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Ethics Id	Date Tabled	Item Number	Study Title	Status	Researcher	Research Institution	Date Submitted

s 22 - Out of scope

E005/009	8/08/2008	6.8	Switching Medicines in the Veteran Population	Final Report	s 47F	University of South Australia	8-Jul-08

s 22 - Out of scope

From:	s 47F
To:	DVA Ethics Committee
Subject:	RE: E005/009 - Progress report: Switching medicines in the veteran population and the impact on health outcomes and costs [TOBECLASSIFIED] [SEC=UNCLASSIFIED]
Date:	Thursday, 3 July 2008 4:30:01 PM

Thanks Madeline. I will forward the final report to the Committee as soon as possible.

Kind regards,

s 47F

From: DVA Ethics Committee [mailto:Ethics.Committee@dva.gov.au]
Sent: Thursday, 3 July 2008 13:20
To: s 47F)
Subject: RE: E005/009 - Progress report: Switching medicines in the veteran population and the impact on health outcomes and costs [TOBECLASSIFIED] [SEC=UNCLASSIFIED]

Dear s 47F

Thank you for your response to our letter regarding progress/final report for the above study. Since the project is now complete a final report to the Committee ensuring that the following is addressed together with any publications etc.

(a) outcome of completed research
(b) any events of significance that have occurred during the study, particularly in relation to adverse outcomes;
(c) maintenance and security of records;
(d) compliance with the approved proposal and protocol; and
(e) compliance with any conditions of approval.

Kind regards

Madeline s 47F
Administrative Support Assistant
DVA Human Research Ethics Committee
Department of Veterans' Affairs
Phone: s 47F

From: s 47F
Sent: Thursday, July 03, 2008 11:57 AM
To: DVA Ethics Committee
Subject: E005/009 - Progress report: Switching medicines in the veteran population and the impact on health outcomes and costs [TO BE CLASSIFIED]

Dear Ms. s 47F

Re: Progress report E005/009: Switching medicines in the veteran population and the impact on health outcomes and costs

s 22 - Out of scope

s 22 - Out of scope

s 22 - Out of scope The research is now completed.

Would the DVA HREC prefer me to submit a progress report or a “final” report for the research? I am able to supply a copy of the PhD thesis and publications arising from the research as part of a final report.

Kind regards,

s 47F

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ORIGINAL REPORT

Brand substitution or multiple switches per patient? An analysis of pharmaceutical brand substitution in Australia[†,‡]

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SUMMARY

Purpose To determine the number of times patients have brand and generic products substituted under Australia's Pharmaceutical Benefits Scheme (PBS) brand substitution policy.

Methods A retrospective cohort study was conducted using Repatriation Pharmaceutical Benefits Scheme (RPBS) pharmacy claims data. Department of Veterans' Affairs (DVA) treatment card holders with at least two dispensings of atenolol, citalopram, enalapril, metformin, omeprazole or ramipril between 1 January 2001 and 28 February 2006 were included. Patients were followed from first dispensing until death, cessation or study end. The main outcome measure was the number of substitutions per patient during follow up. Based on this, patients were defined as non switchers, brand substitution or multiple switchers.

Results Data for 160 145 patients were analysed. Overall more than 80% of patients either had no switches or demonstrated brand substitution. For all study drugs, patients were more likely to be non switchers than have a brand substitution (RR range 2.6 9.4, $p < 0.0001$) and were more likely to be non switchers than multiple switchers (RR range 3.2 35.9, $p < 0.0001$). Patients who switched were more likely to have a brand substitution than multiple switches (RR range 1.2 3.8, $p < 0.0001$). Multivariate logistic regression showed greater odds of being a multiple switcher with increasing number of prescribers and dispensing pharmacies, and increasing length of follow up.

Conclusions Most patients in this study did not substitute products, and those who did were more likely to demonstrate brand substitution than have multiple switches. These results suggest that the brand substitution policy is having its intended effect for most patients. Copyright © 2008 John Wiley & Sons, Ltd.

KEY WORDS generic substitution; pharmaceutical policy; pharmacoepidemiology; Australia

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[†]DVA reviewed the manuscript prior to submission; however, DVA did not control or influence the decision to submit the manuscript for publication. Prescription claims data from the Repatriation Pharmaceutical Benefits Scheme (RPBS) was used for this study. DVA provided access to the RPBS prescription claims data but had no other role in the study design, data analysis and interpretation or writing of the paper.

[‡]Approval to conduct this research was received from the Department of Veterans' Affairs Human Research Ethics Committee on 28 April 2006.

[§]Associate Professor.

[¶]Professor.

INTRODUCTION

In 1990, the minimum pricing policy was introduced to the Pharmaceutical Benefits Scheme (PBS) and Repatriation Pharmaceutical Benefits Scheme (RPBS), the national subsidised schemes for medicine supply in Australia. Since then, only the cheapest product(s) of each PBS and RPBS medicine are available at the patient co-payment price.[1] Patients using more expensive brands pay the price difference between the cheapest and more expensive product in addition to the patient co-payment, in the form of a brand premium. Brand substitution was introduced in December 1994, allowing substitution of products at the time of dispensing provided the prescriber had not specified that substitution could not occur.[2]

The minimum pricing policy was introduced to enable pharmaceutical manufacturers to set higher prices for their products and to provide a price signal to patients;[3] brand substitution enables patients to avoid paying brand premiums.[1] Ideally, patients should remain on the same product following the initial substitution; however, legislation does not prevent supply of multiple products over time to a patient. When there are multiple products for a medicine, patients are faced with differing trade names and in many cases different product appearance. Qualitative Australian research has shown that different names and appearance for the same medicine can contribute to confusion when substitution occurs.[4] Patients may not realise that substituted products are actually the same medicine and double dosing (using both products), poor compliance or therapy cessation may result.[4] In the years since introduction of the brand substitution policy, there have been anecdotal reports and opinions in the literature suggesting that patients receive multiple different products[5–8] and that this may cause confusion.[4,5,9–11] However, the actual extent of the problem is unknown.

A previous evaluation of the minimum pricing policy, which examined the initial brand substitution of products, showed that a significant number of patients switched to cheaper products in the 3 months post-introduction of a brand premium.[3] What remains unclear is how many patients have products substituted over a longer period of time or how widespread is the problem of multiple switches between products. This study examined what happens in practice when patients have prescriptions for medicines with substitutable products dispensed from community pharmacy. We aimed to identify the number of times products are substituted for patients and the extent of multiple switches between products.

METHODS

Study drugs

A retrospective cohort study was conducted using RPBS prescription claims data. The Department of Veterans' Affairs (DVA) pharmacy claims database includes records for all medicines dispensed to veterans subsidised under the RPBS. The eligible treatment population numbered 300 000 in December 2006.[12] Seventy five million prescription records are stored within the dataset, and a client file is also maintained by DVA which includes gender, age and date of death. Each pharmacy claim record includes a patient identifier, the date of supply and date of prescription, a prescriber identifier and dispensing pharmacy identifier, the quantity of medicine supplied and a manufacturer code (indicating the brand or generic product supplied).

Atenolol, citalopram, enalapril, metformin, omeprazole and ramipril were selected as study drugs because they are frequently dispensed on the RPBS,[13] cover a range of therapeutic classes and are generally used in the treatment of long-term conditions. The analysis was limited to strengths and formulations of these medicines with two or more brand and generic products available, listed in Table 1.

Table 1. Included patients

	Atenolol *n* 44 575	Citalopram *n* 18 414	Enalapril *n* 15 752	Metformin *n* 23 456	Omeprazole *n* 67 992	Ramipril *n* 36 814
Strengths and forms studied	50 mg tablets	20 mg tablets	5, 10 and 20 mg tablets	500 and 850 mg tablets	20 mg tablets	1.25, 2.5 and 5 mg tablets
Male patients (%)	24 506 (55)	11 189 (61)	9123 (58)	15 585 (66)	41 060 (60)	23 358 (63)
Median age 28 February 2006 (interquartile range)	82 (79 85)	82 (70 86)	83 (80 87)	81 (76 85)	82 (79 86)	83 (80 86)
Median months follow up (interquartile range)	11 (4 32)	7 (2 19)	16 (5 40)	9 (3 26)	10 (3 28)	8 (2 21)

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Table 2. Brand substitution status of patients

	Atenolol *n* 44 575	Citalopram *n* 18 414	Enalapril *n* 15 752	Metformin *n* 23 456	Omeprazole *n* 67 992	Ramipril *n* 36 814
No switches (%)	35 781 (80)	10 991 (60)	9306 (59)	18 673 (80)	47 017 (69)	32 448 (88)
Brand substitution (%)	5929 (13)	4201 (23)	3543 (22)	3219 (14)	14 639 (22)	3461 (9)
Multiple switches (%)	2865 (6)	3222 (17)	2903 (18)	1564 (7)	6336 (9)	905 (2)
Median switches by multiple switchers (interquartile range)	4 (3 5)	4 (3 5)	4 (3 5)	4 (3 5)	4 (3 5)	3 (3 4)

The study period was from 1 January 2001 to 28 February 2006. Patients were included from their first dispensing post the study start date and followed until discontinuation (defined as more than 90 days since the last dispensing), death or study end, whichever was reached first. Only patients with two or more dispensings were included, as this is the minimum number of dispensings required to receive more than one product.

Identification of switches. Switches were identified if a patient received different brand or generic products of the same strength medicine at consecutive dispensings within 60 days. The 60-day interval was calculated from the data and represents the 90th percentile for time between prescription refills. If the manufacturer code was not recorded, it was assumed that it was the same as the previous dispensing. Of the 4 000 948 claims identified for the products in this study, only 3.0% had no manufacturer code recorded.

Brand substitution status. Patients who received the same product throughout follow-up were classified as non-switchers. Brand substitution was defined if a patient had only one switch, or had a total of two switches involving a switch and then a switch back to the original product. Patients with three or more switches, or who had two switches but received three different products during follow-up were defined as multiple switchers.

Statistical analysis. A multinomial generalised estimating equation (GEE) was used to compare the proportion of patients using each drug with no switches, a brand substitution or multiple switches. For each drug, a multivariate multinomial logistic regression model was used to determine differences in brand substitution status and patient age, gender, duration of follow-up, number of prescribers and number of dispensing pharmacies. No adjustments were made for multiple comparisons. All analyses were undertaken using SAS v9.1 (SAS Inc., Cary, NC, USA).

RESULTS

Total 160 145 patients met the inclusion criteria. A quarter of these patients (39 959) received more than one study drug during follow-up. For all drugs, the majority of patients were male and the median age was over 81 years (see Table 1). The median duration of follow-up was between 7 and 16 months (Table 1).

Over 80% of patients using each medicine either had no switches or demonstrated brand substitution (Table 2). Patients who switched were more likely to have a single brand substitution than multiple switches (Table 3).

Multiple switchers compared to non-switchers

Multivariate logistic regression showed small but statistically significant age differences between multiple switchers and non-switchers (Table 4). There

Table 3. Rate ratio (95% CI) for brand substitution status comparisons

	Atenolol	Citalopram	Enalapril	Metformin	Omeprazole	Ramipril
No switches versus brand substitution*	6.0 (5.9 6.2)	2.6 (2.5 2.7)	2.6 (2.5 2.7)	5.8 (5.6 6.0)	3.2 (3.1 3.3)	9.4 (9.1 9.7)
No switches versus multiple switches*	12.5 (12.0 13.0)	3.4 (3.3 3.5)	3.2 (3.1 3.3)	11.9 (11.3 12.6)	7.4 (7.2 7.6)	35.9 (33.6 38.3)
Brand substitution versus multiple switches*	2.1 (2.0 2.2)	1.3 (1.2 1.4)	1.2 (1.2 1.3)	2.1 (1.9 2.2)	2.3 (2.2 2.4)	3.8 (3.6 4.1)

*$p < 0.0001$ for all comparisons.

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were no gender differences between non-switchers and multiple switchers for patients using atenolol, citalopram, metformin or omeprazole. When all other variables in the model were held constant, the odds of being a multiple switcher compared to a non-switcher increased significantly with a 6-month increase in length of follow-up (Table 4). The odds of being a multiple switcher compared to a non-switcher increased with increasing number of prescribers and dispensing pharmacies for all medicines (Table 4).

Table 4 Factors associated with being a multiple switcher compared to a non-switcher

	Odds ratio of being a multiple switcher compared to a non-switcher for a one unit increase in: (95% CI)			
	Age (years)	Six months of follow-up	Number of prescribers	Dispensing pharmacies
Atenolol	1 006 (1 001–1 011) $p = 0\,0002$	1 240 (1 224–1 256) $p < 0\,0001$	1 351 (1 312–1 392) $p < 0\,0001$	1 226 (1 204–1 249) $p < 0\,0001$
Citalopram	1 014 (1 010–1 019) $p < 0\,0001$	1 607 (1 571–1 643) $p < 0\,0001$	1 663 (1 579–1 752) $p < 0\,0001$	1 695 (1 630–1 763) $p < 0\,0001$
Enalapril	1 012 (1 006–1 019) $p < 0\,0001$	1 313 (1 292–1 333) $p < 0\,0001$	1 355 (1 301–1 412) $p < 0\,0001$	1 322 (1 282–1 364) $p < 0\,0001$
Metformin	1 006 (1 000–1 013) $p = 0\,0433$	1 322 (1 297–1 347) $p < 0\,0001$	1 358 (1 303–1 415) $p < 0\,0001$	1 263 (1 227–1 300) $p < 0\,0001$
Omeprazole	1 012 (1 008–1 015) $p < 0\,0001$	1 349 (1 336–1 363) $p < 0\,0001$	1 552 (1 518–1 588) $p < 0\,0001$	1 338 (1 316–1 361) $p < 0\,0001$
Ramipril	0 992 (0 983–1 000) $p = 0\,0001$	1 342 (1 313–1 373) $p < 0\,0001$	1 227 (1 170–1 286) $p < 0\,0001$	1 136 (1 102–1 171) $p < 0\,0001$

Multiple switchers compared to patients with a brand substitution

For all of the study drugs, multivariate logistic regression showed no significant differences in the age or gender of patients demonstrating brand substitution and multiple switchers. The odds of being a multiple switcher compared to having a brand substitution were significantly greater for patients with longer follow-up (Table 5). The odds of being a multiple switcher compared to having a brand substitution increased with increasing number of prescribers and dispensing pharmacies (Table 5).

DISCUSSION

For all medicines in this study, at least 80% of patients did not switch or demonstrated brand substitution. Patients who switched were more likely to have a single brand substitution rather than multiple switches. Although concerns have been raised that multiple switches occur,[5 8,14] results of this study suggest that for the majority of patients (over 80%) the brand substitution policy is working in its current format.

McManus and colleagues showed that a significant number of patients switched to using co-payment priced products in the 3 months post-introduction of a brand premium and new generics for ranitidine and fluoxetine.[3] Only a single switch in the time period immediately following introduction of the brand premium was considered in their research. Results of the present study confirm that brand substitution occurs for a wider range of government subsidised medicines than originally investigated by McManus and that substitution is sustained over longer periods of time.

Although the majority of patients received the same product throughout follow-up, between 2 and 18% of patients using each study medicine had multiple switches. Multivariate logistic regression showed that multiple switchers attended more pharmacies and had

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Table 5. Factors associated with being a multiple switcher compared to having a brand substitution

	Odds ratio of being a multiple switcher compared to having a brand substitution for a one unit increase in: (95% CI)*		
	Six months of follow up	Number of prescribers	Dispensing pharmacies
Atenolol	1.130 (1.114 1.147)	1.063 (1.031 1.097)	1.069 (1.049 1.089)
Citalopram	1.293 (1.267 1.320)	1.200 (1.149 1.254)	1.255 (1.216 1.295)
Enalapril	1.138 (1.119 1.156)	1.103 (1.061 1.146)	1.196 (1.162 1.232)
Metformin	1.139 (1.115 1.163)	1.125 (1.078 1.174)	1.074 (1.045 1.103)
Omeprazole	1.155 (1.143 1.166)	1.151 (1.128 1.174)	1.109 (1.093 1.125)
Ramipril	1.052 (1.027 1.078)	1.075 (1.022 1.130)	1.067 (1.034 1.101)

*$p < 0.0001$ for all comparisons.

more prescribers than other patients; suggesting that continuity of care between healthcare providers and consumers may play a role in multiple switching. Inadequate transfer of information between healthcare providers, consumers and different healthcare settings can result in poor quality use of medicines and patient harm.[15] To address this problem, the Australian Pharmaceutical Advisory Council (APAC) has developed guiding principles to achieve continuity in medication management when patients move between healthcare settings and providers.[15] Although these principles discuss the potential for patient confusion from multiple brand names and the need to ensure that patients understand changes to brands of their medicine,[15] the issue of multiple brand substitutions is not discussed. Healthcare providers should assume responsibility for maintaining patients on their regular brand of medicine wherever possible to minimise the likelihood of confusion from multiple substitutions. Given the results of this study, consideration should be given for inclusion of this principle in future updates of the guiding principles document.

KEY POINTS

- Most patients in this study did not have brand and generic products substituted.
- Patients who had products substituted were more likely to have a single brand substitution rather than multiple brand substitutions.
- Multiple brand substitutions per patient were not common, and occurred for less than 18% of patients using the medicines in this study.
- Brand and generic substitution of medicines in Australia is being implemented primarily as intended. It is allowing choice, without leading to multiple brand substitutions for the majority of patients.

Data for a 5-year period were available for this study; however, the median length of follow-up was less than 16 months. This level of medication persistence reflects what occurs in practice and is comparable to that seen in other studies.[16 19] It is possible that patients using the medicines in this study switched to other treatments or re-initiated therapy following cessation; however, this was not considered for this study.

Although the analysis was limited to DVA treatment card holders, the medicines studied are equally available on the PBS and the co-payments paid by DVA card holders are the same as PBS concession card holders. A comparison of the DVA population with the wider Australian population has shown that DVA card holders have slightly more GP visits (rate ratio 1.17) and hospitalisations (rate ratio 1.21) per year than other Australians. Despite this, DVA card holders receive only slightly more government subsidised prescriptions (rate ratio 1.13).[20] For this reason, the results are likely to be applicable to other Australians. There is no evidence to suggest that pharmacists are more or less likely to substitute products for DVA card holders than other Australians.

CONCLUSION

Implementation of the minimum pricing policy and brand substitution was intended to give patients a price signal and encourage the use of generics,[3] it was not intended to facilitate multiple switches per patient. For the drugs included in this study, the brand substitution policy appears to be having its intended effect for over 80% of patients that is, allowing choice without facilitating multiple switches. Despite this, some patients have multiple switches and results of this

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study suggested that continuity of care between different pharmacies and different prescribers may play a role.

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REFERENCES

1. Industry Commission. *The Pharmaceutical Industry*, Vol. 1. The Report. Australian Government Publishing Service: Melbourne, 1996; Report No.: 51.
2. Australian Government Department of Health and Ageing. *Schedule of Pharmaceutical Benefits for Approved Pharmacists and Medical Practitioners*. Effective from 1 April 2006. National Capital Printing: Canberra, 2006.
3. McManus P, Birkett D, Dudley J, Stevens A. Impact of the minimum pricing policy and introduction of brand (generic) substitution into the Pharmaceutical Benefits Scheme in Aus tralia. *Pharmacoepidemiol Drug Saf* 2001; **10**: 295 300.
4. Pharmaceutical Health and Rational Use of Medicines (PHARM) Consumer Sub Committee. *Consumer perspectives on managing multiple medicines*. PHARM: Canberra, 2001.
5. Australian Divisions of General Practice Ltd. GPs call for "one switch per script", 2003. Available from http://www.adgp. com.au/client images/5024.pdf [Accessed 25th October 2004].
6. Cain C. Think twice before accepting substitute drugs. *The Advertiser*, 29 December 2006; Section: Opinion. p. 20.
7. Anonymous. Complaints and investigations. Pharmacy Board of South Australia Newsletter. 2004 August.
8. Deakin G, Aufgang M. Controversies in medicine: wrestling with brand choices. *Aust Doctor* 2002; September 13: 42 43.
9. Brooker C. No simple messages on generic substitution. *Pharm News* 2003; August 21:8.
10. Sorensen L, Stokes J, Purdie D, Woodward M, Roberts M. Medication management at home: medication related risk factors associated with poor health outcomes. *Age Ageing* 2005; **34**: 626 632.
11. Peterson G, Naunton M. Simple measures to assist with drug therapy can produce large benefits for elderly patients. *Aust Pharmacist* 2002; **21**(5): 370 373.
12. Department of Veterans' Affairs. DVA treatment population statistics, December 2006. Department of Veterans' Affairs: Canberra, 2006. Available from http://www.dva.gov.au/media/ publicat/Statistics/docs/TpopDec06.pdf [Accessed 29 March 2007].
13. Australian Government Department of Health and Ageing. Pharmaceutical Benefits Pricing Authority Annual Report for the year ended 30 June 2005. Available from http:// www.health.gov.au/internet/wcms/publishing.nsf/Content/ 350C5B2F2D00D2C2CA2570D7001CD22A/$File/04 05% 20PBPA%20Annual%20Report.pdf [Accessed 3rd April 2006].
14. Ferguson H. GP calls for restrictions on generic substitution. Australian Doctor 2006; February 15. Available from: http://www.australiandoctor.com.au/articles/49/0c03ce49.asp. [Accessed 20th February 2008]
15. Australian Pharmaceutical Advisory Council. *Guiding prin ciples to achieve continuity in medication management*. Australian Pharmaceutical Advisory Council: Canberra, 2005.
16. Dailey G, Kim M, Lian J. Patient compliance and persistence with antihyperglycemic drug regimens: evaluation of a Medi caid patient population with type 2 diabetes mellitus. *Clin Ther* 2001; **23**(8): 1311 1320.
17. van Soest E, Siersema P, Dieleman J, Sturkenboom M, Kuipers E. Persistence and adherence to proton pump inhibitors in daily clinical practice. *Aliment Pharmacol Ther* 2006; **24**: 377 385.
18. McManus P, Mant A, Mitchell P, Dudley J. Length of therapy with selective serotonin reuptake inhibitors and tricyclic anti depressants in Australia. *Aust N Z J Psychiatry* 2004; **38**: 450 454.
19. Bourgault C, Senecal M, Brisson M, Marentette M, Gregoire JP. Persistence and discontinuation patterns of antihypertensive therapy among newly treated patients: a population based study. *J Hum Hypertens* 2005; **19**(8): 607 613.
20. Australian Institute of Health and Welfare (AIHW). *Health care usage and costs. A comparison of veterans and war widows and widowers with the rest of the community*. Cat. no. PHE 42. AIHW: Canberra, 2002.

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Pharmaceutical brand substitution in Australia – are there multiple switches per prescription?

Abstract

Background: In Australia, brand substitution by pharmacists has been possible since 1994. There is no limit to the number of substitutions per prescription. Doctors have expressed concern that patients may receive a different product each time their prescription repeats are dispensed, which has the potential to confuse patients. It is unknown how often multiple substitutions per prescription occur.

Objectives: We aimed to identify the number of switches per prescription for a range of medicines and to determine the number of different brand and generic products supplied on each prescription.

Methods: Repatriation Pharmaceutical Benefits Scheme prescription claims between 1 January 2001 and 28 February 2006 were identified for atenolol, citalopram, enalapril, metformin, omeprazole, ramipril, and simvastatin. Original prescriptions with five repeats and all supplies dispensed were included. Switches were identified if a different product was supplied on consecutive repeat dispensings.

Results: 533,279 original prescriptions were included. 488,735 (92%) had no switches on repeats and 37,513 (7%) had only one switch. Only 1% of all prescriptions had more than one switch identified on repeats, and in most cases only two different products were supplied. None of the prescriptions had a different product supplied on each dispensing.

Conclusion and Implications: Multiple switches per prescription are uncommon and multiple different products are rarely supplied on repeats of the same prescription. The rules of the brand substitution policy appear to be adequate in allowing brand choice for patients, without leading to multiple switches per prescription.

Key words: Generic substitution; generic drugs, pharmaceutical policy; pharmaco-epidemiology.

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Quality Use of Medicines and Pharmacy Research Centre, Sansom Institute, School of Pharmacy and Medical Sciences, University of South Australia

In Australia, brand substitution of Pharmaceutical Benefits Scheme (PBS) and Repatriation Pharmaceutical Benefits Scheme (RPBS) medicines has been possible since December 1994, when the brand substitution policy was introduced. Pharmacists can dispense a brand or generic product other than the one prescribed provided the patient agrees to the switch, the substituted products are bioequivalent and the prescriber has not specified that substitution cannot occur. At present, the policy does not limit the number of substitutions that can occur on repeats of an individual prescription. In 2003, the Australian Divisions of General Practice highlighted this and expressed concerns about the potential for patients to receive a different brand of medicine each time their prescription was dispensed, equating to six different brands over the life of a script.[1] They suggested that a limit of one switch per prescription should be enforced.[1] Their concerns about multiple substitutions per prescription arose from the different names and appearance of the various brand and generic alternatives available.

Generic drugs in Australia are marketed under a unique trade name rather than the generic name of the drug. For drugs with multiple brand and generic products, patients are faced with multiple different trade names, and in many cases the product appearance also differs. Qualitative Australian research has found that patients may become confused when products are substituted.[2,3] Between 1998 and 2000, the Pharmaceutical Health and Rational Use of Medicines (PHARM) committee held discussions with representatives from more than 100 consumer groups for a range of chronic conditions, including patients from non-English-speaking backgrounds. It found that patients may not realise that substituted brand and generic products are actually the same drug and problems such as double dosing (i.e. taking both products at the same time) or poor compliance may result.[2] Concerns about multiple switches per prescription and the potential for patient confusion are also held by general practitioners.[3,4] Hassali and colleagues interviewed a convenience sample of 10 Australian general practitioners (GPs) about their views of generic medicines.[3] Some GPs in their sample expressed concerns about the potential for patient confusion when substitution occurred, and some were also critical of the brand substitution policy not preventing multiple switches by pharmacists.[3] In another Australian study 70 GPs were surveyed.[4] Many of the GPs expressed concerns that generic substitution had the potential to confuse patients and some suggested that there should be limits to the number and frequency of brand substitutions.[4] The small sample sizes of these studies limit the generalisability of results; however, there appears to be a perception among Australian prescribers and consumers that brand substitution can cause confusion. The actual extent of the problem is unknown.

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Submitted: April 2007 **Accepted:** June 2007

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of Australia (PSA) has had brand substitution guidelines for pharmacists.[5] These guidelines state that the health and safety of the patient should be the foremost concern when substitution occurs, and that whenever possible the same product should be supplied to patients on chronic therapy.[5] The extent to which pharmacists follow these guidelines is unknown. A survey of 312 pharmacists conducted by the PSA in mid-2006 found that 94% of respondents regularly offered brand substitution to their patients, and more than 70% of respondents reported that less than 20% of prescriptions they dispensed had substitution prohibited by the doctor.[6] Opportunities for patients to be switched are great; however, the extent to which this translates into multiple switches per prescription and multiple different products being supplied is unknown.

Aims

We aimed to identify the number of switches on the repeats of an individual prescription and to determine how often there were multiple switches and multiple products supplied on the same prescription.

Methods

Study drugs

Atenolol, citalopram, enalapril, metformin, omeprazole, ramipril, and simvastatin were selected for study (see Table 1). These drugs were chosen as they are all commonly dispensed on the PBS and RPBS,[7] cover a range of therapeutic classes, and are generally used in the treatment of long-term conditions. All study drugs have bioequivalent brand and generic alternatives available. Strengths and formulations studied are listed in Table 1.

RPBS prescription claims for all study drugs were identified. The first citalopram generic became available on 1 August 2001, and the first simvastatin generic became available on 1 November 2004. For these two drugs, claims were included from the date the first generic became available until the end of February 2006. For all other study drugs, claims identified between 1 January 2001 and 28 February 2006 were included. Each claim record includes a patient identifier, date of prescription, a prescriber identifier, the number of repeats on the prescription, whether the original prescription or a repeat was dispensed, the manufacturer code and the date of supply. Doctors can write PBS prescriptions for each of the study drugs valid for up to six supplies (the original dispensing, plus a maximum of five repeat dispensings); and can only write one PBS or RPBS prescription for each strength of study drug per patient per day.[8] Following these rules, we determined that when the claim record showed the same patient identifier, prescriber identifier, date of prescribing and was for the same strength of drug, repeats of the same prescription had been used at those dispensings. Individual prescriptions were identified and original and repeat dispensings were sorted by date of supply. The total number of dispensings per prescription was calculated.

Inclusion and exclusion criteria

Original prescriptions written for five repeats with all six supplies dispensed within the study period were included.

Data errors were identified if there was more than one claim for an original prescription written by the same doctor on the same day for any patient, or if there were more claims identified for a prescription than allowed by the number of repeats ordered. This led to 16,175 dispensings being excluded (0.3% of identified dispensings).

The manufacturer code in each claim record was used to identify the brand or generic product dispensed. We assumed that the original dispensing was for the brand or generic product

Table 1: Study drugs.

Study drug	Strengths and forms studied	Number of brand/ generic products	Therapeutic category and uses
Atenolol	50 mg tablets	10[a]	Beta blocking agent used in the treatment of cardiovascular conditions including hypertension
Citalopram	20 mg tablets	7	SSRI antidepressant
Enalapril	5 mg, 10 mg and 20 mg tablets	11[a]	Angiotensin converting enzyme inhibitor used in the treatment of cardiovascular conditions including hypertension
Metformin	500 mg and 850 mg tablets	10[a]	Biguanide oral hypoglycaemic agent, used in the treatment of type 2 diabetes
Omeprazole	20 mg tablets	2 (3 from Dec 2004 onwards)	Proton pump inhibitor used in the treatment of acid-related gastrointestinal disorders such as gastroesophageal reflux disease and peptic ulcer disease.
Ramipril	1.25 mg, 2.5 mg and 5 mg tablets	2	Angiotensin converting enzyme inhibitor used in the treatment of cardiovascular conditions including hypertension
Simvastatin	5 mg, 10 mg, 20 mg, 40 mg and 80 mg tablets	4 until August 2005, then 10	HMG CoA-reductase inhibitor used to lower cholesterol

Note:
(a) Single brand and generic products were added or deleted at certain times over the study period. Therefore, the number of products available for the majority of the study period has been shown.

prescribed; switches were then identified if different brand or generic products were supplied on consecutive repeat dispensings of the same prescription. When the manufacturer code was not recorded for a given dispensing (3% of claims), we assumed that it was the same as the previous supply. We calculated the number of switches per prescription and the number of different brand or generic products dispensed over the life of the prescription. Using this method, we could identify a maximum of five switches per prescription and six different products supplied over the life of the prescription.

Results

Overall, 533,279 original prescriptions with five repeats prescribed and all supplies dispensed were identified and included in the study.

Number of switches per prescription

Ninety-two per cent of prescriptions studied had no switches (see Figure 1). When switches were identified on repeats of the same prescription, in the majority of cases there was only one switch per prescription (7% of all prescriptions). Only 1% of all prescriptions identified had more than one switch.

Prescriptions with multiple switches

Ramipril and omeprazole, the drugs with the fewest brand and generic products, had the lowest proportions of prescriptions with more than one switch (0.7%), while citalopram had the highest (3%). Only 1% (n=7,031) of the 533,279 prescriptions studied had more than one switch, and the majority of these (n=5,822) had two switches. Only 0.2% (1,026) of all prescriptions had three switches and 0.03% (161) had four switches. Of the 533,279 prescriptions studied, only 22 had a switch on every repeat dispensing (i.e. five switches per prescription).

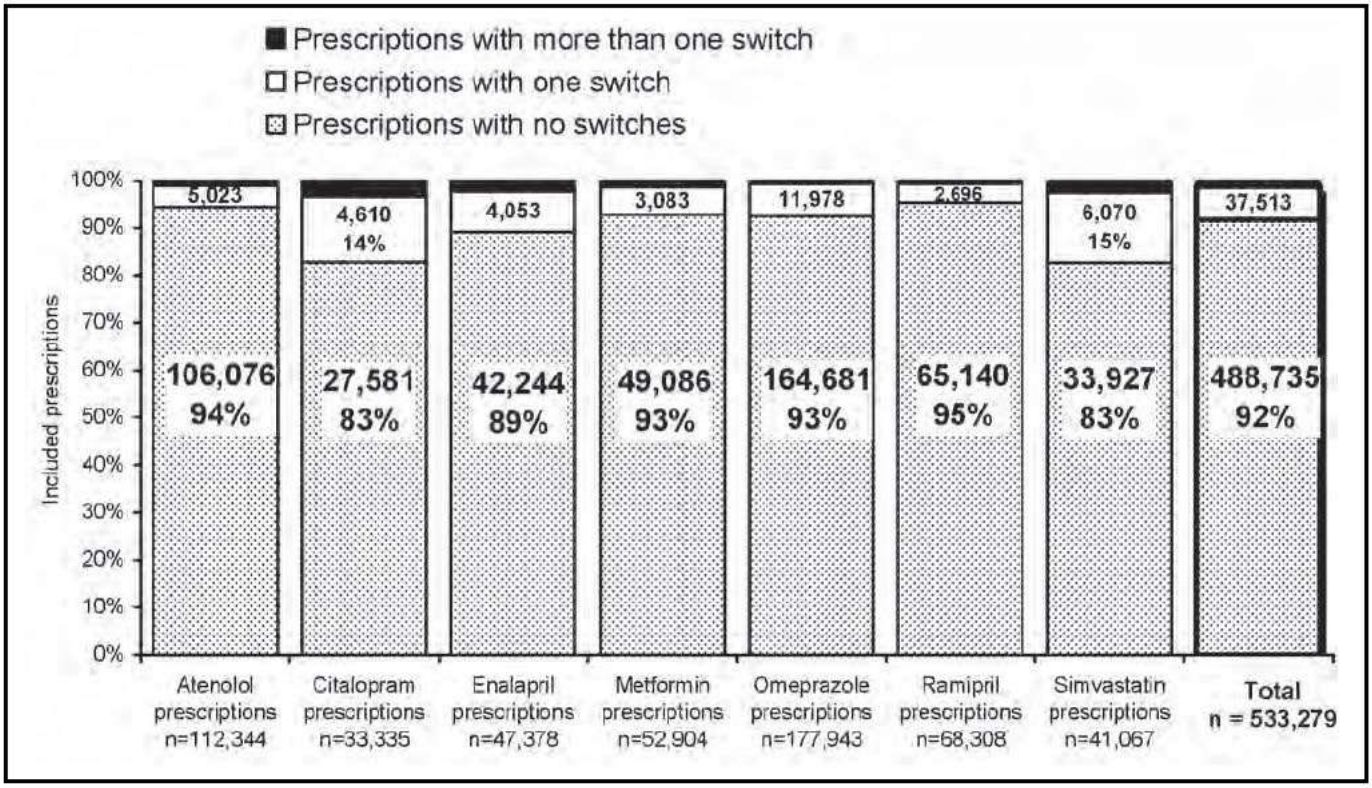
Number of different products supplied per prescription

Our definition of switching means that prescriptions with no switches had the same product supplied on each repeat, and prescriptions with one switch had two different products supplied over the life of the prescription. In most cases, prescriptions with more than one switch also had only two different products dispensed over the life of the prescription (see Table 2). None of the prescriptions included in the study had a different product supplied with each dispensing.

Discussion

To our knowledge, this is the first study that has identified the number of brand substitutions that occur on repeats of the same prescription for any drug. The results show that multiple switches per prescription are uncommon. For 92% of prescriptions studied, the same product was supplied on each dispensing. If switches occurred, there was only one switch per prescription in the majority of cases (7% of prescriptions). Similarly, multiple products were rarely supplied over the life of a prescription, even if there were multiple switches on that prescription. None of the prescriptions studied had a different product supplied on each dispensing.

Figure 1: Prescriptions with and without switches.



Pharmacists appear to consistently supply the same product over the life of most prescriptions, which is in accordance with the PSA guidelines for brand substitution.

The rules of the brand substitution policy do not limit the number of switches per prescription, which led the Australian Divisions of General Practice (now known as the Australian General Practice Network) to express concerns that patients may receive a different product each time their prescription repeats are filled.[1] These concerns have been reflected by consumers[2] and general practitioners[3,4] in qualitative Australian research. Research conducted with consumers using multiple medicines found that confusion from brand substitution may lead to poor compliance or 'double dosing' with two different brands of the same medicine.[2] Our study is the first to quantitatively assess the number of products supplied on repeats of the same prescription. The results show that although the rules of the brand substitution policy do not prevent pharmacists from dispensing a different product on each repeat, this does not occur frequently.

Given the likely inconvenience that a limit of one switch per prescription would incur, and the fact that pharmacists already supply the same product on repeats of prescriptions in most cases, it does not appear necessary to change the rules of the brand substitution policy. A limit of one switch per prescription may be impractical for pharmacists and patients.[9,10] Patients may have their repeats dispensed at more than one pharmacy. If there was a limit of one switch per prescription, pharmacies may need to stock every alternative in order to be able to dispense repeats in these situations.[9] The number of brand and generic alternatives available for some drugs means that stocking all of them is impractical for most pharmacies.[9,10] In addition, if a particular product is out of stock, a limit of one switch per prescription may mean that some patients cannot have their repeats dispensed if their product is out of stock.[10]

We differentiated between the number of switches per prescription and the total number of different products supplied per prescription because the study drugs had different numbers of products available to switch between. Only two ramipril products were available, however a patient could potentially alternate between each product with each repeat dispensing. Although the drugs with the fewest products available (ramipril and omeprazole) had the lowest proportion of prescriptions with multiple switches (0.7%), drugs with multiple products available also had a very small proportion of prescriptions with multiple switches. Only 3% of citalopram prescriptions, 2% of enalapril and simvastatin prescriptions and 1% of atenolol and metformin prescriptions had more than one switch, and in most cases only two different products were supplied over the life of the script. These five drugs all had seven or more products available to switch between for the majority of the study period.

Brand substitution is possible for many other PBS and RPBS medicines in addition to the seven study drugs. The study drugs were chosen because they represent a wide range of therapeutic classes on the PBS and are commonly dispensed on the RPBS. The number of brand and generic products available to switch between and the length of time multiple products have been available varied among the drugs. Despite these differences, in all cases the majority of prescriptions identified for each drug had no switches, and when switches were identified in most cases there was only one switch per prescription. Simvastatin and citalopram had the lowest proportions of prescriptions with no switches than the other medicines studied (83%). In the case of simvastatin, this difference may have been because brand substitution had only recently become possible. Patient-related factors may also have played a role.

We could not tell how many prescriptions were marked "brand substitution not permitted", so we cannot be sure of how often switching was not possible and the influence that this had on the results. However, recent research suggests that substitution is possible for most prescriptions. A survey of Australian doctors found that the majority of prescribers marked less than a quarter of their prescriptions "brand substitution not permitted",[11] and a survey of pharmacists supported this finding.[12]

RPBS claims were studied, therefore only prescriptions dispensed to Department of Veterans' Affairs (DVA) card holders were represented in the analysis. There is no evidence to suggest that pharmacists are more or less likely to substitute brand and generic products for DVA card holders than other patients. The medicines studied are available on both the PBS and RPBS, and

Table 2: Number of products dispensed on prescriptions with multiple switches.

Study drug	Prescriptions with > one switch	Number of different brand or generic products supplied				
		2 products	3 products	4 products	5 products	6 products
Atenolol	1,245	911	323	11	0	0
Citalopram	1,144	682	436	23	3	0
Enalapril	1,081	677	375	26	3	0
Metformin	735	547	184	3	1	0
Omeprazole[a]	1,284	1,231	53	–	–	–
Ramipril[a]	472	472	–	–	–	–
Simvastatin	1,070	631	430	9	0	0
Total	7,031	5,151	1,801	72	7	0

Note:
(a) Only two ramipril products and three omeprazole products were available for substitution.

the subsidised quantities and prices paid by PBS concession card holders are the same as those for DVA card holders. It is likely that the results are equally applicable to other members of the Australian population.

Results of this study indicate that pharmacists consistently supply the same product on each repeat of a prescription in the majority of cases. When switches occur, there is nearly always only one switch per script. Multiple switches per prescription are uncommon and multiple different products are rarely supplied on repeats of the same prescription. The present rules of the brand substitution policy appear to be adequate in allowing brand choice for patients, without leading to multiple switches per prescription.

Acknowledgements

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References

1. Australian General Practice Network [home page on the Internet]. Canberra (AUST): Australian Divisions of General Practice Ltd; 2003 [cited 2004 Oct 25]. *GPs Call for "One Switch per Script*". Available from: http://www.adgp.com.au/client_images/5024.pdf
2. Pharmaceutical Health and Rational Use of Medicines. *Consumer Perspectives on Managing Multiple Medicines*. Canberra (AUST): Consumer Sub-Committee, PHARM; 2001.
3. Hassali M, Kong D, Stewart K. Generic medicines: Perceptions of general practitioners in Melbourne, Australia. *Journal of Generic Medicines*. 2006;3(3):214-25.
4. Sweet G, Wilson S. *The 3D Labels Project*. Melbourne (AUST): Dandenong District Divisions of General Practice, Pharmacy Guild of Australia; 2004.
5. Pharmaceutical Society of Australia. Guidelines for Pharmacists on PBS Brand Substitution. *Australian Pharmacist*. 2004;23(9):668.
6. AMA wrong on brand substitution. *Australian Pharmacist*. 2006;25(7):506.
7. Department of Health and Ageing [publications page on the Internet]. Canberra (AUST): Commonwealth of Australia; 2005 [cited 2006 Apr 3]. *Pharmaceutical Benefits Pricing Authority Annual Report for the Year Ended 30 June 2005*. Available from: http://www.health.gov.au/internet/wcms/publishing.nsf/Content/350C5B2F2D00D2C2CA2570D7001CD22A/$File/04-05%20PBPA%20Annual%20Report.pdf
8. Department of Health and Ageing. *Schedule of Pharmaceutical Benefits for Approved Pharmacists and Medical Practitioners*. Effective from 1 April 2006. Canberra (AUST): Commonwealth of Australia; 2006.
9. Hall A. Proposed generic restriction not practical. *Australian Pharmacist*. 2003;22(2):110.
10. Drug switch confusion debated. *Australian Journal of Pharmacy*. 2003;84:76.
11. Australian Medical Association [publication page on the Internet]. Canberrra (AUST): Federal Secretariat, AMA; 2006 [cited 2006 May 23]. *AMA Brand Substitution Survey.* Available from: http://www.ama.com.au/web.nsf/doc/WEEN-6PX29R/$file/Brand_substitution_survey_results_May_2006.pdf
12. Hall A. The Facts on Brand Substitution. AMA Wrong on Brand Substitution [media release page on the Internet]. Canberra (AUST): Pharmaceutical Society of Australia; 2006 June 1 [cited 2007 July 13]. Available from: http://www.psa.org.au/site.php?id=1054.

Do Pharmacists Adhere to Brand Substitution Guidelines? The Example of Simvastatin

Lisa M Kalisch, Elizabeth E Roughead, Andrew L Gilbert

ABSTRACT

Background: Although pharmacists have been criticised for not following brand substitution guidelines, evidence is lacking. Brand substitution of simvastatin has been possible since November 2004 when the first generic became available; prior to this 2 non-substitutable products were available.

Aim: To identify the rate of switching between brand and generic products of simvastatin.

Method: Analyses were conducted using Repatriation Pharmaceutical Benefits Scheme prescription claims data from 1 November 2002 to 28 February 2006. Switches were identified if different brand or generic products were dispensed consecutively. The change in the rate of switching post-generics was compared to the pre-generics baseline.

Results: Following introduction of generics the switching rate increased to 78.2 switches per 1000 dispensings. Switching was 22 times more likely post-generics compared to pre-generics (rate ratio 21.91 (20.01, 24.00), $p < 0.001$). The rate of switching did not change when 10 products were available for substitution compared to when there were only 4 (RR 1.02 (0.998, 1.041); $p = 0.0664$). Post-generics, 64% of switches occurred when different prescriptions were dispensed consecutively.

Conclusion: Switching between simvastatin products was low prior to generic availability, even though 2 products were available. The switching rate increased when bioequivalent products were available, suggesting that pharmacists practice in accordance with brand substitution legislation. Consumers were most vulnerable to switching when different prescriptions were dispensed consecutively. Pharmacists should be aware of this and take steps to ensure that switches do not occur unnecessarily.

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INTRODUCTION

The Pharmaceutical Benefits Scheme (PBS) and the Repatriation PBS (RPBS) are the government subsidised schemes for supply of medicines in Australia. The RPBS is an expanded version of the PBS list of medicines, which better meets the needs of war veterans and their partners. Patients contribute a co-payment towards the cost of PBS and RPBS medicines and the remainder is subsidised by the government.[1] Since the introduction of the minimum pricing policy in 1990, only the cheapest products of each PBS and RPBS medicine are available to patients at the co-payment price. Patients using more expensive brands pay the price difference between the cheapest and more expensive product in addition to the patient co-payment, in the form of a brand premium. A brand substitution policy was introduced in December 1994, which allows substitution of designated PBS and RPBS products at the time of dispensing and enables patients to avoid paying the brand premium. Brand substitution of PBS and RPBS medicines can occur if patients agree to the product change, if the substituted products are bioequivalent (as indicated by the PBS/RPBS designation) and if the prescriber has not precluded brand substitution from occurring.[1]

The introduction of generic simvastatin products to the Australian market provides a unique opportunity to study brand substitution because, within a short period of time, multiple bioequivalent products were available for substitution. In addition, because two non-substitutable products were originally available it provides an opportunity to examine the extent to which pharmacists follow brand substitution guidelines. A high rate of substitution prior to generic availability would suggest non-adherence by pharmacists to the brand substitution policy, because the products had not been designated bioequivalent.

The Pharmaceutical Society of Australia's brand substitution guidelines for pharmacists, state that the health and safety of patients should be the foremost concern when substitution occurs, and that whenever possible the same product should be supplied to patients on chronic therapy.[2] Anecdotal reports suggest that some prescribers are concerned that pharmacists do not always follow these guidelines or adhere to the rules of the brand substitution policy.[3-7] In 2003, the Australian Divisions of General Practice expressed concern that pharmacists may substitute products multiple times for a patient, which has the potential to confuse patients.[3] A survey of 386 prescribers, conducted by the Australian Medical Association in 2006, found that 75% of respondents thought that some pharmacists substituted brand or generic products even when the prescription was marked 'brand substitution not permitted'.[4] Anecdotal reports have also highlighted concerns among prescribers that some pharmacies may frequently change the generic products that they stock, therefore, patients may receive a different generic product each time the stocked generic product changes.[5-7]

Although brand substitution of PBS and RPBS medicines has been possible for over 10 years, little is known about the extent of brand substitution when new generics are listed for a medicine. The extent to which pharmacists adhere to brand substitution guidelines is also unknown.

This study aimed to identify the rate of switching between brand and generic products of simvastatin. Prior to November 2004 two brand products were available; bioequivalence had not been reported, so brand substitution should not have occurred.[8] Patients could only receive different products at consecutive dispensings if the pharmacy did not have the prescribed brand in stock or if the patient had more than one prescription with different brands prescribed. The first simvastatin generic was PBS listed on 1 November 2004 and at that time bioequivalence was shown for the new generic and the two original brands, so brand substitution was possible. A second generic was PBS listed in April 2005, and by the end of August 2005 ten bioequivalent products were available.

METHOD

The study was conducted using prescription claims data from the RPBS. The pharmacy claims database, maintained by the Department of Veterans' Affairs (DVA), includes records for all medicines dispensed to veterans subsidised under the RPBS.

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Seventy five million prescription records are stored within the pharmacy dataset. A client file is also maintained by the DVA, which includes patient age and gender. We identified all pharmacy claims for simvastatin dispensed between 1 November 2002 and 28 February 2006. Each claim record includes a patient identifier, the date of supply, strength of simvastatin dispensed, manufacturer code (indicating the brand or generic product supplied), prescriber identifier, date of prescription, dispensing pharmacy identifier and whether an original or a repeat prescription was dispensed.

Switches were identified if a patient received different brand or generic products of the same strength of simvastatin at consecutive dispensings, no more than 60 days apart. The 60-day interval was calculated from the data and represents the 95th percentile for time between prescription refills. If the manufacturer code was not recorded for a claim we assumed that it was the same as the previous supply. Of the 1.4 million claims identified for this study, the manufacturer code was missing for only 4%.

For switches identified after 1 November 2004 we determined whether the same or a different prescription was used at consecutive dispensings. The prescription was identified by the date of prescription and the prescriber identifier. Doctors can write PBS prescriptions for simvastatin valid for up to six supplies (original prescription plus a maximum of five repeat dispensings); and can only write one original prescription for each simvastatin strength per patient per day.[8] Therefore, we considered that a patient had repeats of the same prescription dispensed consecutively if consecutive claims showed the same prescriber identifier and date of prescribing, and were for the same strength of simvastatin.

The rate for the supply of different products (switching) at consecutive dispensings was calculated per 1000 prescriptions dispensed each month. The rates pre- and post-generic availability were compared using negative binomial regression analysis.

Patients were categorised as non-switchers, those with only one or two switches and those with three or more switches post-generics ('multiple switchers') for subgroup analyses. Differences in the number of simvastatin prescribers, dispensing pharmacies, dispensings and number of prescriptions used were compared between groups using Poisson regression. All data were analysed using SAS version 9.1 (SAS Institute).

RESULTS

Between 1 November 2004 and 28 February 2006, 48 177 patients received simvastatin. Fifty-six per cent (n 27 142) were male and patients received an average of 11.5 ± 5.4 dispensings. There were 39 786 switches identified post-generics. For 64% of these switches (n 25 311), different prescriptions were dispensed consecutively.

Prior to generic availability, different products were supplied consecutively for 3.6 out of every 1000 prescriptions dispensed. When the first simvastatin generic was introduced in November 2004 the rate of switching increased; to an average rate of 78.2 switches per 1000 prescriptions dispensed from February 2005 to February 2006 (Figure 1). Switches were 22 times more likely to occur post-generics than pre-generics (rate ratio 21.91; 95%CI 20.01 24.00; p < 0.001).

From February to July 2005 when four simvastatin products were available, the rate of switching was 79.0 switches per 1000 prescriptions dispensed. From August 2005 onwards, when 10 simvastatin products were available, the rate of switching was no higher; 77.5 switches per 1000 prescriptions dispensed (RR 1.02; 95%CI 0.998 1.041; p 0.0664).

Table 1. Comparison of multiple switchers and non-switchers

	Multiple switchers (n = 4205)	Non-switchers (n = 25 633)	Rate ratio (95%CI)*
Prescribers	1.93 ±1.07	1.37 ±0.63	1.41 (1.38 1.45)
Dispensing pharmacies	2 56 ±1.61	1.44 ±0.88	1.77 (1.73 1.81)
Original prescriptions	4.54 ±1.65	2.84 ±1.46	1.60 (1.58 1.63)
Dispensings	15.17 ±3.09	9.48 ±5.84	1.60 (1.59 1.61)

*p < 0.0001 for all comparisons

Table 2. Comparison of multiple switchers and patients with one or two switches

	Multiple switchers (n = 4205)	Patients with 1 or 2 switches (n = 18 339)	Rate ratio (95% CI)*
Prescribers	1.93 ±1.07	1.61 ±0.80	1.20 (1.17 1.23)
Dispensing pharmacies	2.56 ±1.61	1.69 ±1.04	1.51 (1.48 1.54)
Original prescriptions	4.54 ±1.65	3.74 ±1.24	1.22 (1.20 1.24)
Dispensings	15.17 ±3.09	13.50 ±3.81	1.12 (1.11 1.13)

*p < 0.0001 for all comparisons

Fifty-three per cent of patients who received simvastatin post-generic availability did not switch products. Thirty-eight per cent of patients had only one or two substitutions, while 9% were multiple switchers. Multiple switchers were likely to have more prescribers, more dispensing pharmacies, more original prescriptions and more simvastatin dispensings than non-switchers and patients who had only one or two switches (Tables 1,2).

DISCUSSION

Results of this study suggest that, in the case of simvastatin, the brand substitution policy is being implemented primarily as intended. Switching was 22 times more likely to occur post-generic availability compared to pre-generics; however, the increase was largely due to patients switching once to a new generic product, rather than patients being switched multiple times. In the 16-month study period, 91% of patients switched twice or less. These results add to previous research where it was shown that in a three-month period after introduction of brand premiums to ranitidine and fluoxetine, 8% and 39% of patients, respectively, switched to cheaper products.[9] Our results demonstrate that substitution is sustained for longer periods after generics are introduced. The size of the premium influenced switching in the earlier study the ranitidine brand premium was only 71c compared to $5.06 for fluoxetine.[9] In the present study, a brand premium comparable to that for ranitidine applied to simvastatin (70c), and over 16 months of follow-up 47% of simvastatin patients had products substituted.

One of the rules governing brand substitution states that products may only be substituted if they are bioequivalent.[1] The results of this study suggest that pharmacists adhere to this rule and rarely substitute products that have not been designated bioequivalent. Prior to introduction of the first simvastatin generic, different products were supplied at consecutive dispensings for only 3.6 out of every 1000 dispensings. A high switching rate pre-generic availability may have suggested that pharmacists substituted products which had not been shown to be bioequivalent. The low pre-generics switching rate suggests that substitution is likely to have occurred only in situations where it was permitted (e.g. when the patients usual

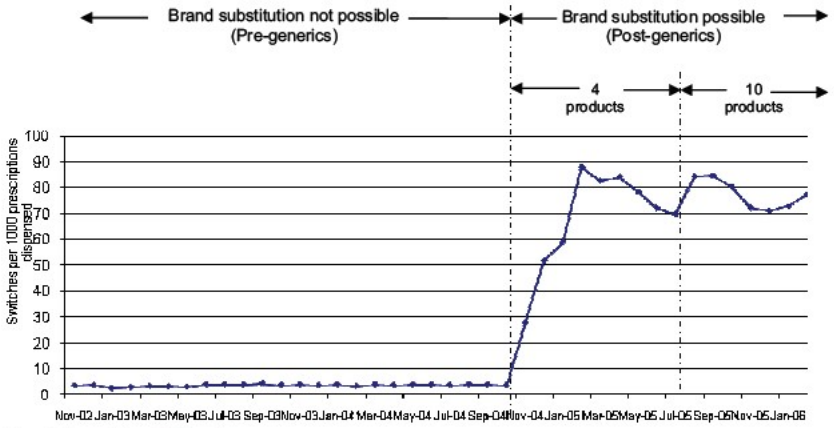

Figure 1. Simvastatin switching rate

product was out of stock), or when patients had more than one prescription written for different brands, dispensed consecutively. The change of legislation allowing brand substitution occurred in 1994 and more than 10 years later, pharmacists are still adhering to this legislation.

It has been suggested that some pharmacies frequently change the generic products that they stock, which has the potential to result in patients receiving a different generic each time the stocked generic product changes.[5-7] The large number of generic products available for some medicines has been suggested as a potential source for patient confusion if brand substitution occurs frequently.[5,7] In this study, the overall rate of switching was no different when ten simvastatin products were available for substitution compared to when only four products were available. Availability of multiple simvastatin products was not associated with increased switching.

A small proportion of patients (9%) were switched multiple times; multiple switchers had multiple prescribers and dispensing pharmacies, suggesting that continuity of care may be associated with multiple brand substitutions. Use of new prescriptions may also play a large role, as different prescriptions were dispensed at consecutive dispensings for the majority of switches identified (64%). A previous study showed that for 92% of prescriptions, pharmacists dispense the same product over the life of the prescription.[10] The product supplied to a patient at the previous dispensing may not be apparent if a different prescription form was used, or if the patient attended a different pharmacy. Pharmacists should be aware of this and take active steps to identify the brand or generic product usually used by a patient, so that multiple brand substitutions do not unnecessarily occur.

The research was conducted using data for DVA card holders. A comparison of the DVA population with the wider Australian population has shown that DVA card holders have only slightly more GP visits (RR 1.17; $p < 0.05$) and hospitalisations (RR 1.21; $p < 0.05$) per year than other Australians.[11] Elderly DVA card holders with no service related disability have a similar number of GP visits and hospitalisations per year compared to other elderly Australians.[11] The likelihood of receiving a prescription at a GP visit is similar for the DVA population and the wider Australian population; however, due to their slightly higher rate of GP visits, DVA card holders receive slightly more government subsidised prescriptions than other Australians (RR 1.13; $p < 0.05$).[11] Differences in health care usage between DVA card holders and the rest of the Australian population are small, and for this reason the results of this study are likely to be applicable to other Australians. In addition, there is no evidence to suggest that pharmacists are any more or less likely to substitute brand and generic products for DVA card holders than other patients.

In conclusion, product substitution increased following introduction of simvastatin generics; however, the increase was due to the large proportion of patients who substituted to a new generic product. The majority of patients did not have products substituted and only a small proportion of patients, 9%, had multiple brand substitutions. Pharmacists adhere to the brand substitution policy and rarely substitute products for which bioequivalence has not been demonstrated.

Acknowledgements
This research was conducted as part of the Veterans' MATES project, funded through the DVA and administered by the University of South Australia.

Competing interests: None declared

References

1. Australian Government Department of Health and Ageing. Schedule of pharmaceutical benefits for approved pharmacists and medical practitioners. Canberra: Commonwealth of Australia; 2007. Available from <www.pbs.gov.au/html/healthpro/publication/list>. Accessed 28 March 2007.
2. Pharmaceutical Society of Australia. Guidelines for pharmacists on PBS brand substitution. Aust Pharmacist 2004; 23: 668.
3. Australian Divisions of General Practice Ltd. GPs call for 'one switch per script'. 2003. Available from <www.adgp.com.au/client_images/5024.pdf>. Accessed 25 October 2004.
4. AMA Federal Secretariat. AMA brand substitution survey. 2006. Available from <www.ama.com.au/web.nsf/doc/WEEN-6PX29R/$file/Brand_substitution_survey_results_May_2006.pdf>. Accessed 23 May 2006.
5. Ferguson H. GP calls for restrictions on generic substitution. Aust Doc 2006; Feb 15.
6. Saunders C. Ticked box holds weight. Aust Doc 2000; Jan 14: 29-30.
7. Deakin G, Aufgang M. Controversies in medicine: wrestling with brand choices. Aust Doc 2002; Sept 13: 42-3.
8. Australian Government Department of Health and Ageing. Schedule of Pharmaceutical Benefits for Approved Pharmacists and Medical Practitioners. Canberra: Australian Government Publishing Service; 2004.
9. McManus P, Birkett D, Dudley J, Stevens A. Impact of the minimum pricing policy and introduction of brand (generic) substitution into the Pharmaceutical Benefits Scheme in Australia. Pharmacoepidemiol Drug Saf 2001; 10: 295-300.
10. Kalisch L, Roughead E, Gilbert A. Pharmaceutical brand substitution in Australia - are there multiple switches per prescription? Aust N Z J Public Health 2007; 31: 348-52.
11. Australian Institute of Health and Welfare. Health care usage and costs. A comparison of veterans and war widows and widowers with the rest of the community. Canberra: AIHW; 2002.

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DVA Human Research Ethics Committee

Minutes of the Meeting held on
Friday 28th April 2006
12th Floor Conference Room DVA National Office

s 22 - Out of scope

s 22 - Out of scope

4.3 Switching medicines in the veteran population and the impact on health outcomes and costs
s 47F , University of South Australia)

This study was considered at the April 2005 meeting and unconditionally endorsed.

The researcher is now seeking approval to add to the drug groups that were originally planned to study. The Committee unconditionally endorsed the changes in protocol.

s 22 - Out of scope

s 22 - Out of scope

s 22 - Out of scope

Australian Government
Department of Veterans' Affairs

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Switching medicines in the veteran population and the impact on health outcomes – change of protocol

Dear Ms s 47F

Thank you for submitting the above change in protocol for consideration by the DVA Human Research Ethics Committee. The Committee considered it at its meeting on 28 April 2006.

The Committee had no ethical or privacy concerns with the change and endorsed the new protocol.

I would like to remind you that, as part of its monitoring role, the Committee must be:

- advised, in writing and before implementation, should protocols change in the future.
- provided with progress reports and/or final reports.

The Committee looks forward to receiving your progress/final report in due course.

DVA HREC approval does not of itself guarantee access to the DVA information requested. Such access is a matter for the appropriate section of DVA, and the researcher remains responsible for negotiating directly with the section owning the data about the requirements for release.

If you would like to discuss this matter further, please contact Carol s 47F in the first instance on s 47F or via the Committee's e-mail address (ethics.committee@dva.gov.au).

The Department of Veterans' Affairs, in partnership with the Department of Health and Ageing, administers an Online Research Register accessible to the public containing veteran related research. We encourage you to share your research by entering your project details in the register once the project commences. The register can be accessed at www.aro.gov.au .

Yours sincerely

Deborah s 47C
Director
Research Support & Development

May 2006

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