

5 Quality use of cardiovascular medicines

This chapter presents information on several aspects of the appropriate use of medicines for cardiovascular disease for which data are available and describes national initiatives aimed at achieving quality use of these medicines where deficiencies have been identified.

5.1 Medicines prescribed for cardiovascular disease

Data on cardiovascular medicines that GPs prescribed or supplied for specific cardiovascular conditions and risk factors (hypertension, lipid disorders and diabetes) were sourced from the BEACH study for the period April 2000–March 2006. For information on this study and details of the method used to analyse the data, see the Appendix.

Over the period 2000–2006, GPs prescribed or supplied medicines to manage most cardiovascular problems (Table 5).

Table 5: Medicines prescribed or supplied by GPs for specific problems, 2000–06

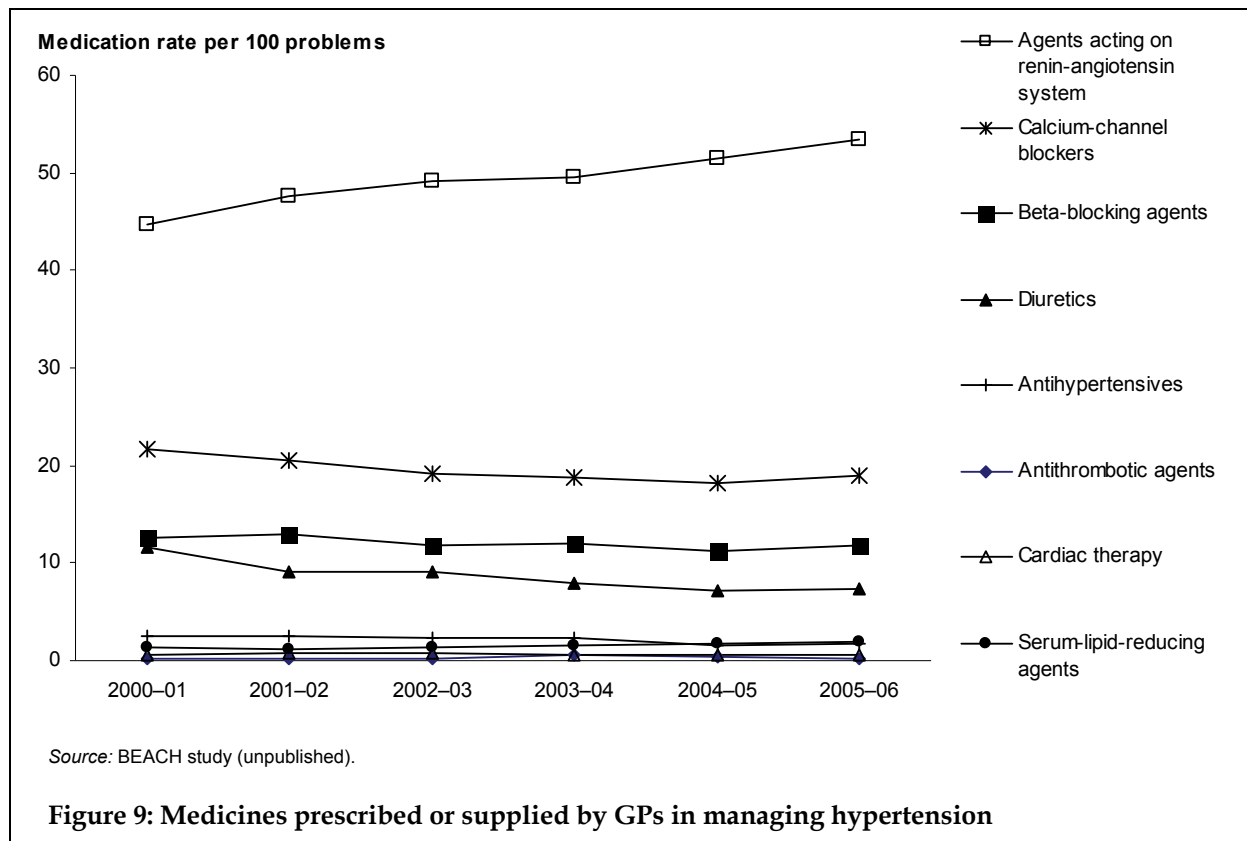
Problem managed	Medicine rate per 100 problems (95%CI)
Arrhythmia	81.1 (78.1–84.2)
Diabetes	72.3 (70.5–74.1)
Heart failure	118.6 (114.2–123.0)
Hypertension	96.5 (95.2–97.9)
Ischaemic heart disease	116.6 (113.1–120.1)
Lipid disorder	65.4 (64.4–66.5)
Peripheral vascular disease	37.4 (32.7–42.1)
Stroke	58.7 (53.3–64.1)

Source: BEACH study (unpublished).

Hypertension is the most common problem managed in general practice, at 6.5% of all problems in 2005–06. Between 2000–01 and 2005–06 the rate of management of hypertension by GPs increased (from 8.6 to 9.4 hypertension problems managed per 100 encounters). In 2005–06, agents acting on the renin–angiotensin system were by far the most popular medicines prescribed or supplied for hypertension (53.4 per 100 problems), followed by calcium-channel blockers (18.9 per 100 problems), beta-blocking agents (11.9 per 100 problems), and diuretics (7.4 per 100 problems), while antihypertensives were seldom prescribed (1.7 per 100 problems) (Figure 9 and Table e1).

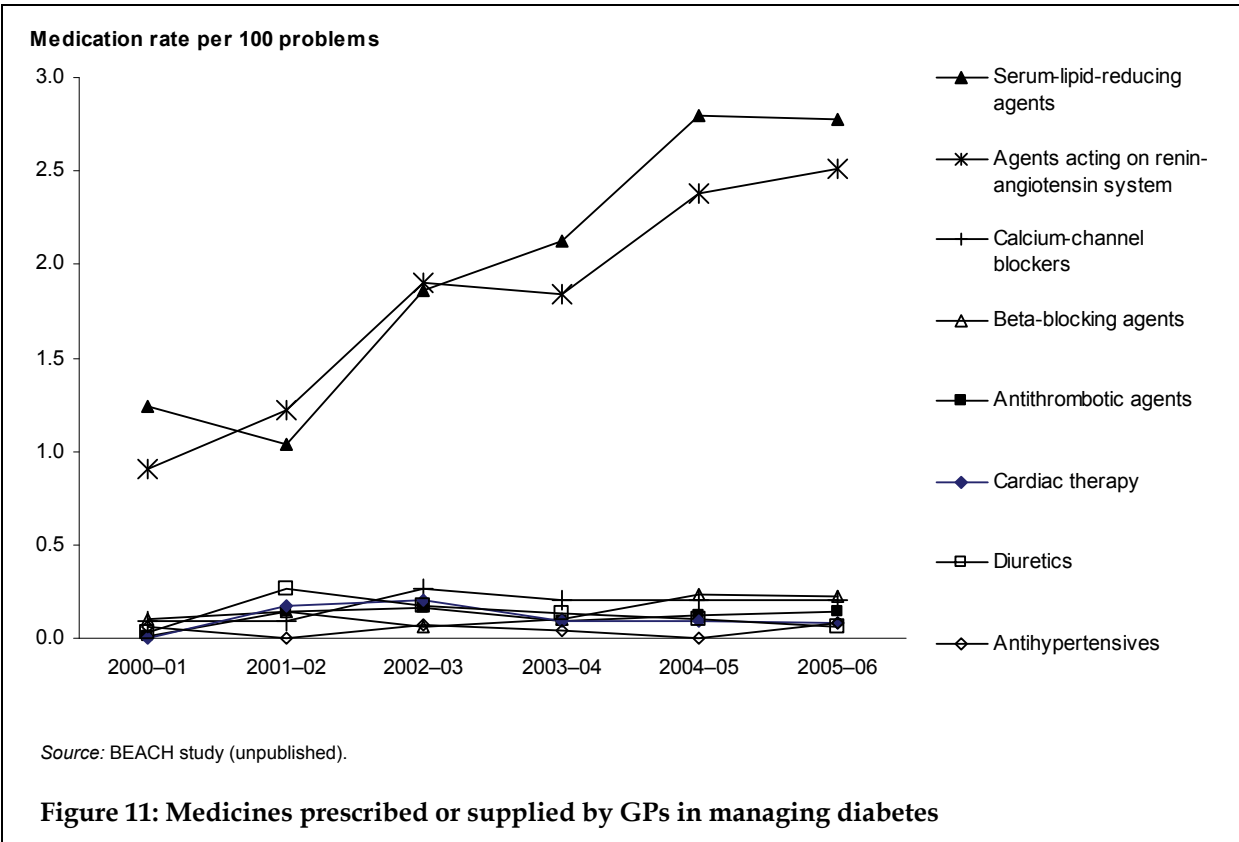
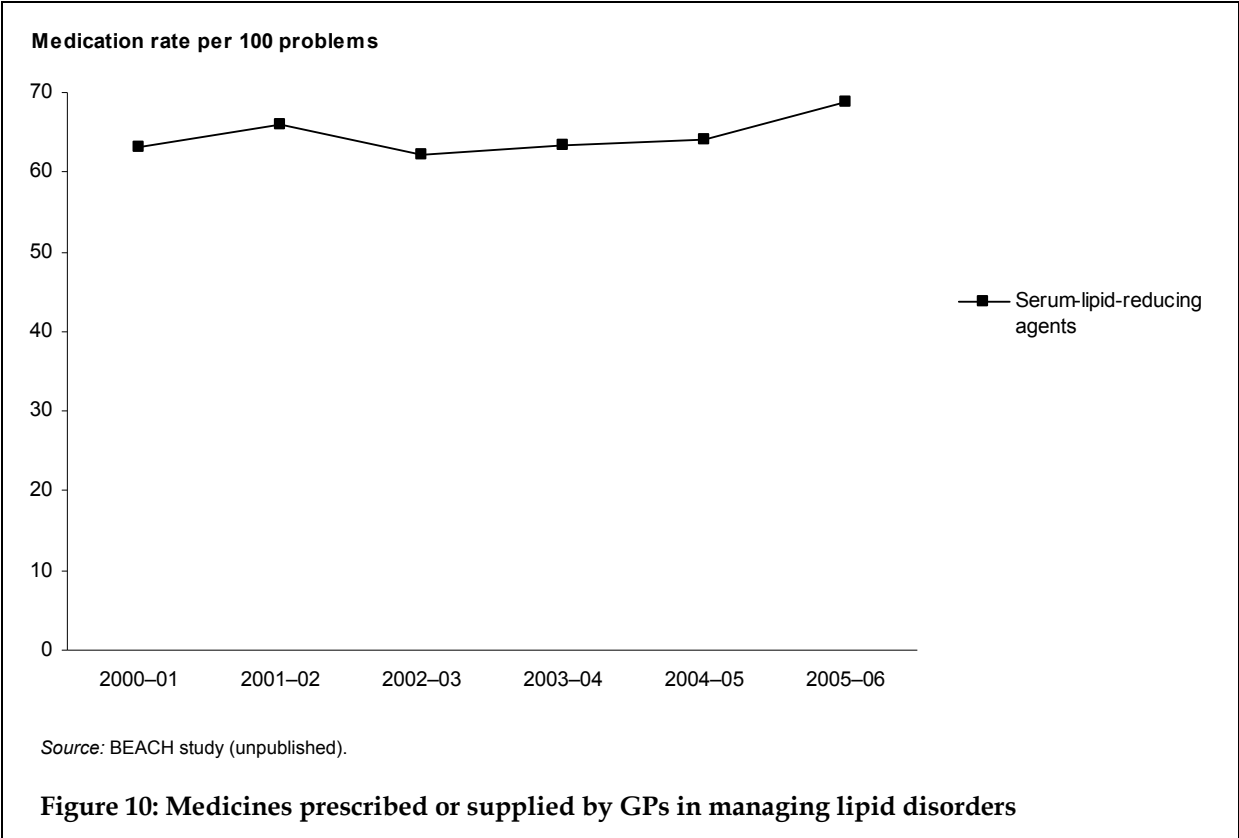
Comparing the rate at which GPs prescribed or supplied cardiovascular medicines for hypertension in 2000–01 and 2005–06, there were statistically significant changes (p value <0.0001): agents acting on the renin–angiotensin system increased, while calcium-channel blockers, diuretics and antihypertensives all fell (Figure 9). Nationwide, these changes equate to an estimated 220,000 additional occasions each year when GPs prescribed or supplied agents acting on the renin–angiotensin system for hypertension, and an annual

reduction by 40,000 for calcium-channel blockers, 80,000 for diuretics and 10,000 for antihypertensives. These trends reflect GPs favouring the newer renin-angiotensin system medicines, which are generally better tolerated than other medicines with blood-pressure-lowering effect.



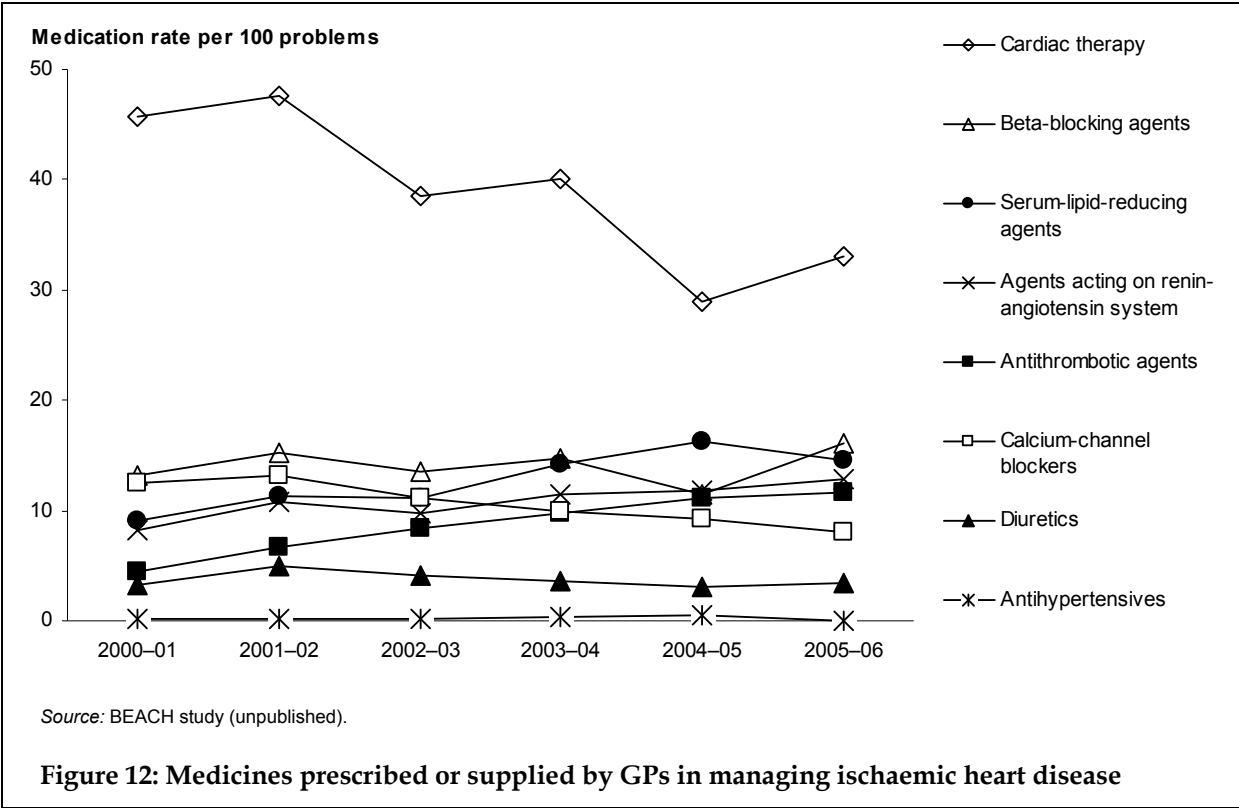
Lipid disorders represented 2.3% of all problems in general practice in 2005-06, with the rate of management of these problems by GPs rising between 2000-01 and 2005-06 (from 2.9 to 3.4 lipid disorder problems managed per 100 encounters). GPs prescribed or supplied serum-lipid-reducing agents in managing lipid disorders at a rate of 68.8 per 100 problems in 2005-06. This rate remained constant over the period 2000-01 to 2005-06 (Figure 10 and Table e2). This means that the increase in overall prescription of serum-lipid-reducing agents (see Figure 6) was due to more lipid disorder problems being managed.

Diabetes accounted for 2.4% of all general practice problems in 2005-06. The rate of management of diabetes by GPs rose between 2000-01 and 2005-06 (from 2.8 to 3.6 diabetes problems managed per 100 encounters). In 2005-06, GPs prescribed or supplied serum-lipid-reducing agents in managing diabetes at a rate of 2.8 per 100 problems and agents acting on the renin-angiotensin system at 2.5 per 100 problems. There was a statistically significant rise (p value <0.0001) in the prescription of both these types of medicines to manage diabetes from 2000-01 to 2005-06 (Figure 11 and Table e3). Nationwide, these changes equate to an estimated 10,000 additional occasions each year when GPs prescribed or supplied agents acting on the renin-angiotensin system for diabetes and the same applies to serum-lipid-reducing agents.



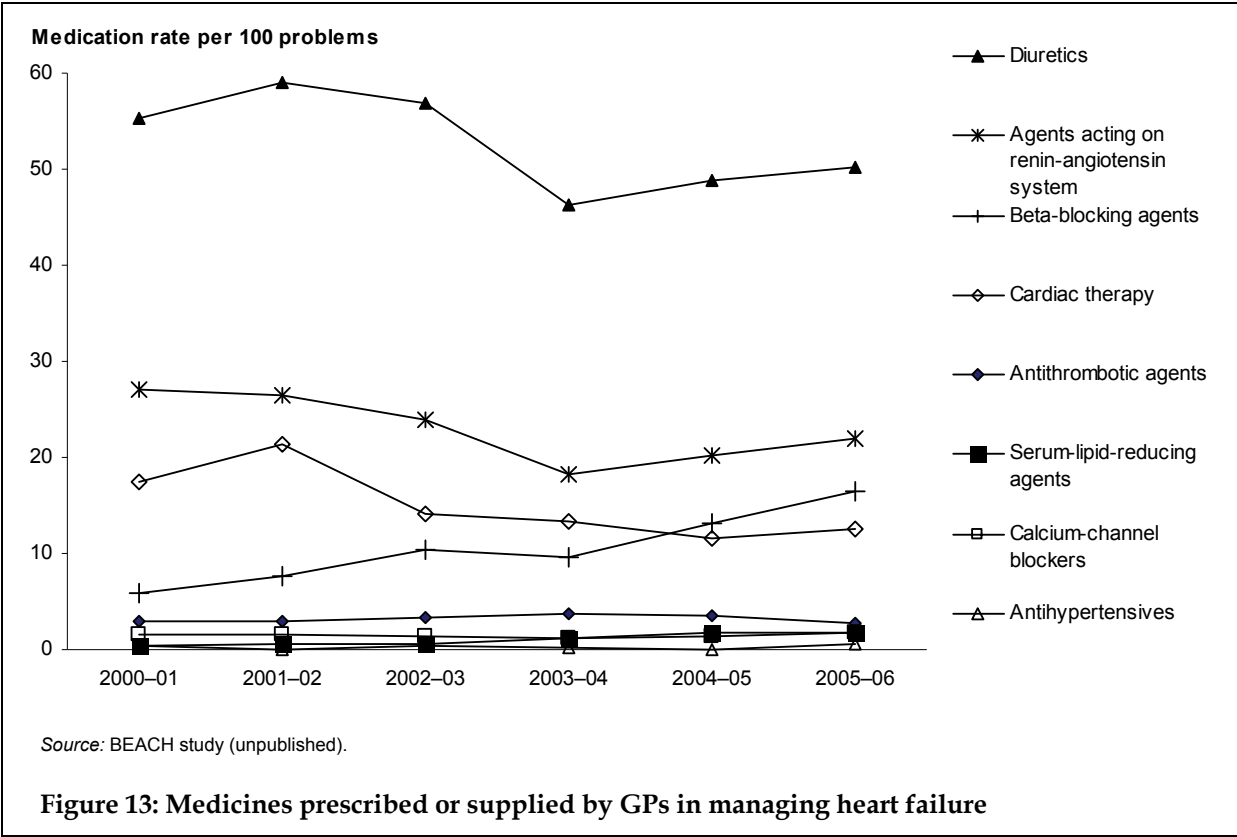
Ischaemic heart disease represented 0.9% of all problems in general practice in 2005-06, with the rate of management of such problems remaining constant over the period 2000-01 to 2005-06 (1.3 ischaemic heart disease problems managed per 100 encounters). In 2005-06, cardiac therapy medicines were the most commonly prescribed or supplied by GPs in managing ischaemic heart disease (33.1 per 100 problems), followed by beta-blocking agents (16.2 per 100 problems), serum-lipid-reducing agents (14.5 per 100 problems), agents acting on the renin-angiotensin system (12.8 per 100 problems), and antithrombotic agents (11.7 per 100 problems) (Figure 12 and Table e4).

Comparing 2005-06 and 2000-01, there were statistically significant differences (p value <0.0001) in the rate of GP prescription and supply of certain medicines: cardiac therapy and calcium-channel blockers fell, while antithrombotic agents and serum-lipid-reducing agents increased (Figure 12). Nationally, these changes amount to an estimated 20,000 additional occasions each year when GPs prescribed or supplied antithrombotic agents for ischaemic heart disease and 10,000 extra occasions for serum-lipid-reducing agents. This suggests GPs are increasingly following recommended guidelines for the treatment of ischaemic heart disease (Therapeutic Guidelines Ltd 2003). Conversely, cardiac therapy medicines were prescribed or supplied for ischaemic heart disease at 40,000 less GP encounters each year and calcium-channel blockers at 10,000 less GP encounters annually.

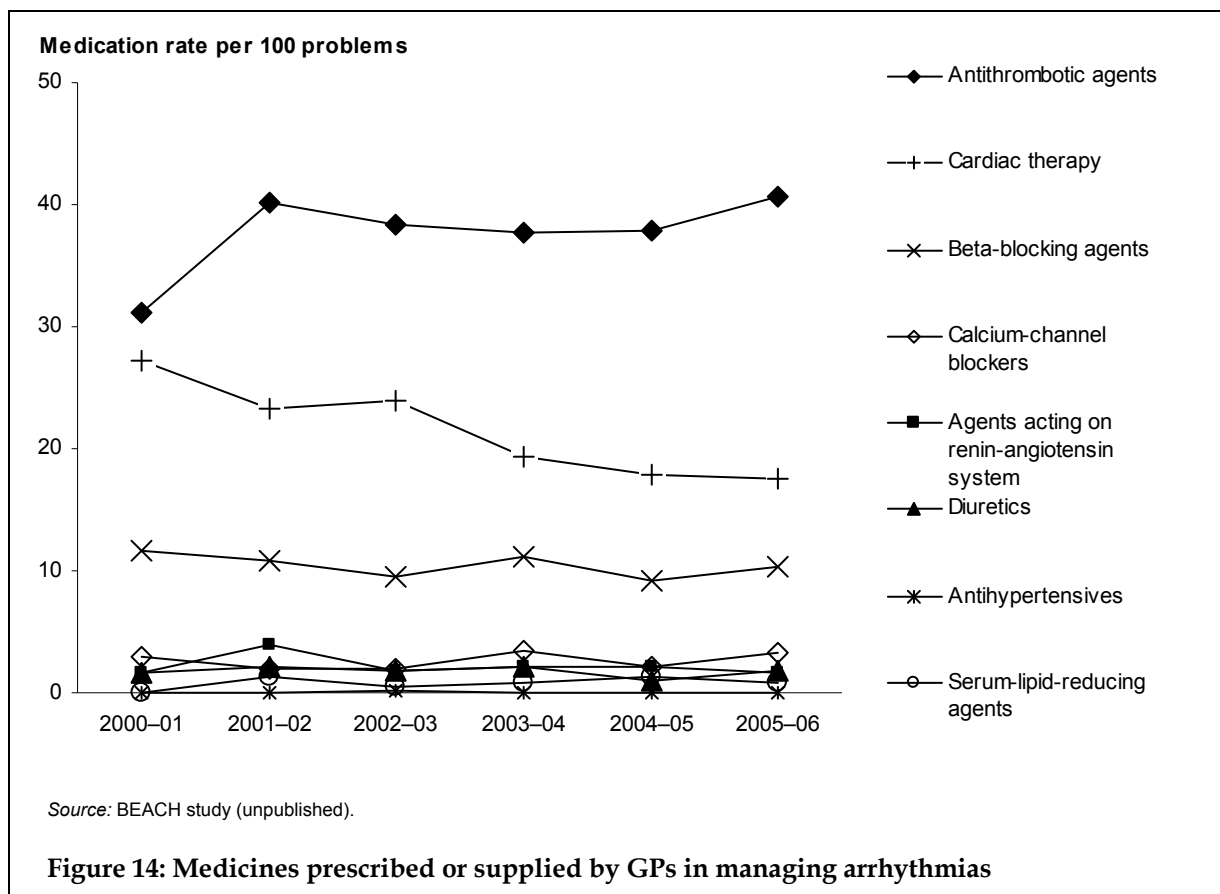


Heart failure made up 0.4% of all problems managed in general practice in 2005-06. Between 2000-01 and 2005-06 the rate of management of heart failure problems was constant (0.7 heart failure problems managed per 100 encounters). In 2005-06, GPs prescribed or supplied mostly diuretics in managing heart failure (50.2 per 100 problems), followed by agents acting on the renin-angiotensin system (21.9 per 100 problems), beta-blocking agents (16.5 per 100 problems), and cardiac therapy medicines (12.6 per 100 problems) (Figure 13 and Table e5).

From 2000-01 to 2005-06 there has been a statistically significant increase in the rate at which GPs prescribed or supplied beta-blocking agents for heart failure (p value <0.0001). Nationally, this represents 10,000 extra occasions per year on which these medicines were prescribed or supplied for heart failure. This trend is encouraging in view of the known under-prescription of beta-blocking agents in people with heart failure but their rate of prescription is still relatively low.

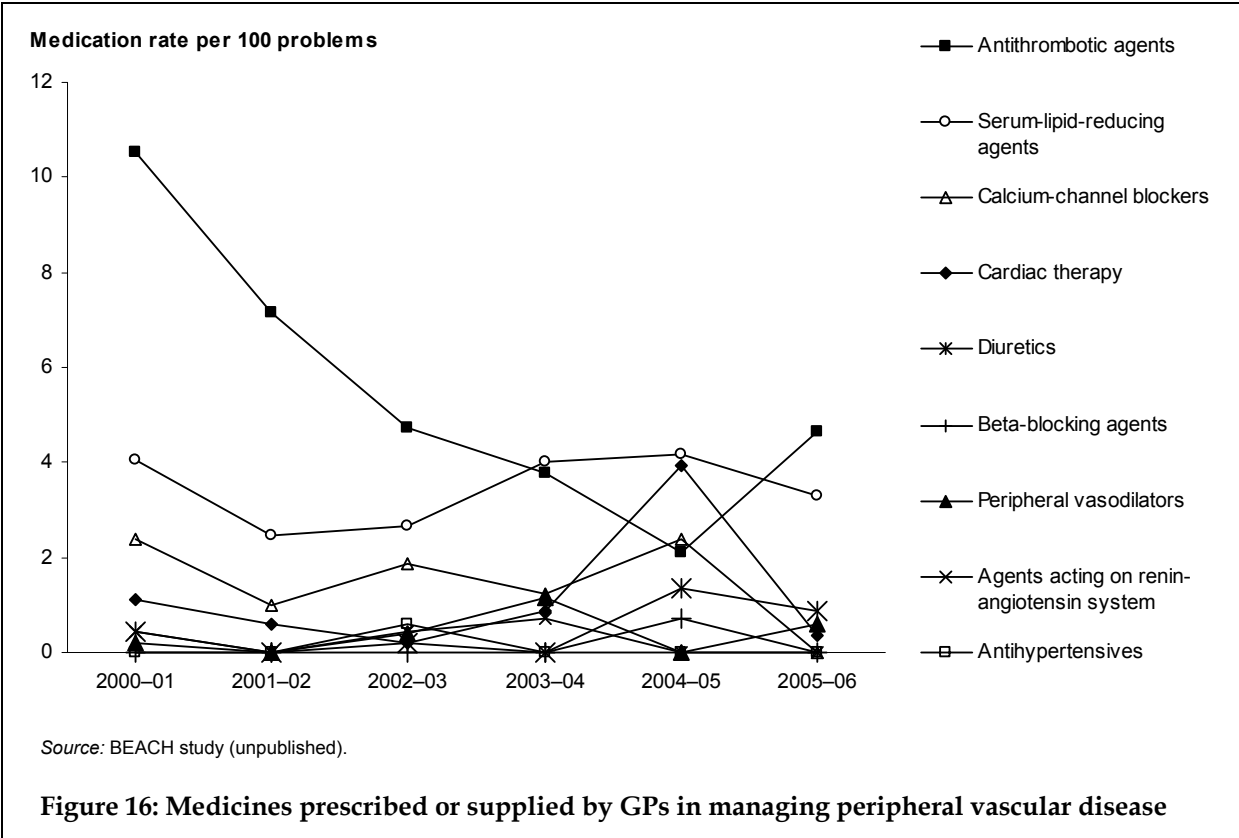
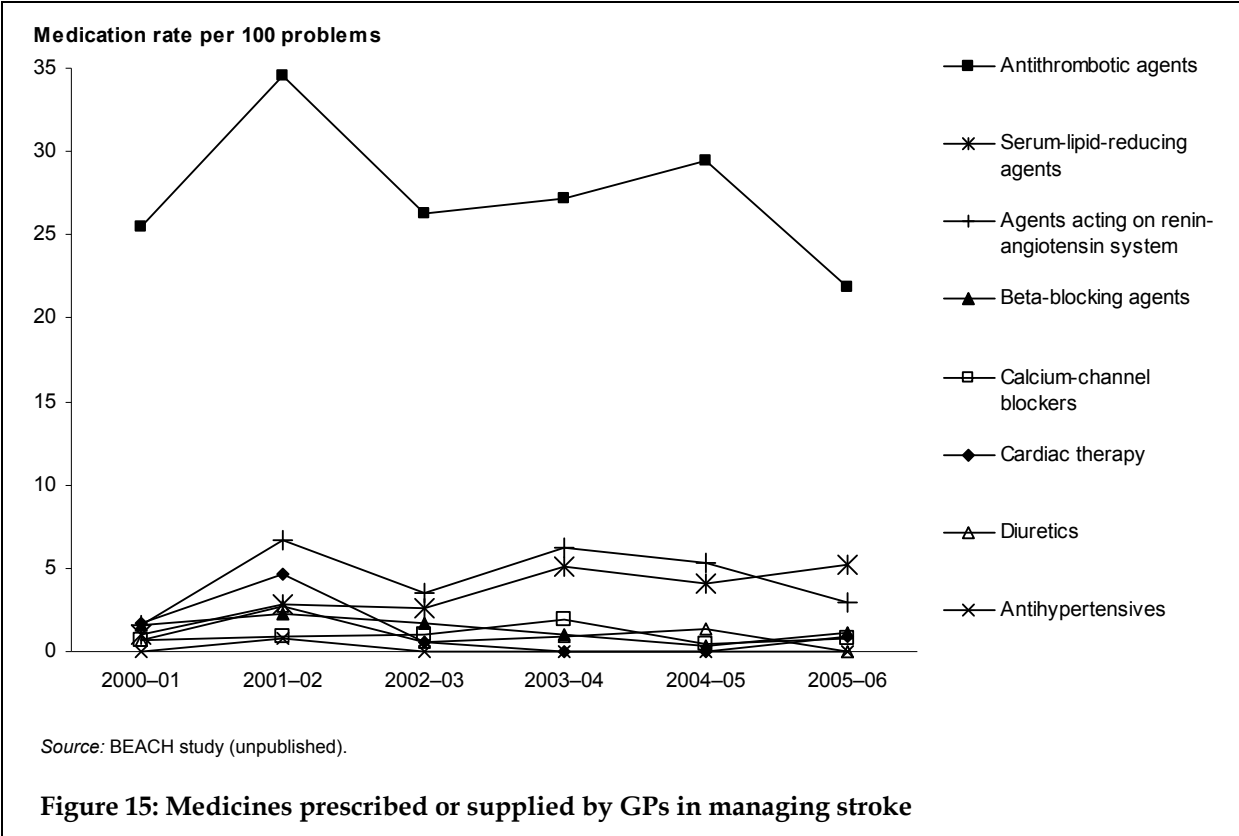


Arrhythmias accounted for 0.8% of all general practice problems in 2005-06. The rate of management of such problems rose over the period 2000-01 to 2005-06 (from 0.8 to 1.1 arrhythmia problems managed per 100 encounters). The medicines that GPs prescribed or supplied most frequently in managing arrhythmias in 2005-06 were antithrombotic agents (40.7 per 100 problems), followed by cardiac therapy (17.5 per 100 problems), and beta-blocking agents (10.3 per 100 problems) (Figure 14 and Table e6). There was a statistically significant fall (p value <0.0001) in the rate of GP prescription or supply of cardiac therapy medicines from 2000-01 to 2005-06.



Stroke represented 0.1% of all problems managed in general practice in 2005-06. Between 2000-01 and 2005-06 the rate of management of such problems was relatively constant (0.2 stroke problems managed per 100 encounters). In 2005-06 the most commonly prescribed or supplied medicines in managing stroke were antithrombotic agents (21.8 per 100 problems), followed by serum-lipid-reducing agents (5.2 per 100 problems), and agents acting on the renin-angiotensin system (2.9 per 100 problems) (Figure 15 and Table e7). There were no statistically significant changes in the rate of GP prescription or supply of any medicines for stroke in 2005-06 compared with 2000-01. Note that these results are based on the small number of stroke problems seen in general practice and therefore should be interpreted with caution.

Peripheral vascular disease accounted for 0.1% of all general practice problems in 2005-06, with the rate of management of such problems being stable between 2000-01 and 2005-06 (0.1 problems managed per 100 encounters). Antithrombotic agents (4.7 per 100 problems) and serum-lipid-reducing agents (3.3 per 100 problems) were the medicines GPs prescribed or supplied most frequently in managing peripheral vascular disease in 2005-06 (Figure 16 and Table e8). There were no statistically significant changes observed in the rate of prescription or supply of medicines for peripheral vascular disease from 2000-01 to 2005-06. However, as the number of peripheral vascular disease problems managed by GPs was small, these results should be regarded with caution.



5.2 Concordance with medicines

Medicines can only be effective if patients actually take them. Concordance with medicines refers to patients using medicines as prescribed, which greatly affects outcomes. For example, people who do not adhere to their medicine therapy are more likely to have uncontrolled blood pressure (Chobanian et al. 2003), and have major cardiovascular events or die (La Rosa et al. 2000, Nelson et al. 2006, Psaty et al. 1990, Rudnicka et al. 2003).

Concordance includes:

- compliance – taking medicines at the prescribed interval and dose (note that sometimes the term ‘concordance’ is used to refer to compliance)
- persistence – continuing taking medicines for the specified treatment period, which is usually lifelong in the case of medicines used to prevent cardiovascular disease or reduce the risk of events such as stroke and heart attack.

This section presents the results of analyses conducted by the Australian Institute of Health and Welfare of compliance and persistence with selected medicines commonly used to prevent and treat cardiovascular disease, in newly prescribed patients studied over 2003–06 using data from the Pharmaceutical Benefits Data System supplied by DoHA. Details of the medicines included, methods used and limitations of the study are given in the Appendix.

HMG COA reductase inhibitors (statins)

Most people dispensed statins in our study were aged 50–79 years, with roughly the same proportions of males and females (52% versus 48%) and more than half being concessional patients (Table 6). Statins were supplied to females at a statistically significant lower rate than for males but the difference was small (411.5 versus 442.4 per 100,000).

People in metropolitan areas were dispensed statins at twice the rate of those living in rural areas, and 30 times the rate of people in remote areas (Table 7). These differences applied to both males and females.

Patients were dispensed statins continuously for a period of 422 days on average (Table 8). At six months from the start of therapy, 83% of patients were persistent with their medicine (that is, one in six patients had discontinued statins), with this proportion dropping to 65% after 24 months (Table 8, Figure A1). These figures are comparable to those of previous studies – 56% persistent after 6 months and 50% after 12 months (Benner et al. 2002); 70% persistent after 6 months (Simons et al. 2000).

The proportion of people who persisted with statins was slightly greater among those living in rural areas than in metropolitan or remote areas (85% versus 82%) after six months (Table A2). After 24 months, this pattern remained – 68% in rural areas versus 62% in metropolitan or remote areas.

People in the most socioeconomically disadvantaged group were supplied statins at a higher rate than those in the least disadvantaged group – for males the difference was 13% and for females it was 27% (Table A3). The proportion of people who persisted with statins at six months in the most disadvantaged group was statistically significantly lower than that in the least disadvantaged group, although the difference was small (Table A4). This difference remained at 24 months.

In the first 12 months of therapy, 77% of newly prescribed patients were assessed as compliant with statins, that is, they had sufficient medicine to use it at the prescribed frequency and dose.

Agents acting on the renin–angiotensin system

For this group of medicines, analyses were limited to concessional and RPBS patients. Those supplied angiotensin II antagonists (plain or combinations) or ACE inhibitors (plain or combinations) in the study were mostly aged 60 years or over, and women represented a larger proportion than men (Table 6). Females were supplied angiotensin II antagonists at a rate 1.5 times that for males. Supply of ACE inhibitors combinations among females was 1.3 times the rate for males, but the difference was not as marked for plain ACE inhibitors.

People in metropolitan areas were dispensed angiotensin II antagonists at nearly twice the rate of those living in rural areas, and 47–58 times the rate of people in remote areas (Table 7). Supply of ACE inhibitors to people in metropolitan areas was 1.7 times the rate of their counterparts living in rural areas, and 29–36 times the rate in remote areas. These differences were present in both males and females.

On average, patients were continuously supplied with these medicines for a period ranging from 432 days for angiotensin II antagonists combinations to 364 days for ACE inhibitors combinations (Table 8). At six months from commencing medicine treatment, 88–91% of patients persisted with their treatment and after 24 months 75–79% were still taking the medicines, depending on the medicine studied (Table 8, Figure A2). International studies have reported similar results – after 12 months 71% persistent with plain ACE inhibitors, 73% with plain angiotensin II antagonists and 67% with medicine combinations, dropping to 58%, 59% and 50% respectively after 36 months (Perreault et al. 2005); 66% persistent with angiotensin II antagonists at 12 months and 56% at 24 months, 59% persistent with ACE inhibitors at 12 months and 47% at 24 months (Bourgault et al. 2005).

The proportion of people persistent with angiotensin II antagonists at six months was slightly greater in rural areas than in metropolitan areas (Table A2). This difference remained after 24 months. For ACE inhibitors, persistence was greatest among patients living in rural areas and lowest in remote areas after six and 24 months.

In the first 12 months of therapy, 87% of newly prescribed patients were assessed as compliant with ACE inhibitors or plain angiotensin II antagonists, and 89% were compliant with angiotensin II antagonists combinations.

Beta-blocking agents

Only concessional and RPBS patients were included in the study of beta-blockers. People dispensed beta-blocking agents were mainly aged 60 years and over, with similar representation of females and males (52% versus 48%) (Table 6). Females were supplied beta-blockers at a slightly higher rate than males (165.0 versus 149.4 per 100,000).

People in metropolitan areas were dispensed beta-blocking agents at 1.6 times the rate of those living in rural areas, and 31–37 times the rate of people in remote areas (Table 7). These differences applied to both males and females.

The average duration of persistence with beta-blocker treatment was 329 days (Table 8). At six months from the start of therapy, 75% of patients continued filling their prescriptions, falling to 53% at 24 months. International studies have shown comparable results – 50% persistent at 12 months and 39% at 24 months (Bourgault et al. 2005); 68% persistent at 12 months and 57% at 36 months (Perreault et al. 2005).

Persistence with beta-blocking agents was slightly greater in rural areas compared with metropolitan areas (77% versus 74%) at six months (Table A2). We observed the same difference after 24 months (55% versus 51%).

Note that in some cases patients are prescribed beta-blocking agents for a limited period and we did not have access to information to identify and exclude those patients from our analysis. Therefore, this may partly account for the large discontinuation rate we found.

Warfarin

Analysis of warfarin supply was limited to concessional and RPBS patients. Most people supplied warfarin were aged 60 years and over, with males and females equally represented (Table 6). There was no difference between males and females in the rate of supply of warfarin.

Males in metropolitan areas were dispensed warfarin at 1.6 times the rate of those living in rural areas, and 36 times the rate of people in remote areas (Table 7). For females, those living in metropolitan areas had 1.9 times the rate of supply of their rural area counterparts and 48 times that of women in remote areas.

On average, patients were dispensed warfarin continuously for a period of 288 days (Table 8). At six months from commencement of therapy, 84% of patients persisted with treatment and by 24 months 57% were still taking the medicine (Table 8, Figure A3). An earlier study showed 85% persistence at 3 months and 77% at 12 months (Hamann et al. 2003).

There was very little difference in the proportion of patients who continued using warfarin in metropolitan, rural or remote areas (Table A2).

Note that in some cases patients are prescribed warfarin for a limited period and we did not have access to information to identify and exclude those patients from our analysis. Hence this may explain part of the large discontinuation rate observed at 24 months.

Other antithrombotic agents

Note that we excluded aspirin from the analysis because it is widely available over-the-counter and this supply is not recorded in the Pharmaceutical Benefits Data System. In addition, aspirin is indicated for other conditions outside the cardiovascular system.

In our study, the group 'other antithrombotic agents' included clopidogrel, dipyridamole and ticlopidine. People dispensed these medicines were mostly aged 60 years and over, with a higher proportion of males than females (59% versus 41%) (Table 6). Males were supplied these antithrombotic medicines at a rate 1.4 times that of females.

People in metropolitan areas were dispensed these antithrombotic agents at twice the rate of those living in rural areas, and 41–47 times the rate of people in remote areas (Table 7). These differences applied to both males and females.

Patients were continuously supplied these antithrombotic agents for a period of 391 days on average (Table 8). After six months of therapy, 90% of patients persisted with these medicines and this proportion fell to 76% after 24 months (Table 8, Figure A3). Previously reported figures are 82% of patients persistent with clopidogrel therapy at 3 months and 62% at 12 months (Hamann et al. 2003).

There was no difference in persistence with these antithrombotic agents in people living in metropolitan, rural or remote areas (Table A2).

People in the most socioeconomically disadvantaged group were supplied these antithrombotic agents at a higher rate than those in the least disadvantaged group – for males the increase was 5% and for females it was 8% (Table A3). The level of persistence with these medicines was similar in all socioeconomic groups (Table A4).

In the first 12 months of therapy, 90% of newly prescribed patients were assessed as compliant with these antithrombotic agents. This means they had enough medicine to take it at the prescribed frequency and dose.

Table 6: Characteristics of the patients studied

	Medicine class							
	HMG COA reductase inhibitors (statins)	Angiotensin II antagonists (plain)	Angiotensin II antagonists (combinations)	ACE inhibitors (plain)	ACE inhibitors (combinations)	Beta-blocking agents	Warfarin	Other antithrombotic agents ^(a)
Number	619,815	255,177	102,624	323,545	47,624	228,221	93,120	155,445
Age group								
0–39 (%)	5.5	2.6	2.2	3.3	2.9	5.0	4.4	1.5
40–49 (%)	14.7	5.6	5.4	6.0	6.3	6.3	3.8	6.2
50–59 (%)	28.7	12.1	12.9	12.1	13.6	12.7	8.0	16.5
60–69 (%)	25.6	29.5	31.9	27.0	30.2	27.3	24.1	24.6
70–79 (%)	18.0	33.4	33.5	31.1	31.9	30.0	37.1	30.1
80+ (%)	7.6	16.9	14.0	20.4	15.1	18.8	22.5	21.1
Females (%)	48.2	59.2	60.8	52.3	57.4	52.1	49.6	40.7
Males (%)	51.8	40.8	39.2	47.7	42.6	47.9	50.4	59.3
Females (rate [95% CI])	411.5 (410.0–413.0)	209.5 (208.4–210.5)	86.6 (85.9–87.3)	234.2 (233.1–235.3)	37.9 (37.5–38.4)	165.0 (164.0–165.9)	64.2 (63.7–64.8)	87.4 (86.7–88.1)
Males (rate [95% CI])	442.4 (440.9–443.9)	142.7 (141.8–143.6)	55.2 (54.6–55.7)	211.1 (210.0–212.1)	27.8 (27.4–28.2)	149.4 (148.5–150.3)	64.1 (63.5–64.7)	125.7 (124.9–126.5)
Patient category								
General (%) ^(b)	41.6	0.0	0.0	0.0	0.0	0.0	0.0	26.2
Concessional (%) ^(c)	54.2	92.3	93.5	91.6	93.2	92.0	89.5	66.6
RPBS (%) ^(d)	4.2	7.7	6.5	8.4	6.8	8.0	10.5	7.2

(a) Includes clopidogrel, dipyridamole and ticlopidine.

(b) Includes general ordinary patients and general patients on safety net.

(c) Includes concessional ordinary patients and concessional patients on safety net.

(d) Includes repatriation patients and repatriation patients on safety net.

Notes

1. Rate per 100,000 population, age standardised to the Australian population at 30 June 2001.

2. The study included newly prescribed patients only. For 'statins' and 'other antithrombotic agents' patients in all categories were included. For all other medicine groups, the analysis was limited to concessional patients and RPBS patients.

3. Age group and category of patients were determined at the time of their first prescription being dispensed.

Source: AIHW analysis of data supplied by DoHA from the Pharmaceutical Benefits Data System.

Table 7: Prescriptions supplied by region of patient residence

Region of residence	Medicine class							Other antithrombotic agents ^(a)
	HMG COA reductase inhibitors (statins)	Angiotensin II antagonists (plain)	Angiotensin II antagonists (combinations)	ACE inhibitors (plain)	ACE inhibitors (combinations)	Beta-blocking agents	Warfarin	
	Rate (95% CI)							
Males								
Metropolitan	285.61 (284.39–286.83)	89.38 (88.69–90.07)	36.19 (35.75–36.63)	125.03 (124.22–125.84)	17.10 (16.80–17.40)	88.71 (88.03–89.39)	38.69 (38.24–39.14)	82.42 (81.76–83.07)
Rural	147.24 (146.37–148.11)	51.41 (50.89–51.92)	18.30 (17.99–18.61)	81.59 (80.94–82.23)	10.13 (9.90–10.36)	57.69 (57.15–58.24)	24.29 (23.94–24.65)	41.29 (40.83–41.75)
Remote	9.55 (9.32–9.77)	1.93 (1.83–2.03)	0.71 (0.65–0.77)	4.35 (4.19–4.49)	0.54 (0.48–0.59)	2.93 (2.80–3.05)	1.06 (0.99–1.14)	1.99 (1.89–2.09)
Females								
Metropolitan	267.56 (266.38–268.75)	134.85 (134.00–135.69)	57.38 (56.82–57.93)	144.43 (143.56–145.30)	23.78 (23.42–24.14)	100.63 (99.89–101.36)	41.46 (40.98–41.93)	57.97 (57.42–58.53)
Rural	136.32 (135.48–137.15)	72.11 (71.49–72.72)	28.27 (27.88–28.65)	85.38 (84.72–86.05)	13.43 (13.16–13.69)	61.48 (60.91–62.05)	21.91 (21.57–22.24)	28.16 (27.78–28.55)
Remote	7.57 (7.37–7.76)	2.49 (2.39–2.61)	0.99 (0.92–1.06)	4.22 (4.07–4.37)	0.71 (0.65–0.77)	2.72 (2.61–2.84)	0.86 (0.79–0.93)	1.24 (1.16–1.32)

(a) Includes clopidogrel, dipyridamole and ticlopidine.

Notes

1. Rate per 100,000 population, age standardised to the Australian population at 30 June 2001.
2. The study included newly prescribed patients only. For 'statins' and 'other antithrombotic agents' patients in all categories were included. For all other medicine groups, the analysis was limited to concessional patients and RPBS patients.
3. Region of residence of patients was determined at the time of their first prescription being dispensed.

Source: AIHW analysis of data supplied by DoHA from the Pharmaceutical Benefits Data System.

Table 8: Persistence with medicines

Medicine class	Number of patients	Average duration of persistence	Proportion of patients persistent at:			
			6 months	12 months	18 months	24 months
		Days	Per cent (95%CI)			
HMG CoA reductase inhibitors (statins)	619,815	422	83.44 (83.34–83.54)	74.65 (74.53–74.77)	68.97 (68.83–69.11)	64.92 (64.77–65.07)
Angiotensin II antagonists (plain)	255,177	393	88.79 (88.66–88.92)	82.38 (82.21–82.55)	78.13 (77.93–78.33)	74.89 (74.66–75.12)
Angiotensin II antagonists (combinations)	102,624	432	90.86 (90.67–91.05)	85.86 (85.62–86.10)	81.95 (81.66–82.23)	79.19 (78.86–79.51)
ACE inhibitors (plain)	323,545	369	88.38 (88.26–88.50)	82.13 (81.97–82.29)	77.99 (77.81–78.17)	74.81 (74.60–75.02)
ACE inhibitors (combinations)	47,624	364	90.62 (90.33–90.90)	85.43 (85.05–85.80)	81.65 (81.19–82.10)	78.82 (78.29–79.34)
Beta-blocking agents	228,221	329	75.15 (74.96–75.34)	63.66 (63.43–63.89)	57.26 (57.01–57.51)	52.89 (52.62–53.16)
Warfarin	93,120	288	83.75 (83.49–84.01)	71.94 (71.57–72.31)	63.23 (62.78–63.68)	56.60 (56.08–57.11)
Other antithrombotic agents ^(a)	155,445	391	90.02 (89.86–90.18)	83.87 (83.65–84.08)	79.42 (79.16–79.68)	76.08 (75.78–76.37)

(a) Includes clopidogrel, dipyridamole and ticlopidine.

Note: The study included newly prescribed patients only. For 'statins' and 'other antithrombotic agents' patients in all categories were included. For all other medicine groups, the analysis was limited to concessional patients and RPBS patients.

Source: AIHW analysis of data supplied by DoHA from the Pharmaceutical Benefits Data System.

As stated earlier, the medicines included in this study of concordance were selected because they are usually indicated for lifelong use in the prevention and treatment of cardiovascular disease. However, we observed that a considerable proportion of newly prescribed patients were dispensed one script only for these types of medicines, ranging from 14% to 27% (Table 9). Assuming patients were dispensed the cheapest PBS item in the relevant medicine class, this equates to a minimum cost to government and patients of \$7.4 million. It is likely that this early discontinuation of medication is due to side effects that occur in the first month of therapy. Although the rates of side effects with many of these medicines are low in clinical trials, patients in the real world may attribute side effects to medicines more commonly and stop taking them.

Table 9: Newly prescribed patients dispensed one prescription only

Medicine class	Total newly prescribed patients (number)	Newly prescribed patients dispensed one script only		Minimum cost for patients dispensed one script only ^(a) (\$)
		(number)	% of total newly prescribed patients	
Beta-blocking agents	393,879	105,460	26.8	834,189
ACE inhibitors (combinations)	61,701	11,462	18.6	265,918
ACE inhibitors (plain)	416,001	69,619	16.7	960,742
Warfarin	116,698	18,497	15.9	143,907
Other antithrombotic agents ^(b)	197,389	31,093	15.8	1,016,741
Angiotensin II antagonists (combinations)	127,190	18,962	14.9	414,130
Angiotensin II antagonists (plain)	317,389	46,862	14.8	908,186
HMG COA reductase inhibitors (statins)	792,338	110,022	13.9	2,857,271
Total				7,401,084

(a) Assumes that patients who filled one script only were dispensed the cheapest preparation in the relevant medicine class available on the Pharmaceutical Benefits Scheme in 2006. Calculations used 2006 prices.

(b) Includes clopidogrel, dipyridamole and ticlopidine.

Note: For 'statins' and 'other antithrombotic agents' patients in all categories were included. For all other medicine groups, the analysis was limited to concessional patients and RPBS patients.

Source: AIHW analysis of data supplied by DoHA from the Pharmaceutical Benefits Data System.

Overall, the results of our study indicate a high level of discontinuation of medicines that are generally intended to be taken long-term. This represents a significant waste of resources and a lost opportunity to prevent cardiovascular disease with medicines known to be effective. Note that due to the limitations of the data set, discontinuation rates may have been over-estimated to some extent (see Methods section in the Appendix for details).

Previous research has shown that, across a wide range of medical disorders, about 75% of medicines are taken as prescribed, and that compliance decreases as the number of daily doses increases (Cramer 2002, Claxton et al. 2001).

Factors associated with poor concordance with medicines include:

- treatment of a condition with no symptoms (such as high blood pressure and high blood cholesterol)
- presence of depression
- inadequate follow-up or discharge planning

- side effects of medicine
- poor communication between health professional and patient
- patient's lack of understanding of their condition
- patient's lack of belief in the benefit of treatment
- complexity of treatment
- missing doctor's appointments and
- cost of medicines (Osterberg et al. 2005, WHO 2003).

We do not have access to patient information that would allow us to explore the reasons for discontinuing medicine treatment in our study. The fact that for the most part our analyses were confined to concessional patients, for whom out-of-pocket expenses on medicines would be relatively low, suggests that cost does not play a big role. However, research indicates that one in five sicker Australians omits a medicine owing to cost (Schoen et al. 2005).

According to international studies, people with a history of coronary heart disease, stroke, heart failure, diabetes or hypertension are more likely to keep taking lipid-lowering and blood-pressure-lowering medicines than those without these conditions (Benner et al. 2002, Chapman et al. 2005). As patients' medical histories are not recorded in national databases in Australia, we were unable to look into this issue in our analyses.

5.3 National Prescribing Service initiatives

The National Prescribing Service (NPS) conducts a range of initiatives to promote quality use of medicines (National Prescribing Service 2004, 2005). For more information on the NPS, see the Appendix. Among NPS activities relating to cardiovascular disease medicines are:

- education and quality assurance programs for health professionals using a range of publications and interventions, including clinical audits, education visiting, peer group discussions and case studies. Over the period 1999–2004, a considerable proportion of GPs has participated in such a program covering hypertension (52%), lipid disorders (37%), heart failure (15%), antithrombotics (6%), as well as multiple medicine use (7%) and medicine reviews (8%). Note that these figures cannot be added together as GPs may have participated in more than one program activity.
- publications for health professionals on newly listed or revised cardiovascular medicines.
- telephone advice line for health professionals (Therapeutic Advice and Information Service) and for consumers (Medicines Line), where cardiovascular medicines are a frequent topic. Calls relate mostly to medicine interactions and adverse drug reactions.
- information material for consumers on self-management of heart failure
- information program for consumers to encourage older people to be more active in managing their medicines
- Medicines List to help consumers who take multiple medicines keep track of their medicines.

Clinical audits provide an opportunity for GPs to reflect on their prescribing practice. One-fifth of Australian GPs had reviewed their management of hypertension through NPS

clinical audits between 1999 and 2004. For management of lipid disorders, the corresponding proportion was one-tenth.

A NPS study involved 5,247 GPs who voluntarily participated in one of four clinical audits on hypertension held in 1999, 2001, 2003 and 2004, and provided self-reported data for 105,086 adult patients with a history of hypertension (National Prescribing Service, unpublished). The objectives of the audits were to review management of hypertension against guidelines, identify ideal target blood pressure for individual patients and optimise blood pressure control, and review the selection of antihypertensive medicine.

Note that as GPs participating in the clinical audits were self-selected and the data were self-reported, the sample of GPs or their patients may not represent the whole of Australia and therefore these results may not be generalised and we should be cautious when interpreting them. For some measures, the survey questions changed over time and direct year-to-year comparisons are not entirely appropriate, but the results give an indication of the trends.

Results showed that management of hypertension in general practice had improved between 1999 and 2004. Target blood pressures were likely to be consistent with guideline recommendations and more patients were achieving control of their blood pressure – 70% in 2004. The proportion of patients using one blood-pressure-lowering medicine fell from 52% in 1999 to 45% in 2004, in favour of combinations of medicines (data not shown).

The most commonly prescribed agents with blood-pressure-lowering effect were ACE inhibitors, calcium-channel blockers and beta-blockers (Table 10). The increasing use of combination products resulted in increasing overall use of low-dose thiazide diuretics, ACE inhibitors and angiotensin II antagonists.

Table 10: Medicines with blood-pressure-lowering effect prescribed

Type of antihypertensive medicine prescribed	1999	2001	2003	2004
	Per cent of patients			
Low-dose thiazide diuretics	14	11	10	10
High-dose thiazide diuretics	7	7	5	4
Beta-blocking agents	24	24	24	24
Calcium-channel blockers	37	33	33	31
ACE inhibitors	46	41	36	36
Low-dose thiazide and ACE inhibitor combination	n/a	6	9	10
Angiotensin II antagonists	13	17	20	22
Low-dose thiazide and angiotensin II antagonist combination	n/a	8	13	14
Alpha-blocking agents	4	3	3	3
Other antihypertensive medicines	12	6	4	5

Source: National Prescribing Service, unpublished.

In accordance with guidelines (Therapeutic Guidelines Ltd 2003), there was an increase in patients using a blood-pressure-lowering medicine most suited to their coexisting health conditions (58% in 1999 versus 81% in 2004). However, the proportion of patients with coexisting heart failure prescribed ACE inhibitors was low at 54–62% (Table 11). Similarly, fewer than 52% of patients with a history of myocardial infarction were prescribed beta-blockers or ACE inhibitors. GPs reported simultaneous use of medicines known to

exacerbate hypertension in 24% of patients in 2001, 19% in 2003 and 17% in 2004. Complementary medicines that could raise blood pressure were reported in 1–2% of patients with hypertension.

Table 11: Patients with hypertension and a coexisting condition prescribed blood-pressure-lowering medicines with favourable or unfavourable effects on coexisting conditions

Coexisting condition	Medicines with effect on coexisting condition	2001	2003	2004
	Favourable effect	Per cent of patients		
Heart failure	ACE inhibitor	58	62	54
	Beta-blocking agent	26	35	32
Microalbuminuria/proteinuria	ACE inhibitor or angiotensin II antagonist	n/a	39	45
Previous myocardial infarction	Beta-blocking agent	49	45	49
	ACE inhibitor	52	50	51
	Beta-blocking agent plus ACE inhibitor	23	23	26
Angina	Beta-blocking agent or calcium-channel blocker	76	64	45
	Unfavourable effect			
Bradycardia	Beta-blocking agent	22	23	21
Bilateral renal stenosis	ACE inhibitor or angiotensin II antagonist	41	54	32

Source: National Prescribing Service, unpublished.

5.4 National Institute of Clinical Studies initiatives

The National Institute of Clinical Studies (NICS) has initiated a range of activities to improve clinical practice in Australia. For more information on NICS, see the Appendix. Two NICS initiatives relating to cardiovascular disease medicines are described here.

Reducing time to thrombolysis

Forty-seven hospitals came together in 2002 to form a national emergency department collaborative whose aim was to develop and implement programs that would reduce waiting times for treatment, including time to thrombolysis (National Institute of Clinical Studies 2004a). There is overwhelming evidence that early thrombolysis (treatment with clot-busting medicines) leads to less morbidity and deaths in patients with myocardial infarction. While patients get benefit from treatment up to 12 hours after the onset of symptoms, the beneficial effect is substantially higher if patients are treated within 90 minutes of the onset of symptoms.

The Australian national benchmark for time from assessment in the emergency department to start of thrombolysis ('door-to-needle' time) is 30 minutes. In South Australia three emergency departments participated in the collaborative, resulting in their average time to thrombolysis dropping from 58 minutes to 44 minutes, with 75% of patients receiving thrombolysis within 30 minutes after the collaborative, compared with 16% previously. Each organisation used different models and developed processes that suited them to achieve these improvements.

Heart failure

NICS developed a program to improve the quality of care for people with heart failure, which had been identified as an area with major gaps between actual clinical practice and best practice (National Institute of Clinical Studies 2004b). It is a collaboration with the National Prescribing Service, National Heart Foundation of Australia and Divisions of General Practice.

As part of the program, NICS conducted a study to identify barriers to managing heart failure in general practice (Phillips et al. 2004). Concerns about possible side effects of the medicines and lack of awareness of their effectiveness were common reasons for suboptimal use of ACE inhibitors. Under-use of beta-blocking agents was due mainly to concerns about side effects, contraindications and coexisting conditions, being unaware of their value and lack of experience initiating treatment with these medicines.

Among other objectives, the program encourages doctors to prescribe appropriate medicines at optimal doses, particularly ACE inhibitors and beta-blocking agents, through a range of interventions. Evaluation results of the program will be available in 2007.

5.5 National Primary Care Collaboratives

The Australian Primary Care Collaboratives program, an initiative of the Australian Government Department of Health and Ageing, aims to improve clinical health outcomes, reduce lifestyle risk factors and maintain good health in people with chronic and complex conditions. Its initial focus is on promoting quality improvement in primary health care in the prevention, management and underpinning clinical and business systems relating to cardiovascular disease and diabetes. Program activities started in February 2005 (National Primary Care Collaboratives 2006).

Results to date for participating practices show marked improvements in the:

- proportion of patients with coronary heart disease taking aspirin
- proportion of patients with coronary heart disease taking a statin (cholesterol-lowering agent)
- proportion of patients who had a myocardial infarction in previous year taking beta-blocking agents
- proportion of patients with coronary heart disease with blood pressure below 140/90 mm Hg (Table 12).

Table 12: Quality practices in management of coronary heart disease among participants in Australian primary care collaboratives

Indicator	Group 1		Group 2	
	At start	After 17 months	At start	After 9 months
	Per cent			
Patients with coronary heart disease taking aspirin	43	66	54	62
Patients with coronary heart disease taking a statin	41	73	62	71
Patients who had a myocardial infarction in previous year taking beta-blocking agents	29	63	41	64
Patients with coronary heart disease with blood pressure below 140/90 mm Hg	36	51	30	48

Notes

1. 157 general practices participated in Group 1 and 159 in Group 2 nationally. The mean of the results from all participating practices is shown.
2. Results shown here are current at the time of preparing this report but the collaboratives are continuing so more recent information will be available in future.

Source: National Primary Care Collaboratives 2006.

5.6 Section 100 initiative

Despite Indigenous Australians having poorer health than other Australians, expenditure on PBS medicines among Indigenous people was one-third that for other Australians in 2001–02 (AIHW 2005). The supply of PBS medicines to remote area Aboriginal and Torres Strait Islander Health Services under Section 100 of the National Health Act of 1953 is an initiative introduced in 1999 to improve access to PBS medicines for Indigenous people.

Under these arrangements, patients attending approved remote area Aboriginal and Torres Strait Islander Health Services are able to get medicines from an on-site dispensary at the health service, without the need for a prescription form and without charge.

In 2001–02 the Australian Government spent \$35.9 million on all medicines for Indigenous people, including \$10.9 million on PBS medicines supplied under Section 100 arrangements to remote area Aboriginal and Torres Strait Islander Health Services, compared with \$4,671.4 million and \$1.2 million for non-Indigenous people respectively (AIHW 2005).

The Section 100 arrangements benefit 36% of the Aboriginal and Torres Strait Islander population and have resulted in an increase of \$36.4 million expenditure on PBS medicines for Indigenous people from 2000–01 to 2002–03 associated with, for example, increased access to ACE inhibitors (Kelaher et al. 2004).

5.7 Drug-adverse events

Drug-adverse events are medicine problems that result in harm to the patient. They may arise from over-use and under-use of medicines, as well as from reactions to medicines and interactions between medicines. Although there may be a low likelihood of individual drug-adverse events occurring, the large numbers of people taking medicines increase the potential for events and presents a major problem. The risk is higher for people taking

multiple medicines, particularly older people. It has been estimated that 2–3% of all unplanned hospitalisations in Australia are related to medicines, rising to about 20% among people aged over 65 years (Australian Council for Safety and Quality in Health Care 2002). Medicines for heart disease and hypertension and anticoagulants are among the most commonly involved in drug-adverse events.

According to a survey run in South Australia, 52% of respondents used complementary medicines in 2004, 50% had used conventional medicines on the same day, and 53% did not report the use of complementary medicines to their doctor (MacLennan et al. 2006). It is not unusual for younger women to give complementary medicines to older relatives with chronic diseases without first checking safety of interactions with conventional medicines (Gowan 2006).

One in ten patients presenting to a GP has had a medicine incident in the preceding six months, defined as an 'unintended event due to the use of medicine that could have harmed or did harm the patient' (Miller et al. 2006). About 8% of these patients were hospitalised as a result and GPs thought 23% of all medicine incidents could have been prevented. The most common reason given for a medicine incident was a recognised medicine side effect (72%), followed by medicine sensitivity (12%) and allergy (11%).

Factors that may lead to drug adverse events in hospital include omission of therapy, overdose, administration of the wrong medicine, failure to read or misreading the patient chart, prescription errors, and dispensing errors in hospital pharmacies. In general practice, there may be communication problems, inadequate review of patient history, lack of protocols, or errors in assessment leading to the use of an inappropriate medicine or dose, prescribing errors and administration errors. Problems with medicines may also arise from lack of communication in the transition between hospital and community care, and when patients consult several health care providers who may not know the patient's full medical history and medicines they are taking (Australian Council for Safety and Quality in Health Care 2002).

Information on deaths and hospitalisations associated with drug-adverse effects is available from the National Mortality Database and the National Hospital Morbidity Database, respectively. The data shown here refer to the ICD-10 and ICD-10-AM codes defined as 'drugs, medicaments and biological substances causing adverse effects in therapeutic use' and are limited to those medicines that are relevant to cardiovascular disease. This category includes correct medicine properly administered in a therapeutic or prophylactic dose as the cause of any adverse effect. It excludes accidents in the technique of administration of medicines, accidental overdoses of medicines, wrong medicines given or taken in error, and medicines taken inadvertently.

In 2004 there were 301 deaths with adverse effects of medicines that may be used to prevent or treat cardiovascular disease recorded (Table 13). Drug-adverse effects were the underlying cause in 29 deaths (9.6%) and an associated cause in 272 deaths (90.4%), indicating that for most of these deaths the drug-adverse effect was not considered the main cause of death. Anticoagulants were the medicines most commonly reported as causes of death.

Table 13: Deaths with adverse effects of medicines used to prevent or treat cardiovascular disease, 2004

Medicine class (ICD-10 code)	Underlying cause deaths	Associated cause deaths	Total deaths
Anticoagulants (Y44.2)	19	211	230
Anticoagulant antagonists, vitamin K and other coagulants (Y44.3)	0	21	21
Thrombolytic drugs (Y44.5)	0	10	10
Salicylates (Y45.1)	4	10	14
β-Adrenoreceptor antagonists, not elsewhere classified (Y51.7)	1	1	2
Cardiac-stimulant glycosides and drugs of similar action (Y52.0)	0	5	5
Other antidysrhythmic drugs, not elsewhere classified (Y52.2)	4	9	13
Angiotensin-converting-enzyme inhibitors (Y52.4)	1	1	2
Antihyperlipidaemic and antiarteriosclerotic drugs (Y52.6)	0	2	2
Loop (high-ceiling) diuretics (Y54.4)	0	1	1
Other diuretics (Y54.5)	0	1	1
Total	29	272	301

Notes

1. Some of the medicines listed in this table are used to treat a range of conditions outside the cardiovascular system. The particular condition for which the medicine was indicated is not recorded.
2. Underlying cause of death is the disease or injury initiating the sequence of events leading to death, that is, the main cause.
3. Associated cause of death is any disease or injury, other than the underlying cause of death, contributing to death.

Source: AIHW National Mortality Database.

There were 28,449 hospital separations with codes for adverse effects of medicines that may be used to treat or prevent cardiovascular disease recorded in 2004–05, representing 0.4% of all separations and 32% of all separations with adverse effects of any medicine (Table 14). Their number increased with age, with 81% of such hospitalisations occurring in patients aged 65 years and over. This probably reflects the fact that older people are both more likely to take medicines and to be hospitalised. Anticoagulants were the most commonly recorded medicines with adverse effects, accounting for 32% of the total (9,127 separations), followed by cardiac-stimulant glycosides and medicines of similar action (3,223 separations). Overall, most drug-adverse events occurred in hospital (42–91%), but up to 18% happened at home, depending on the medicine class considered. The proportion of hospitalisations with codes for adverse effects of medicines used to treat or prevent cardiovascular disease remained constant from 2003–04 to 2004–05.

A study conducted in Western Australia showed that between 1991 and 2002, rates of drug-adverse events causing admission to hospital or extending hospital stay doubled for people aged 60 years and over (Burgess et al. 2005). In those aged 80 years and over, the increase was even more marked and cardiovascular medicines were the most frequently associated with hospitalisations with drug-adverse events. For people aged 60 years and over, anticoagulants were the most common medicines implicated in drug-adverse events causing hospitalisation in 2002 and had had the largest increase over time.

Table 14: Hospitalisations with adverse effects of medicines used to prevent or treat cardiovascular disease, 2003–04 and 2004–05

Medicine class (ICD-10-AM code)	Number separations	
	2003–04	2004–05
Anticoagulants (Y44.2)	8,587	9,127
Anticoagulant antagonists, vitamin K and other coagulants (Y44.3)	115	71
Antithrombotic drugs (Y44.4)	37	364
Thrombolytic drugs (Y44.5)	146	91
Salicylates (Y45.1)	1,334	1,259
Predominantly β -adrenoreceptor antagonists, not elsewhere classified (Y51.5)	206	204
α -Adrenoreceptor antagonists, not elsewhere classified (Y51.6)	105	115
β -Adrenoreceptor antagonists, not elsewhere classified (Y51.7)	2,411	2,707
Cardiac-stimulant glycosides and drugs of similar action (Y52.0)	2,803	3,223
Calcium-channel blockers (Y52.1)	739	792
Other antidysrhythmic drugs, not elsewhere classified (Y52.2)	1,217	1,363
Coronary vasodilators, not elsewhere classified (Y52.3)	1,254	1,222
Angiotensin-converting-enzyme inhibitors (Y52.4)	1,445	1,564
Other antihypertensive drugs, not elsewhere classified (Y52.5)	2,443	2,803
Antihyperlipidaemic and antiarteriosclerotic drugs (Y52.6)	303	395
Peripheral vasodilators (Y52.7)	56	68
Antivaricose drugs, including sclerosing agents (Y52.8)	10	14
Other and unspecified agents primarily affecting the cardiovascular system (Y52.9)	119	118
Benzothiadiazine derivatives (Y54.3)	441	508
Loop (high-ceiling) diuretics (Y54.4)	773	846
Other diuretics (Y54.5)	1,588	1,595
Total separations with adverse effects of medicines used to treat or prevent CVD	26,132	28,449
Total separations with adverse effects of any medicine	83,022	90,371
Total separations	6,841,225	7,018,850

Notes

1. Some of the medicines listed in this table are used to treat a range of conditions outside the cardiovascular system. The particular condition for which the medicine was indicated is not recorded.
2. Hospitalisations with adverse effects of medicines coded as a principal or additional diagnosis are shown.

Source: AIHW National Hospital Morbidity Database.

Australian Council for Safety and Quality in Health Care initiatives

The former Australian Council for Safety and Quality in Health Care (now Australian Commission on Safety and Quality in Health Care) identified various strategies shown to reduce medicine problems. These include:

- computerised prescribing by doctors with clinical decision support systems
- computerised drug-adverse event alerts
- individual patient medicine supply in hospitals, where medicines are labelled, supplied and stored for individual patients

- clinical pharmacy services, which provide patient and staff education
- monitoring and medicine review
- effective transfer of information between hospital and community settings
- community-based medicine management and case conferencing, and
- discharge medicine management (Australian Council for Safety and Quality in Health Care 2004).

The Council sponsored a national medication safety breakthrough collaborative aimed at reducing patient harm associated with medicines by 50% in participating facilities (Australian Council for Safety and Quality in Health Care 2005). The collaborative began in September 2003 with 100 teams from all states and territories focussing on medicine processes in acute hospitals and improving medicine practices at the interface between acute hospitals and the community. Many teams achieved a 50% reduction in harm in the area they chose, such as antithrombotic agents and cardiovascular medicines. Strategies used included:

- taking a multidisciplinary approach to improvement
- implementing education programs to raise awareness
- revising systems with the potential to cause harm
- developing tools to reduce medicine omission
- developing systems to identify patients at risk of medicine mismanagement or harm
- developing guidelines for using high-risk medicines
- using patient information material and medicine cards to keep patients informed and involved in their own medicine management, and
- implementing systems for communication with general practitioners.

This initiative is now disseminating knowledge of successful practices to others.

Veterans' MATES

The Australian Government Department of Veterans' Affairs developed the Veterans' Medicines Advice and Therapeutics Education Services (Veterans' MATES) program to improve the use of medicines in the veteran community. The program uses data from RPBS prescription claims to identify veteran patients who may be at risk of drug-adverse events and provides information that may help improve the management of patients' medicines. Veterans' GPs are the main focus of the program, but it also involves patients, their carers, community pharmacists and other specialists to encourage better communication and raise awareness of patients' chronic conditions (Department of Veterans' Affairs 2006).

The program is delivered in modules every three months. Modules delivered to date include:

- a review of medicines among veterans who use five or more medicines each month to discuss the medicines being taken and why, and how patients were managing medicines and if there were any unwanted side effects (38,500 patients and their 11,000 doctors)
- medicines for heart failure (13,000 patients and their 6,500 doctors)
- heart medicines for patients with diabetes (17,500 patients, their 8,000 doctors and 5,000 community and hospital pharmacies)
- arthritis medicines and their risks for patients with heart failure or diabetes

- using multiple medicines safely (46,000 patients and their 12,500 doctors).

Home medicines reviews

The Australian Government introduced the Home Medicines Review (HMR) in October 2001. The HMR is a program where the patient's GP and a pharmacist collaboratively review their use of medicines and develop an agreed medicine management plan. It usually entails a visit to the patient's home by a pharmacist accredited to conduct medicine reviews, after a referral from the patient's GP and consent from the patient.

The objectives of the HMR are: to detect and resolve potential medicine-related problems that interfere with the desired health outcomes for the patient; to promote collaboration between the patient, their carer where appropriate, the GP, pharmacists and other relevant health professionals to improve the patient's health and quality of life; and to improve patients' and health professionals' knowledge and understanding about medicines.

An Australian study found that HMRs resolved medicine related problems in 56% of cases and in a further 20% the problem had improved at follow-up (Gilbert et al. 2002).

From the start of the program to April 2005 there were over 70,000 HMRs conducted nationally (Urbis Keys Young 2005). About 74% of HMRs were for people aged 65 years and over, and 62% were provided to women. Older men, young people with chronic disease, Indigenous Australians, people living in rural and remote areas, and people from diverse cultural and linguistic backgrounds have to date tended to have less access to HMRs than other Australians. Only about 15% of GPs have made referrals for HMRs so far, indicating that HMRs have not been used by a large number of patients who might benefit from them.