Generic substitution of commonly used medications: Australia-wide experience, 2007–2008

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ABSTRACT

Objective: To study the extent of brand substitution and switching in three commonly used classes of drugs available on the Pharmaceutical Benefits Scheme (PBS).

Design, setting and participants: Assessment of PBS claim records for a 1-year period from 1 August 2007 to 31 July 2008 for long-term concession cardholders drawn from a 10% random sample of the Australian population. The target drug classes were: statins (pravastatin, simvastatin), calcium channel blockers (CCBs) (amlodipine, felodipine, nifedipine), and selective serotonin reuptake inhibitor (SSRI) antidepressants (fluoxetine, fluvoxamine, paroxetine, sertraline).

Main outcome measures: Proportion of patients who were non-switchers (single brand only) and multiple switchers (two or more brand switches).

Results: We retrieved information relating to 935 334 prescriptions for 122 000 patients. Of those patients filling at least four prescriptions for a product, 41 174 patients received statins, 27 230 received CCBs and 21 342 received SSRIs. More than half the patients received only one brand during the study period: 57% for statins, 60% for CCBs, and 63% for SSRIs. Multiple switching was recorded for 24% of patients with statins, 19% with CCBs, and 21% with SSRIs, with smaller proportions receiving three or more brands: 14% for statins, 10% for CCBs, and 12% for SSRIs. Multiple switching was more common among younger patients for all drug classes (28% for those aged < 50 years v 18% for those aged ⩾ 80 years).

Conclusion: Generic substitution with multiple switches is occurring in a small proportion of patients being treated with statins, CCBs or SSRIs. The potential for patient confusion appears to be relatively small, but this may change with recent incentives included in pharmacy reimbursement arrangements.

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Brand substitution with generic forms of Australian Pharmaceutical Benefits Scheme (PBS) medicines has been possible since 1994, with potential cost savings for patients. Although doctors and patients have expressed reservations about the bioequivalence of generic products,[1-4] this is no longer felt to be a major issue,[5] except perhaps for epilepsy which has a very narrow therapeutic window.[6] Concern has since been expressed that multiple brand switches (permissible under current PBS regulations) might lead to patient confusion and poor adherence or persistence.[7,8] However, there is little firm evidence to support this concern and some evidence that it is not a problem.[9]

A study examining dispensing under the Repatriation Pharmaceutical Benefits Scheme during 2001–2006 found that brand substitution and multiple switches were uncommon and therefore of little practical concern.[10,11] Here, we have analysed the extent of brand substitution and switching for products in selected drug classes listed on the PBS during the 12 months to 31 July 2008, a period immediately before changes in reimbursement arrangements for Australian pharmacies, which included a financial incentive for dispensing non-premium generic medicines.

METHODS

Data source

We analysed PBS claims for prescriptions for long-term concession cardholders drawn from a 10% random sample of the Australian population, using data from de-identified records held by Medicare Australia. We focused on products from three commonly prescribed drug classes that require long-term therapy and have multiple generic brands available: statins (pravastatin, simvastatin; up to 14 brands listed); calcium channel blockers (CCBs) (amlodipine, felodipine, nifedipine; up to nine brands listed); and selective serotonin reuptake inhibitor (SSRI) antidepressants (fluoxetine, fluvoxamine, paroxetine, sertraline; up to 13 brands listed). Most of these drugs are priced below the general patient copayment threshold, and such prescriptions are not recorded in the Medicare Australia database. Hence, the study was restricted to patients classified as "long-term concessional", defined as patients with no record of a "non-concessional" (ie, general) prescription since June 2002. Concessional patients are estimated to receive 65% of all PBS drugs (under copayment data received for use with Weighted Average Monthly Treatment Cost calculations, Pharmaceutical Benefits Advisory Committee Drug Utilisation Sub-Committee).

Brand switching analysis

We identified a cohort of concessional patients prescribed these drugs during the 1-year period from 1 August 2007 to 31 July 2008. Given our previous findings of high discontinuation rates in patients using lipid or antihypertensive drugs,[12,13] we limited our reporting to patients who filled four or more prescriptions for the same drug during the year, to minimise the impact of poor compliance or change in dose. Apart from excluding patients with less than four prescriptions for a product in the 1-year period, we made no attempt to differentiate between treatment episodes, new initiations, cessations, poor compliance or dose changes.

The drug brand was identified using the manufacturer code included in the PBS claim made by the pharmacy. A "premium" brand was defined as a product for which an additional premium was paid by the patient; this was usually the originator's brand. For the small number of records where brand identification was missing (around 1%), it was conservatively assumed that the brand was the same as the previous script dispensed.

"Brand switching" was defined as a patient receiving different brands of the same strength of medicine at consecutive dispensing occasions. Same-day dispensing, very small in extent, was assigned the brand supplied and both scripts were included in the brand and switch counts. Patients who

received the same brand throughout the period were classified as non-switchers. "Brand substitution" was defined if a patient had at least one switch from one brand to another. Patients with two or more switches were classified as "multiple switchers".

Multiple switch rates were compared between male and female patients and between 10-year age groups. The group with the smallest proportion of multiple switchers was selected as the reference group, and pairwise comparisons with other groups were reported using odds ratios and 95% confidence intervals.

Ethics approval

Patients remained anonymous during this investigation, and ethics approval was obtained from the Medicare Australia Ethics Committee.

RESULTS

We retrieved information on 935 334 prescriptions for 122 000 patients. Of the patients collecting four or more scripts for an item, 41 174 patients received a statin, 27 230 received a CCB and 21 342 received an SSRI. There was a modest excess of female patients overall, and those prescribed SSRI drugs were younger than those receiving the other two classes (Box 1). Based on the type of prescriber of each patient's first prescription, more than 90% of prescriptions were written by a general practitioner.

Brand substitution findings are summarised in Box 2. More than half the patients received only one brand during the study period: 57% of those with statins, 60% with CCBs, and 63% with SSRIs. Brand substitution was common (43% of patients with statins, 40% with CCBs, and 37% with SSRIs), with multiple switching recorded for 24% of patients with statins, 19% with CCBs, and 21% with SSRIs. Smaller proportions received three or more brands (14% with statins, 10% with CCBs, and 12% with SSRIs).

1 Demographics of patients receiving ⩾ 4 prescriptions*

	Statins (*n* = 41 174)	CCBs (*n* = 27 230)	SSRIs (*n* = 21 342)
Sex			
Male	16 552 (40%)	10 959 (40%)	6 593 (31%)
Female	24 622 (60%)	16 271 (60%)	14 749 (69%)
Age group (years)			
< 50	996 (2%)	699 (3%)	6 468 (30%)
50–59	2 594 (6%)	1 710 (6%)	2 943 (14%)
60–69	9 427 (23%)	5 871 (22%)	4 150 (19%)
70–79	18 641 (45%)	11 581 (43%)	4 709 (22%)
⩾ 80	9 516 (23%)	7 369 (27%)	3 072 (14%)
Mean age (years)	72.6	73.3	59.4

CCB = calcium channel blocker. SSRI = selective serotonin reuptake inhibitor.
* Data are number (%) of patients unless otherwise specified. ◆

2 Brand substitution by patients filling four or more prescriptions, by drug class*

	Statins (*n* = 41 174)	CCBs (*n* = 27 230)	SSRIs (*n* = 21 342)
No. of prescriptions filled			
4–7	7 320 (18%)	6 730 (25%)	9 518 (45%)
8–11	14 811 (36%)	7 866 (29%)	6 338 (30%)
⩾ 12	19 043 (46%)	12 634 (46%)	5 486 (26%)
Mean scripts/patient	10.3	10.0	8.6
No. of brands dispensed			
1	23 608 (57%)	16 466 (60%)	13 412 (63%)
2	11 743 (29%)	8 074 (30%)	5 338 (25%)
3	4 178 (10%)	2 097 (8%)	1 891 (9%)
4	1 253 (3%)	505 (2%)	541 (3%)
⩾ 5	392 (1%)	88 (0.3%)	160 (1%)
Mean brands/patient	1.6	1.5	1.5
No. of brand switches			
0	23 608 (57%)	16 466 (60%)	13 412 (63%)
1	7 606 (18%)	5 713 (21%)	3 372 (16%)
2	4 878 (12%)	2 829 (10%)	2 220 (10%)
3	2 273 (6%)	1 191 (4%)	977 (5%)
4	1 287 (3%)	562 (2%)	632 (3%)
⩾ 5	1 522 (4%)	469 (2%)	729 (3%)
Mean switches/patient	0.9	0.7	0.8
Premium brand prescriptions†	107 064 (25%)	86 376 (33%)	62 482 (32%)

CCB = calcium channel blocker. SSRI = selective serotonin reuptake inhibitor.
* Data are number (%) of patients unless otherwise specified. Percentages may not sum to 100% due to rounding. † Number (%) of prescriptions filled. ◆

There was wide variation in the proportion of multiple switching between products, ranging from 6% for felodipine to 30% for fluvoxamine (Box 3). There appeared to be a trend towards a higher proportion of multiple switches for products with more brands listed on the PBS.

A significant relationship was observed between multiple switching and age in all drug classes, with more switching at younger ages (Box 4). Multiple switching was recorded for 28% of those aged less than 50 years compared with 18% of those aged 80 years or older (odds ratio, 1.75; 95% CI, 1.65–1.86). There were no major differences in multiple switching between male and female patients (24%, 19% and 22% of men, and 24%, 18% and 20% of women for statins, CCBs and SSRIs, respectively). A substantial proportion of prescriptions filled were for the premium brand (25% of statins, 33% of CCBs, and 32% of SSRIs), at extra cost to the patient.

DISCUSSION

In an environment where generic substitution is encouraged, we found that between a quarter and a third of prescriptions for statin, CCB or SSRI drugs were for the original brand products, for which patients paid an extra premium. Brand substitution occurred with around 40% of patients, who received more than one brand of these medicines during a 1-year period. Furthermore, 19%–24% of patients made multiple switches. These results indicate potential for patient confusion, especially in the presence of polypharmacy.[7,8] However, there is little hard evidence that confusion is actually occurring on any large scale,[9] nor are we aware of any major dataset describing any relationship between generic substitution, patient confusion and rates of hospitalisation.

Our findings were broadly consistent across drugs used for cholesterol control, blood pressure reduction, and antidepressant therapy. These drug classes were selected because they are widely used and have multiple generic brands available.

3 Extent of brand substitution and multiple switching, by drug product

Product	Year of, or time since, first generic	No. of generics*	Multiple (⩾ 3) brands†	Multiple (⩾ 2) switches†
Statins				
Pravastatin	2005	up to 11	13%	26%
Simvastatin	> 5 years	up to 14	14%	26%
CCBs				
Amlodipine	2007	up to 9	16%	25%
Felodipine	> 5 years	up to 3	1%	6%
Nifedipine	> 5 years	up to 8	5%	18%
SSRIs				
Fluoxetine	> 5 years	up to 11	11%	21%
Fluvoxamine	> 5 years	up to 4	15%	30%
Paroxetine	> 5 years	up to 10	15%	26%
Sertraline	2004	up to 13	11%	19%

CCB = calcium channel blocker. SSRI = selective serotonin reuptake inhibitor. * Listed on the Pharmaceutical Benefits Scheme in July 2008. † Proportion of patients. ◆

The higher frequency of switching in younger patients is intriguing. As all patients paid the same concessional price, this is not a financial issue. We might speculate that older patients are less willing to accept a brand switch, and this could be a useful protective mechanism against any potential confusion.

Just under half the patients taking statins or CCBs collected 12 or more prescriptions in the 1-year period, compared with around a quarter of SSRI patients. While statins and CCBs have been linked to poor persistence,[12,13] these data indicate that there is a substantial group of patients who are both adherent and persistent. On the other hand, the patient selection criteria used in this analysis would have largely overridden issues of poor persistence. The smaller proportion of patients collecting 12 or more SSRI scripts suggests that the use of these drugs may be more episodic than chronic in this patient population.

An examination of patients receiving atenolol, citalopram, enalapril, metformin, omeprazole, ramipril and simvastatin during the 5 years to early 2006 found that 92% of patients had no switches, and only 1% were multiple switchers. The authors concluded that: "The rules of the brand substitution policy appear to be adequate in allowing brand choice for patients, without leading to multiple switches per prescription".[10] Our findings stand in contrast to these results, but there are differences between the two studies: the sampling in the previous study was devoted to the Repatriation Pharmaceutical Benefits Scheme, some of the drugs differed from those in our study and, most importantly, there were fewer generic alternatives available in the earlier period. Furthermore, we used a different definition of multiple switching, including return to an earlier brand as a switch. When using a similar definition of multiple switching to that used in the earlier study,[11] we found that 10%–14% of patients received three or more brands in the 1-year period. Although we studied a different population (concession cardholders), the extent of multiple switching seems to have increased since 2006.

Cost savings to third-party payers or patients for generic drugs in Australia are smaller than in other countries. In the United States, significant cost savings have been reported.[14] In a recent survey of patient perceptions, most Americans appreciated the cost-saving value of generic drugs, but few were actually eager to use them.[4] Returning to the issue of bioequivalence, a meta-analysis of drugs used in cardiovascular disease concluded that evidence did not support the notion that premium drugs were superior to generic drugs, yet a substantial number of editorials counselled against the interchangeability of generic drugs.[5]

There are some limitations in our analysis. Only concession cardholders were studied for a period of 12 months; however, they represent around 65% of Australian patients using these medicines. We acknowledge a lack of medical history, and we did not determine how long these patients had used the medicines before the study. Treatment cessation was not taken into account in the analysis, and no allowance was made for new generic products added to the PBS during the study period. However, these limitations are largely overshadowed by the large number of patients we sampled.

In summary, we did not identify any major extent of brand switching during this 1-year period, but this may change following the introduction of incentives for generic dispensing in pharmacy reimbursement arrangements.

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COMPETING INTERESTS

Michael Ortiz is a full-time employee of Solvay Pharmaceuticals, who commissioned this project. Solvay had no input into the concept, design,

4 Proportion of patients with multiple (⩾ 2) switches, and odds ratios, by age group

Age group (years)	Statins		CCBs		SSRIs		All classes	
	%	Odds ratio (95% CI)	%	Odds ratio (95% CI)	%	Odds ratio (95% CI)	%	Odds ratio (95% CI)
< 50	33%	1.77 (1.54–2.04)	29%	2.14 (1.80–2.55)	28%	2.51 (2.23–2.82)	28%	1.75 (1.65–1.86)
50–59	30%	1.55 (1.41–1.71)	23%	1.55 (1.36–1.76)	25%	2.16 (1.89–2.47)	26%	1.58 (1.48–1.68)
60–69	26%	1.23 (1.15–1.32)	20%	1.35 (1.23–1.47)	21%	1.75 (1.54–1.99)	23%	1.33 (1.27–1.40)
70–79	23%	1.08 (1.02–1.14)	18%	1.14 (1.06–1.23)	17%	1.31 (1.15–1.50)	21%	1.15 (1.10–1.20)
⩾ 80*	22%	1.00	16%	1.00	13%	1.00	18%	1.00

CCB = calcium channel blocker. SSRI = selective serotonin reuptake inhibitor. * Pairwise comparison reference group. ◆

intellectual development or analysis of this study, or preparation or approval of the manuscript prior to submission. Leon Simons has received speaker fees in the past (unrelated to this study). Gordon Calcino is an independent contractor who was paid by Solvay Pharmaceuticals to undertake the data extraction and analysis for the project.

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