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Exploring the association between stroke and acute myocardial infarction and statins adherence following a medicines co-payment increase

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Exploring the association between stroke and acute myocardial infarction and statins adherence following a medicines co-payment increase

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ABSTRACT

Objectives: Patient contributions (co-payments) for one months' supply of a publicly-subsidised medicine in Australia were increased by 21% in January 2005 (US\$2.73-\$3.31 for social security recipients and \$17.05-\$20.58 for others). This study investigates the relationship between patients' use of statin medication and hospitalisation for acute coronary syndrome and stroke, following this large increase in co-payments.

Methods: We designed a retrospective cohort study of all patients in Western Australia who were dispensed statin medication between 2004 and 05. Data for the cohort was obtained from State and Federal linked databases. We divided the cohort into those who discontinued, reduced or continued statin therapy in the first six months after the co-payment increase. The primary outcome was two-year hospitalisation for acute coronary syndrome or stroke-related event. Analysis was conducted using Fine and Gray competing risk methods, with death as the competing risk.

Results: There were 207,066 patients using statins prior to the co-payment increase. Following the increase, 12.5% of patients reduced their use of statin medication, 3.3% of patients discontinued therapy, and 84.2% continued therapy. There were 4343 acute coronary syndrome and stroke-related hospitalisations in the two-year follow-up period. Multivariate analysis demonstrated that discontinuing statins increased the risk of hospitalisation for acute coronary syndrome or stroke-related events by 18% (95%CI = 0.1%–40%) compared to continuing therapy. Subgroup analysis showed that men aged <70 years were at increased risk of 54–63% after discontinuing statins compared to those continuing, but that women and older men were not.

Conclusion: Discontinuing statin medication after a large increase patient cost contribution was associated with higher rates of acute coronary syndrome and stroke-related hospitalisation in men under 70 years. The findings highlight the importance of continued adherence to prescribed statin medication, and that discontinuing therapy for non-clinical reasons (such as cost) can possibly have negative consequences particularly for younger men.

Introduction

Affordability of medication is an issue faced worldwide by individuals, families and governments. Out-of-pocket spending on medical services can create barriers to healthcare access and utilisation,

including the use of medications.¹ In Australia, the Federal Government subsidizes the cost of a wide range of prescription medicines through the Pharmaceutical Benefits Scheme (PBS). Patients make a contribution (co-payment) toward the cost of each dispensed medicine and the remaining cost is paid by the Federal government through the PBS.

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Co-payments are lower for social security beneficiaries than the general community. Social Security beneficiaries in Australia are also known as concessional beneficiaries. Co-payments are increased each January at a rate equivalent to the consumer price index unit (CPIU) of approximately 3%, however in 2005 copayments were increased by 21% (from AU\$3.80–\$4.60 (US\$2.73–\$3.31) for social security beneficiaries and from AU\$23.70–\$28.60 (US\$17.05–\$20.58) for general beneficiaries)^{2,3}; the second largest copayment increase in the history of the PBS.

Previous research has demonstrated that rising prescription costs may be followed by a reduction in medication adherence for some people, even for essential medications, and this can result in poorer health outcomes.^{4–9} International research has also demonstrated that the reduction in medication adherence due to cost impacts on health service utilisation through increased hospitalisation and emergency department visits.^{10–15} Dispensing of statins (HMGCoA reductase inhibitors) – indicated for the primary and secondary prevention of cardiovascular disease (CVD) including coronary heart disease (CHD) and stroke^{16,17} was temporarily reduced following the 2005 consumer co-payment increase in Australia.^{8,9} This led to an immediate 5% reduction in statin dispensings after the co-payment increase. However, the monthly increases in quantity for statin medication remained unchanged demonstrating an immediate but not an ongoing impact of statin utilisation.⁸

In 2014–15, across Australia there were 1.1 million hospitalisations associated with CVD representing 11% of all hospitalisations nationally.¹⁸ However, the risk of hospitalisation due to a cardiovascular event is different for males and females, and across age groups.¹⁸

There is potential for a disruption in statin use, as a result of copayment increases making medicines less affordable, to adversely affect health, such as acute coronary syndrome (ACS) and stroke, which could result in additional hospitalisation.

The purpose of this study was to investigate the relationship between consumers who discontinued, reduced adherence or continued statin medications after the January 2005 PBS co-payment increase and ACS or stroke-related hospitalisations using whole-population linked data.

Methods

Data sources and ethical considerations

Individual-level data were obtained from both State and Federal databases. Data from the PBS (2002–2010) were linked to the Western Australia (WA) Hospital Morbidity Data Collection (HMDC) (2000–2010) and Mortality Register (2000–2010) by the WA Data Linkage Branch and the Australian Institute of Health and Welfare.¹⁹ The PBS dataset captures information about all claims for subsidised medicines dispensed at PBS-approved pharmacies and hospitals. Approval for this study was obtained from the ethics committees of the WA Department of Health, University of Western Australia and University of Notre Dame. A waiver of consent was granted by the approving ethics committees and de-identified data were provided to the research team in accordance with the principles of the Privacy Act, 1988 (Australian Government). The waiver of consent was granted as neither explicit consent nor an opt-out approach was appropriate as we were seeking whole-population linkage. Hence, the research participants do not know that their data were used in the research. The HMDC and mortality registry data custodian is the WA Department of Health, and the PBS data custodian is the Australian Department of Health.

Study design and cohort

We designed a retrospective cohort study using the WA whole-population linked datasets. WA has been shown to be representative of Australia's eight jurisdictions.²⁰

The cohort included all individuals who were established statin users as of December 31, 2004, before the co-payment increase of January

2005.

Statin users were identified in the PBS dataset using the Anatomical Therapeutic Chemical (ATC) codes (simvastatin C10AA01, pravastatin C10AA03, fluvastatin C10AA04, atorvastatin C10AA05, cerivastatin C10AA06, rosuvastatin C10AA07).²¹ Statin medications were chosen as it has previously been demonstrated that statin dispensings fell by 5% in the year following the January 2005 co-payment increase compared to the dispensing trend in the previous four years.⁸ Additionally, statins are an essential medication used for primary and secondary prevention of coronary heart disease and stroke events.^{22,23}

An established statin user was defined as an individual who had at least 60 days of statin medication supplied in the last three months of 2004 or 150 days of statin medication supplied in the last six months of 2004. Individuals were excluded from the study if they died prior to July 2005, were aged less than 18 years in 2004 or if they had an excess supply of medication in 2004. Excess supply was defined as a medication possession ratio (MPR) > 150% in 2004.²⁴ This was determined based on a review of the data and on Australian regulations that allow for up to six months supply of a medication at once in special circumstances.²⁵ Prior to mid-2012, medicines were not captured in the PBS dataset if they were priced below the co-payment. For social security beneficiaries, all statin medications were above the co-payment for the entire observation period, and hence records were complete in the PBS dataset for these individuals. However, for general beneficiaries, two low dose statin formulations (fluvastatin 20 mg and simvastatin 5 mg) were below the co-payment, and hence these medicines were not captured for general beneficiaries during the study period.²⁶ For social security beneficiaries, fluvastatin 20 mg and simvastatin 5 mg represented 0.7% of all statin dispensings in 2004.

Established statin users were categorised into three groups that either: continued, reduced adherence or discontinued statin medication use in 2005, after the co-payment increase. These groups were defined using the statin MPR adherence level for each individual in 2004 compared to the first six months of 2005. Continued use was defined as a change in statin MPR adherence of <20% or MPR ≥80% in the first six months of 2005. We defined the reduced group as those individuals with a 20% reduction in adherence pre- and post-the January 2005 co-payment increase. Previous research has defined non-adherence as an MPR of <80% (20% below optimum),²⁴ and we used this as the basis for defining a further meaningful reduction in MPR.

Based on clinical consultation, cessation of use was considered to have occurred if there was no dispensing of a statin medication in the first six months of 2005. Sensitivity analysis using a three-month overlap from 2004 identified if there was any under-estimation of the MPR in 2005 to account for standard end-of-year fluctuations in dispensing frequency due to the PBS safety-net rules. The safety-net rule is when the patient co-payment drops to zero dollars for social security beneficiaries, and to the social security level for general beneficiaries if they reached the safety-net annual expenditure threshold.²⁷ In 2004, the safety-net threshold for the combined family spending on medication was \$197.60 for social security beneficiaries and \$726.80 for general beneficiaries.² Once the threshold is reached, it has been shown historically that consumers stock pile medication whilst it is at the lower price or free until the end of the year when the threshold ends.²⁷ This results in a large increase in the number of dispensing compared to the start of the next year where consumers are using their excess supply from the prior year.²⁷

Replication of the creation of the statin user groups using 2003–2004 data, where there was no unusually large consumer co-payment increase, was undertaken in order to provide a baseline trend of the proportion of the population that may have discontinued or reduced medicine use as a result of the co-payment during normal years where copayment increased just in-line with inflation.

Outcomes

The follow-up for this study was the two-year period from July 2005 to June 2007. The primary outcome was time to first hospitalisation for ACS or stroke. ACS and stroke were identified in the principal diagnosis field of the HMDC data using the International Statistical Classification of Diseases and Related Health Problems, tenth revision, with Australian modifications (ICD-10-AM) codes I20.0 or I21 (for ACS) and I60–I61, I63, I64 (for stroke).²⁸ Codes were selected according to prescribing guidelines of statin use in at risk patients in Australia.²⁹

Statistical analyses

Continuous data were summarized with means ($\pm$ SD) and categorical data were summarized as percentages. Differences among the three statin groups were initially analysed by crude one-way ANOVA for continuous variables and chi-squared tests for categorical variables.

Since death is a competing risk for the primary outcome, univariate and multivariate Fine and Gray competing risk models were used to determine the subdistribution hazard ratios (sHR) between the three statin user groups.³⁰ All-cause death was selected as a competing risk to allow for everyone to have the opportunity for hospitalisation. Results are presented as sHR and 95% confidence intervals (CI). The characteristics were stratified by age (<60, 60–69, $\geq$ 70 years) sex, and history of previous statin usage (new user in 2004 and existing user in 2002/03). Proportional hazard assumptions were assessed graphically as well as a formal test (stptest) to ensure the cumulative incidence of the event over time was constant.

Variables of clinical relevance in the multivariate Fine and Gray models included: age, sex, socio-economic disadvantage (quintiles of Index of Relative Socio-Economic Disadvantage with 1 representing most disadvantage and 5 representing least disadvantage),³¹ residential remoteness (based on Accessibility and Remoteness Index Australia (ARIA) categorised as major cities, inner regional, outer regional, remote, very remote and unknown),³² beneficiary status (general or social security beneficiaries), Charlson Comorbidity Index (CCI), previous CHD (2000–2004; ICD-10-AM codes: I20–I25),²⁸ previous stroke (2000–2004; ICD-10-AM codes: I60–I61, I63–I64),²⁸ previous coronary artery revascularisation procedure (CARP) (2000–2004), current ACS (Jan–Jul 2005; principal diagnosis field ICD-10-AM codes I20.0, I21), current stroke (Jan–Jul 2005; principal diagnosis field ICD-10-AM codes I60–I61, I63–I64), current CARP (Jan–Jul 2005), diabetes medications (2004; ATC A10), cardiovascular medications (2004; ATC C01–C10 (except C10AA)), previous statin usage (2002–2003), number of medications in 2004, and statin MPR in 2004. Change in the number of unique medications dispensed in the last six months of 2004 compared to the first six months of 2005 was reported descriptively. Characteristics were calculated using the PBS dataset (based on the last 3 months of 2004) and the HMDC dataset.

Statistical significance was set at the two-sided 5% level. Analyses were completed using Stata SE version 15 (StataCorp., College station, Texas, USA)).

Results

Characteristics of the study cohort by statin group are shown in Table 1. Overall, there were 207,066 individuals identified as a current statin user at the end of December 2004. Reduction in adherence after the January 2005 co-payment increase was observed in 25,838 (12.5%) and cessation of statin therapy was observed in 6753 (3.3%). The three groups had significant differences in characteristics except for sex and taking diabetic medications in 2004. Compared to the continued group, patients who reduced adherence or discontinued statin therapy tended to be younger, general beneficiaries (i.e. paying a higher co-payment amount), took more medications, had less CHD or stroke history and had a shorter history of statin use. Additionally, those who discontinued

Table 1

Characteristics of the study cohort (n = 207,066) by type of statin use following co-payment increase.

Characteristic	Continued (n = 174,475, 84.2%)	Reduced adherence (n = 25,838, 12.5%)	Ceased (n = 6,753, 3.3%)	P value
Demographics				
Age (years)	65.9 $\pm$ 11.0	63.7 $\pm$ 12.0	62.9 $\pm$ 12.7	<0.01
Female	47.8	48.2	48.1	0.36
Socio-economic disadvantage:	10.6	11.3	11.4	<0.01
Most (1)	17.9	18.0	18.0	
2	24.9	24.2	22.7	
3	19.3	19.4	20.0	
4	25.8	25.5	26.3	
Least (5)	1.5	1.6	1.6	
Unknown				
Remoteness:				<0.01
Major cities	66.4	67.8	68.1	
Inner regional	19.6	18.0	17.1	
Outer regional	11.2	11.0	11.4	
Remote	2.2	2.3	2.5	
Very remote	0.5	0.7	0.9	
Unknown	0.1	0.1	0.1	
Beneficiary:	73.6	67.5	64.1	<0.01
Social security	26.4	32.5	35.9	
General				
Comorbidity history				
CCI (2000–2004):				
CCI average ($\pm$ SD)	0.42 (1.18)	0.43 (1.22)	0.44 (1.31)	<0.01
0	82.2	82.2	82.0	<0.01
1–2	12.0	12.0	12.1	
3–5	4.5	4.5	4.5	
6+	1.3	1.3	1.4	
Previous CHD or Stroke admission (2000–2004)	12.0	11.8	9.5	<0.01
Previous CARP (2000–2004)	5.1	4.8	3.3	<0.01
Current ACS (Jan–Jun 2005)	0.5	0.5	0.2	<0.01
Current Stroke (Jan–Jun 2005)	0.1	0.2	0.1	<0.01
Current CARP (Jan–Jun 2005)	0.3	0.3	0.1	<0.01
Medication history:				
Diabetes (2004)	16.0	16.4	16.6	0.12
Cardiovascular (2004)	72.3	68.1	64.7	<0.01
Statins (2002–2003)	90.2	82.6	74.5	<0.01
Average number of other medications in 2004 ($\pm$ SD)	8.9 (6.5)	9.1 (7.0)	9.4 (7.5)	<0.01
Average statin MPR 2004 ($\pm$ SD)	93.6 (15.6)	92.9 (17.7)	88.0 (24.3)	<0.01
^a Average statin MPR 2005 ($\pm$ SD), Median (IQR)	97.2 (21.4) 100 (83.3–100.7)	52.1 (16.5) 50 (40.3–66.7)	–	
^a Mean change in number of medications (2004–2005) (SD) & median (IQR)	–0.7 $\pm$ 2.9 0 (–2–1)	–1.0 $\pm$ 3.4 –1 (–2–0)	–3.6 $\pm$ 4.8 –2 (–2–5)	<0.01

Results are expressed as mean (SD = standard deviation) for continuous variables and percentages for categorical variables.

CCI = Charlson comorbidity index, CHD = coronary heart disease, CARP = coronary artery revascularisation procedures, ACS = acute coronary syndrome, MPR = medication possession ratio, IQR = interquartile range.

^a Variable not included in adjusted models.

statins were also likely to discontinue at least two other medicines and those that reduced statins were also likely to discontinue at least one other medication compared to those who continued therapy.

Replication of the study as a sensitivity analysis using data from 2004, when there was no large consumer co-payment increase, demonstrated that 2.4% of patients discontinued and 10.9% reduced statin medication in 2004. Compared to 2005, there was an increase of 0.9% in those who discontinued statin therapy and 1.6% who reduced statin therapy, implying a combined absolute increase of 2.5%; the likely proportion reducing as a result of the co-payment change [INSERT Table 1].

Overall, 4343 (2.1%) of the study cohort had at least one admission to hospital due to ACS or stroke as a primary diagnosis during the two-year follow up period. By statin group this was 2.2% for the discontinued group, 2.1% for the reduced adherence group and 2.1% for the continued group ($p = 0.76$). In addition, there were 3955 (1.9%) deaths in the follow-up period, 2.7% for the discontinued group, 2.4% for the reduced adherence group and 1.8% for the continued group ($p < 0.01$).

Unadjusted analysis showed no significant association in the risk of hospitalisation for those who discontinued statin therapy compared to those who continued (sHR 1.06; 95% CI 0.90–1.25) (Table 2). Similarly, the reduced adherence group demonstrated no significant difference in the risk of hospitalisation compared to the continued group (sHR 1.01; 95% CI 0.92–1.10).

In the adjusted Fine and Gray models, time to first ACS or stroke related hospitalisation was associated with discontinuing statin medication over the two-year period compared to continuing therapy (adjusted sHR 1.18, 95% CI 1.00–1.40). However, there was no significant difference for those who reduced adherence compared to those who continued using statins (Table 2).

The association between hospitalisation and statin group varied with age and gender (Table 3). For males aged less than 70 years who discontinued statin medications, there was a 54–63% increased risk of hospitalisation compared to males less than 70 years who continued therapy. However, there was no association for males who reduced adherence compared to those who continued. For females, no associations were observed in any age groups in the risk of hospitalisation for those who either reduced adherence and/or discontinued medication.

Discussion

This study investigated the association between statin use following a large co-payment increase in subsidised medicines in Australia and the

Table 2
Time to first ACS or stroke hospitalisation by statin group (n = 207,066).

Variable	Statin Therapy Group		
	Continued	Reduced Adherence	Ceased
Number of admissions	3648 (2.1%)	545 (2.1%)	150 (2.2%)
Number of competing risks	3147 (1.8%)	624 (2.4%)	184 (2.7%)
Unadjusted sHR (95% CI)	1.00 (reference)	1.01 (0.92–1.10)	1.06 (0.90–1.25)
P value	–	0.841	0.463
Adjusted sHR (95% CI)	1.00 (reference)	1.04 (0.95–1.14)	1.18 (1.00–1.40)
P value	–	0.94	0.046

ACS, acute coronary syndrome; CI, confidence interval; sHR, subdistribution hazard ratio; Number of competing risks refers to the number of deaths. Adjusted for age, sex, socio-economic disadvantage, residential remoteness, beneficiary status, Charlson Comorbidity Index, previous coronary heart disease, previous stroke, previous coronary artery revascularisation procedure, current acute coronary syndrome, current stroke, current coronary artery revascularisation procedure, diabetes medications, cardiovascular medications, previous statin usage (2002–2003), number of medications in 2004, and statin medication possession ratio in 2004.

Table 3

Time to first ACS or stroke hospitalisation by statin group stratified by age and gender.

Variable	Statin Therapy Group		
	Continued	Reduced Adherence	Ceased
Female, age < 60 yr (n = 23,825)			
Number of admissions	154 (0.8%)	35 (0.9%)	4 (0.3%)
Number of competing risks	74 (0.4%)	13 (0.3%)	5 (0.4%)
Unadjusted sHR (95% CI)	1.00 (reference)	1.11 (0.77–1.61)	0.41 (0.15–1.12)
P value	–	0.578	0.082
Adjusted sHR (95% CI)	1.00 (reference)	1.17 (0.81–1.70)	0.43 (0.16–1.19)
P value	–	0.406	0.103
Female, age 60 to 69 yr (n = 31,677)			
Number of admissions	265 (1.0%)	39 (1.0%)	9 (1.0%)
Number of competing risks	170 (0.6%)	37 (1.0%)	8 (0.9%)
Unadjusted sHR (95% CI)	1.00 (reference)	1.06 (0.52–1.95)	1.01 (0.52–1.95)
P value	–	0.744	0.985
Adjusted sHR (95% CI)	1.00 (reference)	1.11 (0.80–1.56)	1.00 (0.51–1.98)
P value	–	0.528	0.991
Female, age ≥ 70 yr (n = 43,561)			
Number of admissions	1006 (2.7%)	132 (2.7%)	37 (3.2%)
Number of competing risks	1037 (2.8%)	195 (4.0%)	66 (5.7%)
Unadjusted sHR (95% CI)	1.00 (reference)	1.06 (0.76–1.48)	1.06 (0.52–1.95)
P value	–	0.744	0.985
Adjusted sHR (95% CI)	1.00 (reference)	0.97 (0.81–1.17)	1.16 (0.83–1.61)
P value	–	0.777	0.390
Male, age < 60 yr (n = 37,434)			
Number of admissions	454 (1.5%)	98 (1.7%)	37 (2.3%)
Number of competing risks	154 (0.5%)	46 (0.8%)	17 (1.1%)
Unadjusted sHR (95% CI)	1.00 (reference)	1.14 (0.92–1.42)	1.53 (1.09–2.14)
P value	–	0.236	0.013
Adjusted sHR (95% CI)	1.00 (reference)	1.09 (0.87–1.36)	1.63 (1.16–2.29)
P value	–	0.451	<0.01
Male, age 60 to 69 yr (n = 33,529)			
Number of admissions	621 (2.1%)	88 (2.4%)	29 (3.2%)
Number of competing risks	318 (1.1%)	80 (2.2%)	14 (1.5%)
Unadjusted sHR (95% CI)	1.00 (reference)	1.10 (0.88–1.38)	1.48 (1.02–2.15)
P value	–	0.395	0.038
Adjusted sHR (95% CI)	1.00 (reference)	1.04 (0.83–1.31)	1.54 (1.05–2.26)
P value	–	0.715	0.026
Male, age ≥ 70 yr (n = 37,040)			
Number of admissions	1148 (3.6%)	153 (3.9%)	34 (3.4%)
Number of competing risks	1394 (4.3%)	253 (6.4%)	74 (7.5%)
Unadjusted sHR (95% CI)	1.00 (reference)	1.09 (0.92–1.28)	0.96 (0.69–1.36)
P value	–	0.341	0.838
Adjusted sHR (95% CI)	1.00 (reference)	1.03 (0.87–1.22)	0.97 (0.68–1.38)
P value	–	0.742	0.868

CI, confidence interval; sHR, subdistribution hazard ratio; Number of competing risks refers to the number of deaths. Adjusted for socio-economic disadvantage, residential remoteness, beneficiary status, Charlson Comorbidity Index, previous coronary heart disease, previous stroke, previous coronary artery revascularisation procedure, current acute coronary syndrome, current stroke, current coronary artery revascularisation procedure, diabetes medications, cardiovascular medications, previous statin usage (2002–2003), number of medications in 2004, and statin medication possession ratio in 2004.

risk of subsequent hospitalisation for ACS or stroke.

After accounting for the competing risk of death, and controlling for other factors, we showed that patients who discontinued their statin therapy following the co-payment increase had an 18% higher two-year risk of ACS or stroke-related hospitalisations compared with those who continued their therapy. When stratified by age and gender, men aged less than 70 years had an increased risk of hospitalisation for these conditions when discontinuing statin therapy compared with men of the same age who continued statin use.

Replication of the study in a year when there co-payment increase was not unusually large (3% in 2004) demonstrated that in 2005 the discontinuation and reduction of statins was 2.5% above background discontinuation rate. Extrapolating this in the WA population it is estimated that 32,591 stable statin users in WA may have discontinued or reduced adherence to statins as a result of the 21% co-payment increase. Therefore, a proportion of hospitalisation may be attributed to the increase in medication costs.

Internationally, studies on statin medication have shown that rising prescription costs are followed by a reduction (but not cessation) of medication use, which affected health service utilisation including hospitalisation and emergency department visits.^{10,12,14,15} Additionally, reduction of statin medication has been shown in other studies to have a negative effect on health outcomes.³³

We did not find an association between hospitalisation and statin reduction at a MPR change of at least 20%. Further analysis demonstrated those that discontinued medication also discontinued an additional two medications on average, compared to the continued group who did not discontinued any additional medication. The reduced group discontinued an average of one additional medication. This behavior might explain some of increased hospitalisation risk experienced by the discontinued statin group compared with the reduced adherence group.

Previous systematic reviews have demonstrated that poor statin adherence is associated with an increased risk of cardiovascular disease and hospitalisations.^{33,34} A recent meta-analysis demonstrated that statin therapy for primary prevention reduced the risk of major vascular events irrespective of age.³⁵ Additionally, men aged 70 years or less have a higher rate of hospitalisation due to CVD compared to women.¹⁸ The findings of our study are consistent with men being at a greater risk of CVD hospitalisation and that poor adherence to statin medication is associated with an increased risk of hospitalisation. Interestingly, a recent systematic review has challenged the current approaches to CVD prevention suggesting that statin usage may lead to unhealthy behaviours that may actually increase the risk of CVD.³⁶

A retrospective cohort study in United States demonstrated that following a policy change that eliminated the co-payments for statin therapy from a mean monthly cost of US\$24.28 there was a significant reduction in rates of hospitalisation and emergency department presentations (relative change 0.90; 95% CI: 0.80–0.92).³⁷ No co-payment decreases of this magnitude have occurred in Australia during the past 30 years, however, the Australian Government introduced a \$1 discount (at the dispensing pharmacists' discretion) on co-payments in 2016. The impact of this policy change has not yet been examined. The previous research examining the impact of the 2005 co-payment increase may have informed the policy decisions not to increase co-payments above inflation since this time.^{8,9}

Our findings should be interpreted in the context of the study's limitations. Firstly, this study uses an observational design, we cannot confirm whether a causal relationship exists between the co-payment increase and hospitalisation for ACS or stroke. Additionally, not all the discontinuation or reduction in adherence of statins may be attributed to the co-payment change. A sensitivity analysis in a year with no large co-payment increase demonstrated that an additional 2.5% of stable statin users discontinued or reduced their statin usage in 2005. Secondly, this study is specific to statin therapy. Statins are used for primary and secondary prevention of coronary artery disease that is predominantly

an asymptomatic condition except in the case of angina. Hence, the findings may not be generalisable to other medications or primarily symptomatic conditions, as symptoms may return when use is stopped with consumers more likely to continue to take the medication. Thirdly, a small number of ACS and stroke events will not be captured in the HMDC dataset, approximately 3%. This includes any hospitalisations outside WA or any events that occurred that did not require admission to hospital. Also, the PBS dataset during the study period did not capture medications priced under the general beneficiary co-payment (AU \$28.60 as at January 2005). Consequently, we will have under-captured some of the cheaper cardiovascular and diabetes medicines dispensed to general beneficiaries. Lastly, as the January 21% co-payment increase affected other medication categories, future research should explore if individuals choose between different medication categories to adhere to but not to others.

Despite these limitations, the strength of this study lies in the use of high quality individual-level administrative data that enabled specific patient characteristics and demographic information to be detailed and adjusted for in the analysis. Whole-of-population administrative data also eliminates selection and recall biases, and overcomes low response or loss-to-follow-up that may be problems with other types of observational studies. We recognise that the study data are ageing, being from 2005, however this was the last time there was a large increase (above normal CPIU increase) in co-payments in Australia.

The findings of this study are of relevance in Australia and other health systems where cost containment strategies are constantly being reviewed.

Conclusion

We found that discontinuing statins was associated with an increased two-year risk of ACS or stroke hospitalisation following a 21% increase in consumer co-payment. Men aged less than 70 years who discontinued their statin therapy had higher risk of ACS or stroke-related hospitalisation. The association was not found in men of other ages and women. This study will help to inform future policy makers on the potential implications of introducing a larger than usual medication co-payment increase.

Authors Statement

Karla L Seaman: Conceptualization, Methodology, Writing – original draft, Formal analysis, Data curation. Max K Bulsara: Writing – review & editing, Supervision, Formal analysis. Frank M Sanfilippo: Writing – review & editing, Supervision, Methodology. Anna Kemp-Casey: Writing – review & editing, Supervision, Methodology. Elizabeth E Roughead: Writing – review & editing, Supervision, Methodology. David B Preen: Writing – review & editing, Supervision, Methodology. Caroline Bulsara, Writing – review & editing, Supervision. Gerald F Watts, Writing – review & editing, Supervision.

Declaration of competing interest

The author reports no conflicts of interest in this work.

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Abbreviations

SD: standard deviation
 CCI: Charlson comorbidity index
 CHD: coronary heart disease
 CARP: coronary artery revascularisation procedures
 ACS: acute coronary syndrome
 MPR: medication possession ratio
 IQR: interquartile range
 CI: confidence interval
 sHR: subdistribution hazard ratio
 PBS: Pharmaceutical Benefits Scheme
 Statins: HMGCoA reductase inhibitors
 CVD: cardiovascular disease
 WA: Western Australia
 HMDC: Hospital Morbidity Data Collection
 ATC: Anatomical Therapeutic Chemical
 ICD-10-AM: International Statistical Classification of Diseases and Related Health Problems, tenth revision, with Australian modifications.