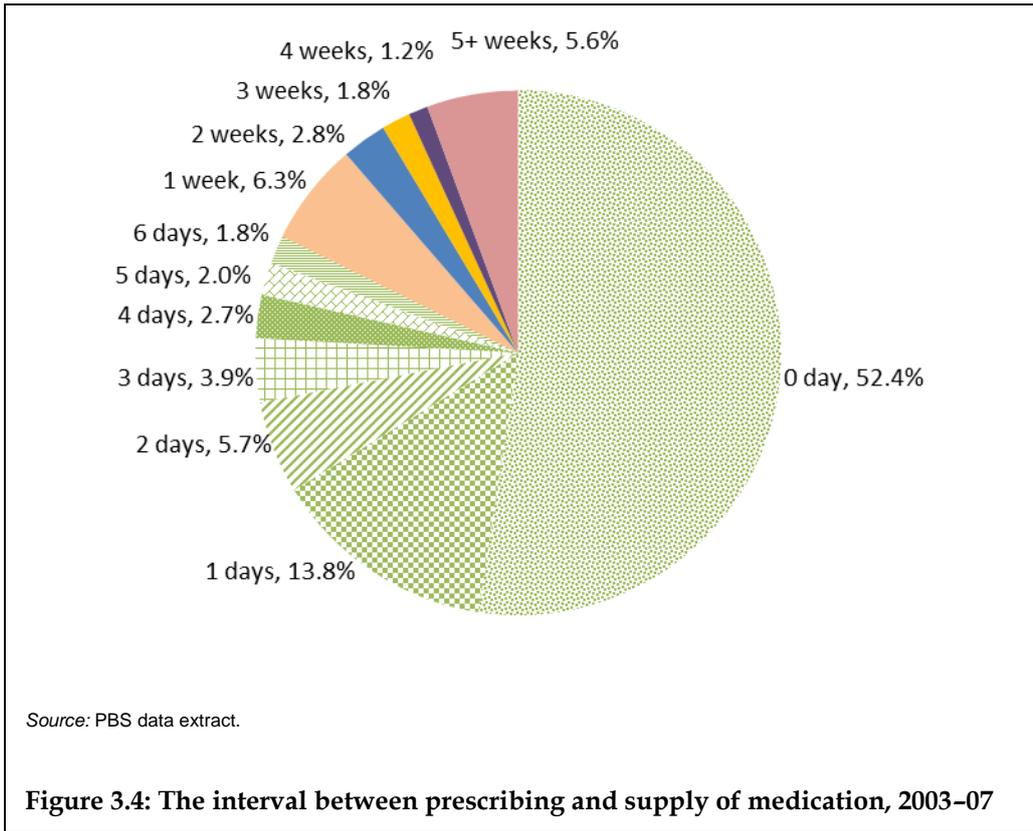
Note: The prescriber major specialty information was missing for 114 patients.

Source: PBS data extract.

Time taken to fill the first prescription

Over half (52.4%) of the initiating cohort had their first script filled on the day it was prescribed (Figure 3.4). An additional 30% had their prescription filled within 1-6 days of prescription. By the end of the 4th week, almost all patients in the initiating cohort (94.4%) had filled their first antiresorptive prescription.

A small group (5.6%), however, took 5 weeks or more to fill their prescription.



4 The first 12 months of antiresorptive supply

A total of 232,921 patients received their first antiresorptive supply during the 5-year study period between 1 July 2003 and 30 June 2006, and met the criteria to be included in the follow-up cohort (see Appendix B).

This chapter examines their first 12 months of antiresorptive supply. Twelve months is a short time span to characterise any underlying trends in the use of antiresorptive medicine which is generally recommended for long-term use. The length of time monitored is nevertheless sufficient to follow certain drug supply patterns.

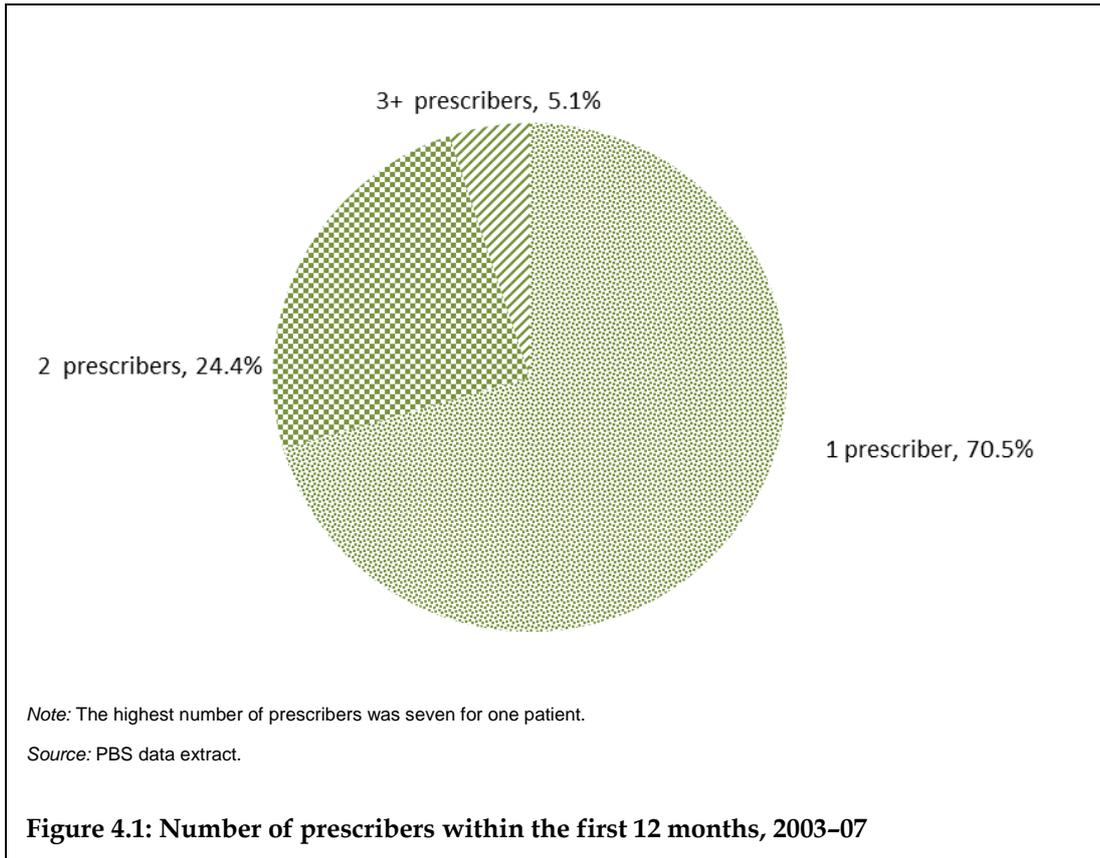
Four aspects of the medicine supply were examined:

- the number of antiresorptive prescribers per patient
- the extent of drug switching
- how much of prescribed antiresorptives in the first 12 months was supplied to patients
- the cost of the first 12 months of antiresorptive therapy.

How many prescribers?

Continuity of care with the same physician is important for ensuring quality of care, and it has been shown to reduce adverse reactions, increase personal satisfaction and adherence to treatment (Gray et al. 2003; Ionescu-Ittu et al. 2007). The PBS data suggest that the majority of patients in the follow-up cohort (70.5%) had only one medical professional prescribing antiresorptive medication during the first 12 months of treatment (Figure 4.1). About a quarter (24.4%) of the follow-up cohort received antiresorptive prescriptions from two prescribers in the first 12 months.

Only a small group (5.1%) received prescriptions from three or more prescribers. This suggests that continuity of care is high for those on antiresorptive therapy.



Drug switching

Patient tolerance, compliance and side effects may influence the changing type or routine of administration of therapy on an individual basis (RACGP 2010). During the first 12 months of treatment only 8.5% of patients in the follow-up cohort switched from the initiating antiresorptive to another type (Figure 4.2).

The great majority of the follow-up cohort (91.5%) stayed on the initiating antiresorptive throughout the first 12 months (Figure 4.2).

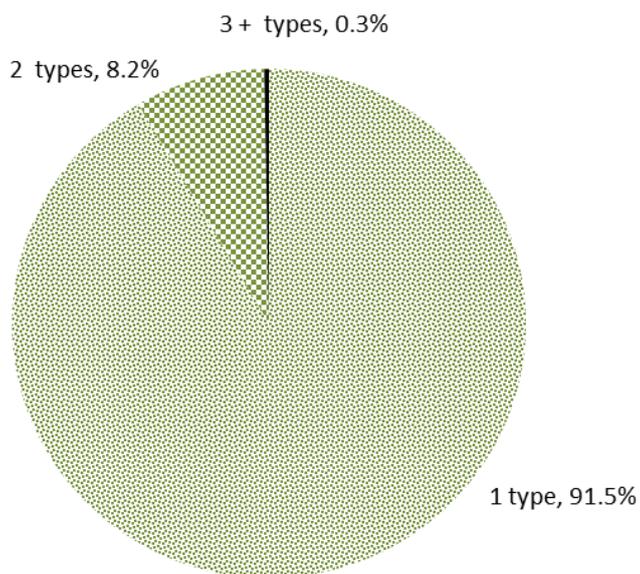


Figure 4.2: Antiresorptive switching in the first 12 months, 2003-07

Note: Different doses of a drug were classified as the same drug. For example, alendronate 10 mg and 70 mg were grouped together, as were risedronate 5 mg and 35 mg.

Source: PBS data extract.

It was not possible to determine from the PBS data whether a person had stopped taking the initial drug once the alternative drug was supplied. Concurrent use of multiple antiresorptive drugs is not recommended by the Royal Australian College of General Practitioners (RACGP 2008).

The type of drug that people were started on appears to have influenced whether drugs were switched within the first 12 months. Those who started on alendronate sodium or risedronate sodium with calcium were least likely to change drugs in the first 12 months. One in 13 (7-8%) of these people switched to another antiresorptive. In comparison, one in six people (15.7%) who started on disodium etidronate and calcium carbonate switched drugs during the same period.

A greater proportion of the follow-up cohort switched their antiresorptives as more antiresorptive alternatives became available through the PBS in 2006 (Table 2.3). While around one in 20 patients in the follow-up cohort changed drugs in their first year of treatment in 2003-04 and 2004-05 (5.0% and 4.9%), one in 6 (16.2%) did so in 2005-06.

Were enough antiresorptives supplied in the first 12 months?

Two measures were used to examine the extent of antiresorptive supply to enable compliance:

- proportion of patients who received enough antiresorptives
- number of days to filling the last prescription in the 12-month follow-up period.

Proportion of patients who received enough antiresorptives

As noted earlier, while full compliance is recommended, 75–80% compliance is regarded as the level required to obtain the therapeutic benefits of bisphosphonates. To be either fully or 75–80% compliant, a patient must have been dispensed with a certain volume of the medications.

The minimum number of prescriptions needed to be filled in 12 months to be fully compliant with the therapy can be obtained by:

$$\text{the number of prescriptions needed for full compliance} = 365 \text{ days} * 100\% / \text{days covered by a pack}$$

The minimum number of prescriptions needed to be filled in 12 months to be adequately compliant with the therapy can be obtained by:

$$\text{the number of prescriptions needed for adequate compliance} = 365 \text{ days} * 75\% / \text{days covered by a pack}$$

Simply being dispensed with an adequate volume of the medications does not, of course, guarantee compliance in terms of the timing and dosages that were actually consumed. It does, however, mean that it was at least possible for compliance to occur.

Table 4.1 summarises the achievable compliance level for a given level of supply for each antiresorptive available from 2003 to 2007. As it is shown in Table 2.3, most antiresorptives that were available from 2003 to 2007 contained comparable numbers of defined daily dosages per pack. One pack supply of all antiresorptives covered 28 or 30 days, except for disodium etidronate and calcium carbonate which covered 90 days.

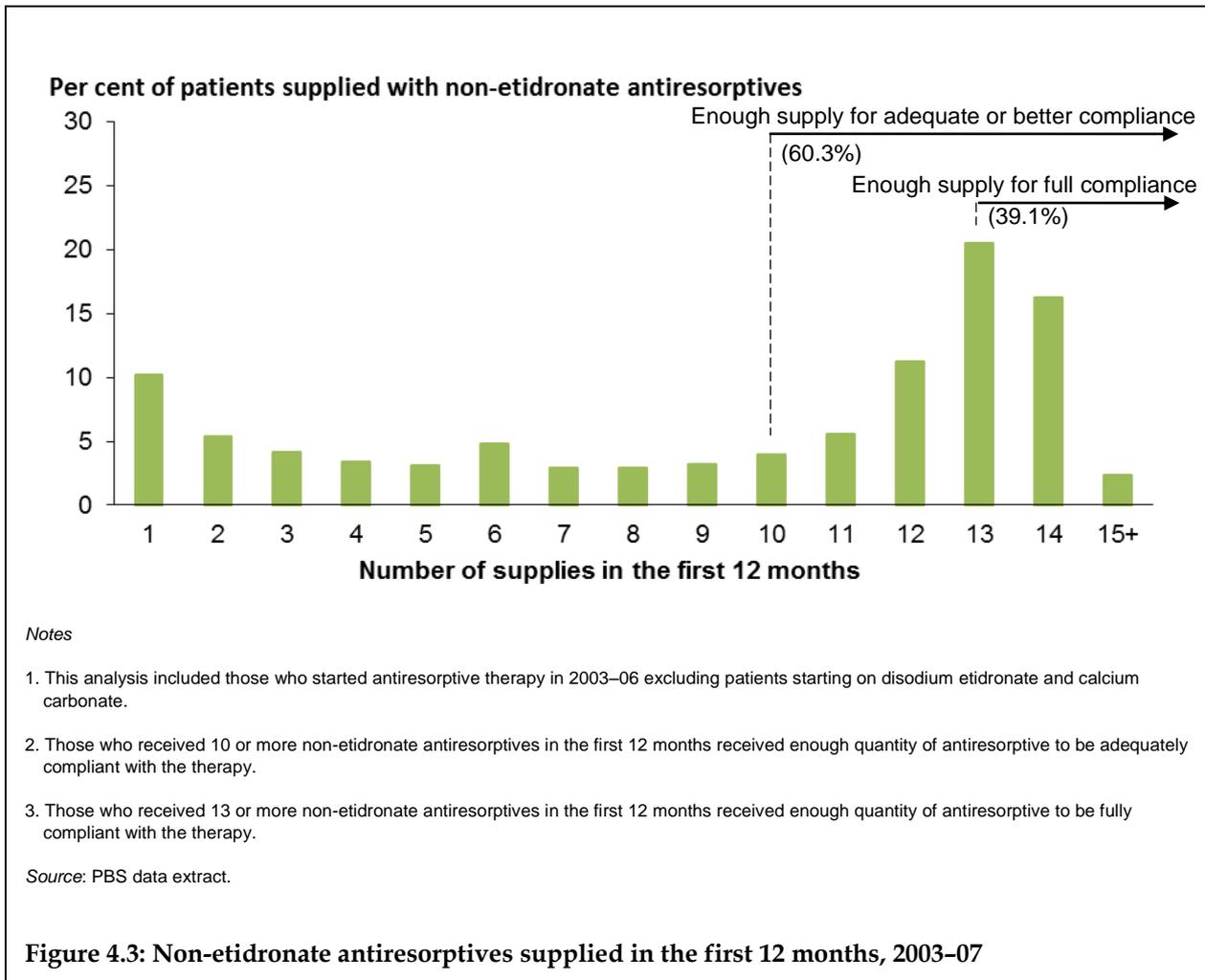
Table 4.1: Number of antiresorptives supplies and the achievable compliance level

Achievable compliance level with supplied antiresorptives	28 days per pack	30 days per pack	90 days per pack
	Number antiresorptive supplies in 12 months		
Below adequate compliance (<75%)	0–9	0–9	0–3
Adequate compliance (75-99%)	10–12	10–12	4
Complete compliance (100%+)	13+	13+	5+

Note: One pack supply of disodium etidronate and calcium carbonate covered 90 days. All other antiresorptives available from 2003 to 2007 covered 28 or 30 days.

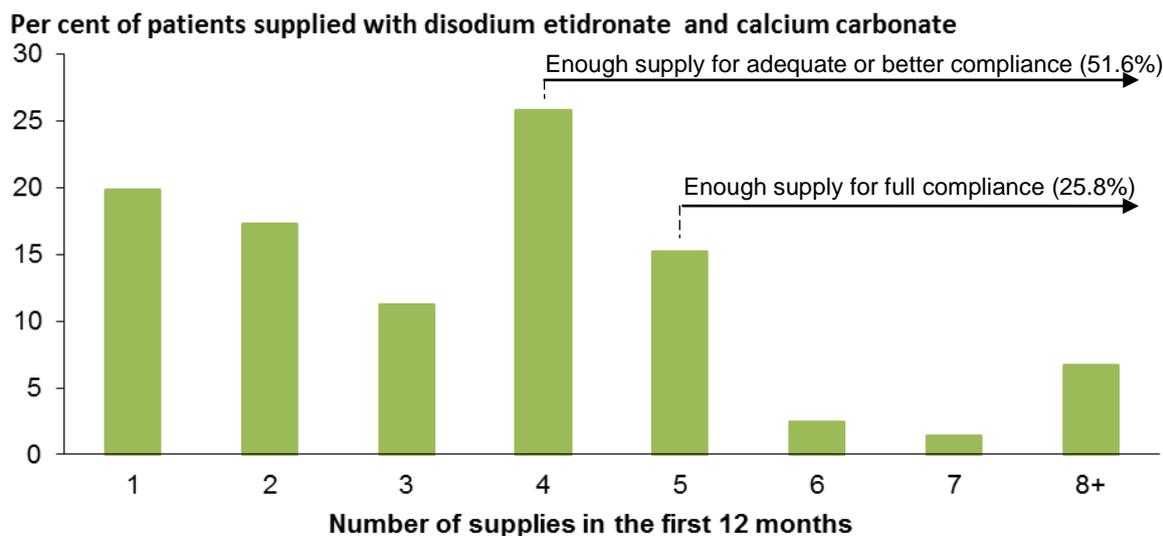
Among the patients in the follow-up cohort who were supplied with non-etidronate antiresorptives, three out of five (60.3%) filled 10 or more antiresorptive prescriptions (Figure 4.3) and thus received enough medicine to meet at least an adequate compliance criteria.

About 2 in 5 (39.1%) who received non-etidronate antiresorptives filled 13 or more scripts during the first 12 months of their treatment, and thus received enough medicine to be fully compliant.



Of those who started on disodium etidronate and calcium carbonate, just over a half (51.6%) received four or more supplies in 12 months, and thus received enough medicine to meet at least an adequate compliance criteria (Figure 4.4).

A quarter (25.8%) of those who started on this antiresorptive filled five or more prescriptions over the 12-month period, and thus received enough medicine to be fully compliant (Figure 4.4).



Notes

1. This analysis included those who started on disodium etidronate and calcium carbonate treatment in 2003–06.
2. Those who received four or more disodium etidronate and calcium carbonate in the first 12 months received enough quantity of antiresorptive to be adequately compliant with the therapy.
3. Those who received five or more disodium etidronate and calcium carbonate in the first 12 months received enough quantity of antiresorptive to be fully compliant with the therapy.

Source: PBS data extract.

Figure 4.4: Disodium etidronate antiresorptive supplied in the first 12 months, 2003–07

Table 4.2 summarises the levels of antiresorptive supply in the first 12 months across all subtypes. The overall level of antiresorptive supply resembled that of people who were supplied non-etidronate antiresorptives, as this group constituted the majority of the follow-up cohort.

Table 4.2: Levels of antiresorptive supplies in the first 12 months, 2003–07

Coverage of 12 months dosage	Number	Per cent
<25%	45,420	19.5
25–49%	25,907	11.1
50–74%	21,202	9.1
75–99%	48,867	21.0
100%+	91,525	39.3
Total	232,921	100.0

Notes

1. Covers individuals starting treatment in 2003–06.
2. 100%+ supply equates to five or more supplies for those starting on disodium etidronate and calcium carbonate, and 13 or more supplies for those starting on other antiresorptives.

A substantial number of the follow-up cohort (91,525 people) received more than enough to cover 12 months of antiresorptive therapy (Table 4.2). The explanations for this 'over supply' may include:

- some patients in the follow-up cohort switched antiresorptive type during the first 12 months
- some patients in the follow-up cohort who reached the safety net threshold for the PBS medicine stockpiled their medicine before the end of the calendar year to obtain medicine at a reduced price.

In January 2006, the PBS safety net 20-day rule was introduced to prevent people from obtaining medicine more than 20 days earlier than they needed it (Department of Health and Ageing 2005). This rule applied at least to part of the follow-up period.

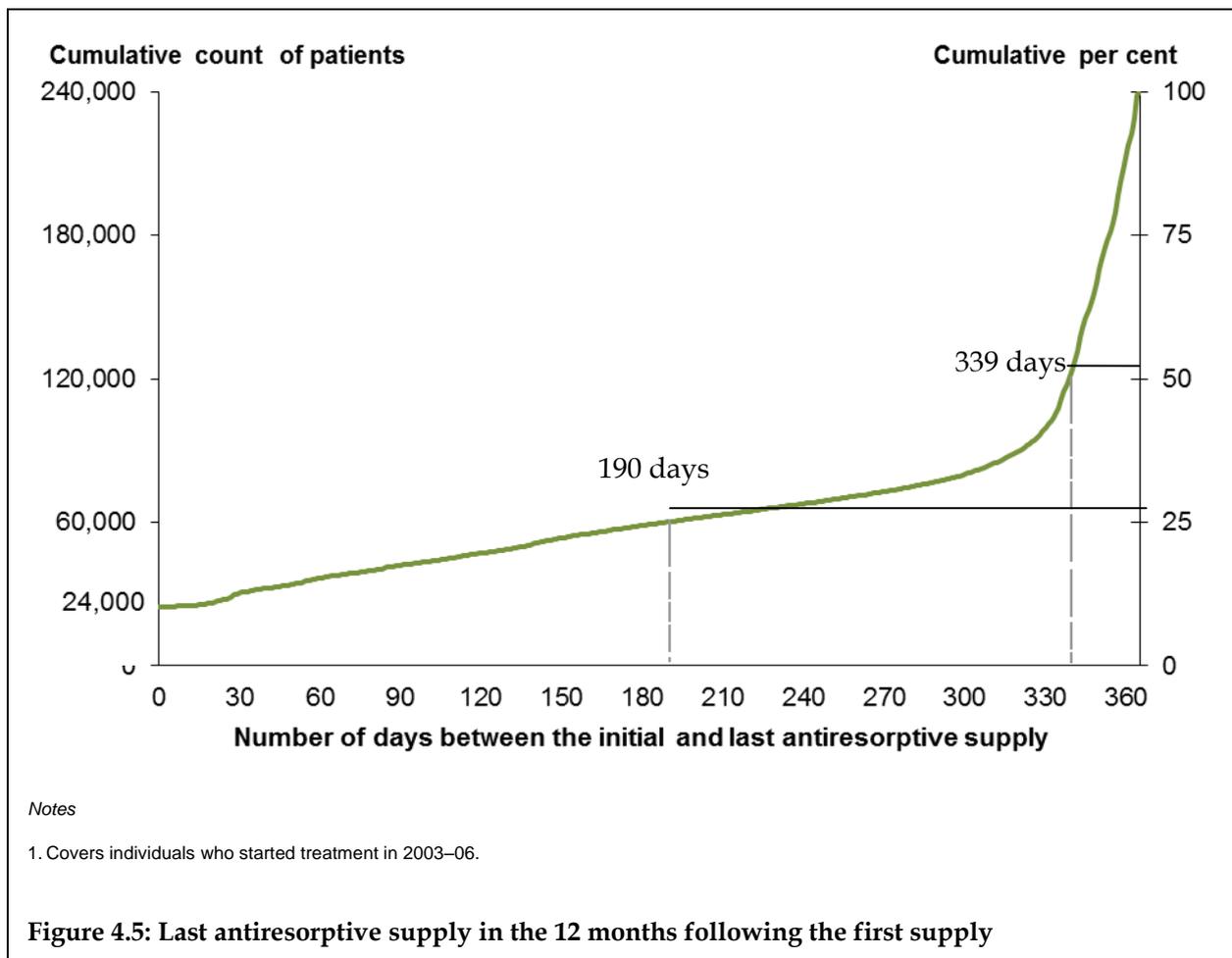
Number of days to non-renewal

Approximately half of the follow-up cohort (117,719 people or 50.5%) received the last recorded antiresorptive supply 339 or more days (approximately 11 months) after the first supply (Figure 4.5). This indicates that about half of the follow-up cohort was continuing to receive their antiresorptive supply 12 months after the commencement of the therapy. Those who were taking antiresorptive that covered 28 or 30 days per pack had just enough to cover until the end of the 12-month period. Those who were taking disodium etidronate calcium carbonate had more than enough to cover until the end of the 12-month period.

A sizable proportion of the follow-up cohort, however, received their last recorded supply of antiresorptive well before the completion of the 12-month monitoring period.

About one in 10 (23,967 people or 10.3%) in the follow-up cohort received only one supply of antiresorptive in the first 12 months.

About a quarter of the follow-up cohort received their last supply of antiresorptive by 190 days, or just after 6 months from the commencement of the therapy.



Average yearly cost of antiresorptive therapy

The average yearly total cost per person (sum of the cost to PBS and patient co-payment) for antiresorptive therapy for the 3-year period from July 2004 to June 2006 was \$516. The annual average cost declined slightly from \$525 per person in 2004–05 to \$498 per person in 2006–07.

This decline is at least partly accounted for by a decrease in the PBS-dispensed price of antiresorptives from 1 July 2003 to 30 June 2007 (Table 4.3). The first generic¹ alendronate became available through the PBS in December 2005 (Alendro Once Weekly), and the PBS-dispensed prices of antiresorptives started decreasing from that time.

¹ A drug that is comparable to another drug in content, dosage, strength, manner of administration, performance characteristics and intended use. The generic version became available after the first patent for Fosamax expired.

Table 4.3: PBS-dispensed price (\$) antiresorptives for osteoporosis available from July 2003 to June 2007

Antiresorptive type	Subtype	Brands	PBS schedule publication month																			
			Nov 2002	Aug 2003	Nov 2003	Feb 2004	May 2004	Aug 2004	Dec 2004	Apr 2005	Aug 2005	Dec 2005	Apr 2006	Aug 2006	Dec 2006	Jan 2007	Feb 2007	Mar 2007	Apr 2007	May 2007	Jun 2007	
Bisphosphonates	Alendronate sodium ^(a)	Fosamax 10 mg ^(b)	59.5	59.6	59.6	59.6	59.6															
		Fosamax Once Weekly	55.9	55.9	55.9	55.9	55.9	55.9	56.0	56.0	56.0	54.7	54.5	53.1	53.1	53.1	53.1	53.1	52.6	52.6	52.6	
		Alendro Once Weekly ^(c)										54.5	53.7	52.3	52.3	52.3	52.3	52.3	51.8	51.8	51.8	
	Risedronate sodium	Actonel	55.9	55.9	55.9	55.9	55.9	55.9	56.0	56.0	56.0	54.5	53.7	52.3	52.3	52.3	52.3	52.3	52.3	52.3	52.3	52.3
		Actonel Once Weekly	55.9	55.9	55.9	55.9	55.9	55.9	56.0	56.0	56.0	54.5	53.7	52.3	52.3	52.3	52.3	52.3	52.3	52.3	52.3	52.3
		Disodium etidronate and calcium carbonate	Didrocal	80.5	80.6	80.6	80.6	80.6	80.6	80.6	80.6	71.2	71.2	71.4	69.4	69.4	69.4	69.4	69.4	69.4	69.4	69.4
Combination bisphosphonates	Alendronate sodium with cholecalciferol	Actonel Combi											53.7	52.3	52.3	52.3	52.3	52.3	52.3	52.3	52.3	
	Risedronate sodium and calcium carbonate	Fosamax Plus												52.3	52.3	52.3	52.3	52.3	51.8	51.8	51.8	
SERM ^(d)	Raloxifene hydrochloride	Evista	60.6	60.6	60.6	60.6	60.6	60.6	60.6	60.6	60.7	59.0	59.2	57.7	57.7	57.7	57.7	57.7	57.7	57.7	57.7	
Other	Strontium ranelate	Protos 2 g																	52.3	52.3	52.3	

(a) Three generic alendronate sodium (tablet equivalent to 70 mg alendronic acid), (Chem mart Alendronate, GenRx Alendronate, and Terry White Chemists Alendronate) were listed on the PBS in December 2006 under the PBS item number 8511Y. The availability of these was limited to only two months as they were subsequently deleted from the PBS on February 2007. For the two months these products were available through the PBS, their dispense price was \$52.30. These were not included in the table due to their limited period of availability.

- (b) Fosamax 10 mg was deleted from the PBS in May 2004.
- (c) Alendronate Once Weekly was the first generic alendronate.
- (d) SERM stands for selective estrogen receptor modulator.

Source: Department of Health and Ageing (2011b).

5 Discussion

This study described the pattern of antiresorptive supply for management of osteoporosis to a cohort of people who began their antiresorptive therapy from 1 July 2003 to 30 June 2007. The study focused on examining:

- demographic characteristics of those who started on antiresorptive therapy
- medical specialists involved in prescribing antiresorptives
- changes in antiresorptive supply over time
- levels of antiresorptive supplies to support compliance with the therapy.

Key findings

The study found between 2003 and 2007:

- the majority of those who started antiresorptive therapy were females and aged 65 years and over
- alendronate and risedronate (both bisphosphonates), recommended as the first-line therapy for osteoporosis were the most widely supplied antiresorptives
- primary care physicians (GPs and OMPs) played a major role in prescribing antiresorptive medicines
- two in 5 patients did not receive the quantity of antiresorptives required to maintain sufficient regular intake of this medication during the first 12 months of therapy
- a sizable proportion of patients stopped receiving antiresorptives by 6 months after the initiation of therapy, short of the duration needed to establish therapeutic effects
 - a quarter of the patients stopped receiving antiresorptive supply within 6 months of initiation of antiresorptive therapy
 - one in 10 patients received just one supply of antiresorptives.

Taking antiresorptives regularly, and as directed, is important for effective management of osteoporosis. For antiresorptive therapy to be effective, 36 to 60 months of regular medication is considered to be optimal (Watts & Diab 2010).

In order to ensure the antiresorptives are taken regularly and as directed, the supply of a certain quantity of the drugs over a specific period of time is required. This study, however, found that many patients who started on antiresorptive therapy in the years 2003–06 did not receive enough medication to be adequately compliant in the first 12-month period both in terms of quantity and duration.

The PBS data pertain to supply of antiresorptives and not whether these were taken in accordance to dosage and frequency as advised by the doctors. The amount of antiresorptives supplied sets the natural limit of the amount that can be taken by the patients. Seen in this light, the actual compliance rate with the therapy among the follow-up cohort is likely to be lower than that suggested by the supply data analysis.

It is noteworthy in this context that prior to April 2007, only those who had a confirmed case of minimal trauma fracture(s) were eligible for antiresorptive therapy through the PBS. This meant that many in this study suffered painful fractures that were a physical prompt to

commencing therapy. It is likely that many of the more recent patients who use the medication as a primary prevention strategy have not experienced fractures of this sort. Thus, it is possible that the compliance rate among more recent patients to antiresorptive therapy may be lower than what was found in this study.

This study found that about half of the initiating cohort discontinued their antiresorptive therapy within 6 to 7 months of initiation; a trend consistent with previous studies (Jackevicius et al. 2002; Cramer et al. 2003; Haynes et al. 2002, Sambrook 2006). It appears that shortly after treatment initiation is a critical time to establish compliance with antiresorptive treatment. The Royal Australian College of General Practitioners indeed recommends GPs provide regular monitoring and follow-up of all patients with osteoporosis 3 to 6 months after initiating pharmaceutical intervention and annually thereafter (RACGP 2010). The causes of the drop-out from antiresorptive therapy would be a worthwhile area of enquiry to improve the quality use of medicine in the area.

Appendix A PBS data

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

Year	PBS subsidy status					
	<u>Concessional beneficiaries</u>			<u>General beneficiaries</u>		
	Co-payment	Safety net threshold	PBS safety net contribution	Co-payment	Safety net threshold	PBS safety net contribution
2003	\$3.70	\$192.40	\$0.00	\$23.10	\$708.40	\$3.70
2004	\$3.80	\$197.60	\$0.00	\$23.70	\$726.80	\$3.80
2005	\$4.60	\$239.20	\$0.00	\$28.60	\$874.90	\$3.80
2006	\$4.70	\$253.80	\$0.00	\$29.50	\$960.10	\$4.60
2007	\$4.90	\$274.40	\$0.00	\$30.70	\$1,059.00	\$4.90

Table A.2: The medical specialties included in the GPs/ OMPs

<u>Other primary care medical practitioner</u>
General medicine
Vocationally registered GP
Family medicine program trainee
Fellow of College of GPs
Royal Australian College of General Practitioners (RACGP) trainee
Remote OMP, Outer metro OMP
Medicare plus pre-1996 OMP (restricted and unrestricted)
Local rural/remote relief
Rural and remote area placement program
Procedural GP (recognised and non-recognised)
Other non-specialist

Appendix B The study cohorts

The Department of Health and Ageing provided the PBS data extract of antiresorptives for management of osteoporosis processed by Medicare Australia from 1 January 2003 to 31 December 2007. The record selection steps noted below were followed to define the initiating cohort and follow-up cohort (refer to Figure A2.1).

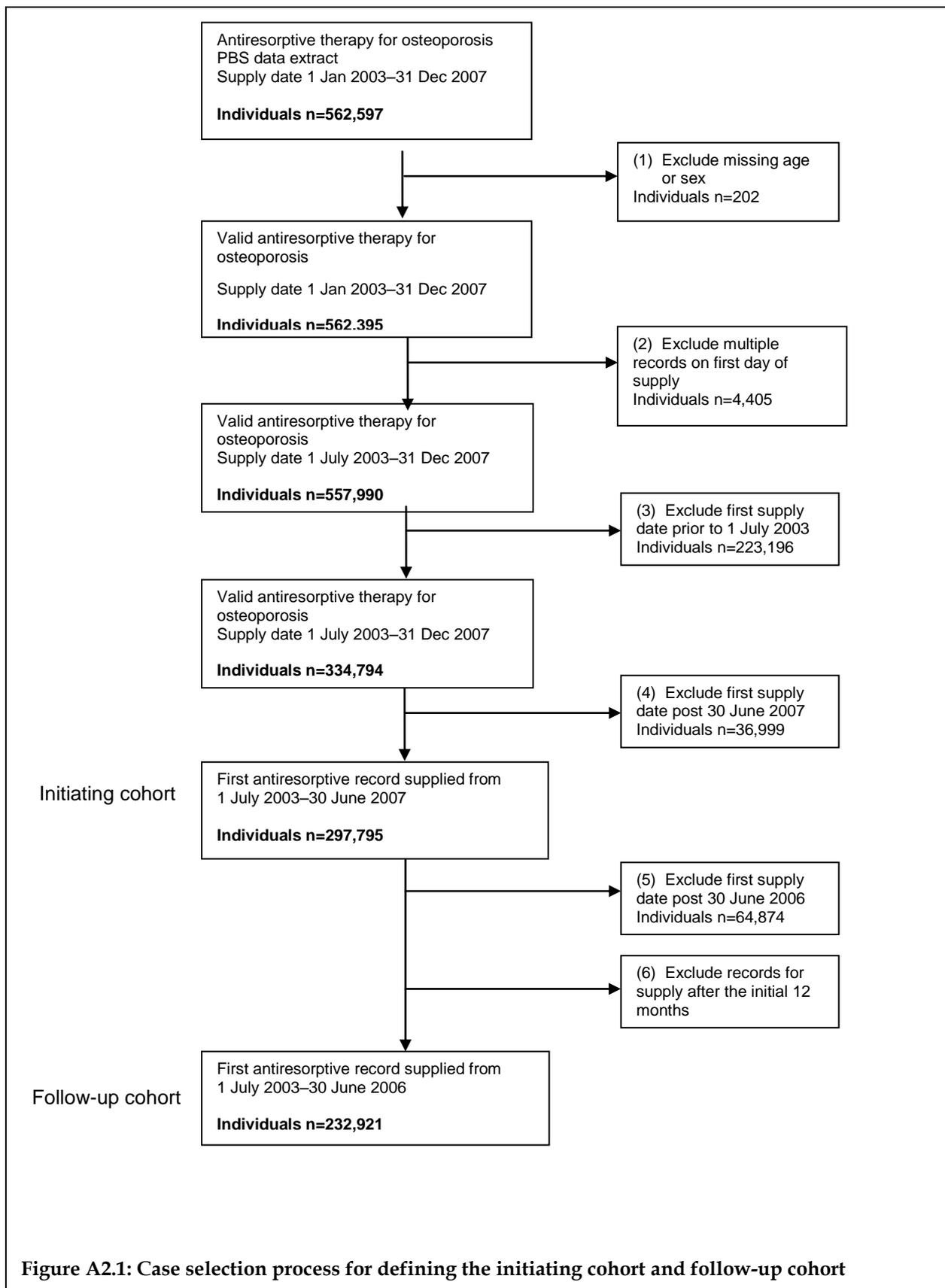


Figure A2.1: Case selection process for defining the initiating cohort and follow-up cohort

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