Journal of Population Therapeutics and Clinical Pharmacology
INCORPORATING FETAL ALCOHOL RESEARCH
Journal de la thérapeutique des populations et de la pharmacologie clinique

Original Research
DOI: 10.22374/1710-6222.25.1.1

REDUCED OUT-OF-POCKET COSTS AND MEDICATION ADHERENCE – A POPULATION-BASED STUDY

Shenzhen Yao[1]; Lisa Lix[2]; Yvonne Shevchuk[1]; Gary Teare[3]; David F. Blackburn[1]

[1]College of Pharmacy & Nutrition, University of Saskatchewan, Saskatoon, Saskatchewan; [2]Department of Community Health Sciences, University of Manitoba, Winnipeg, Manitoba; [3]Health Quality Council, Saskatoon, Saskatchewan.

Correspondence may be directed to David Blackburn, PharmD: d.blackburn@usask.ca

Submitted: April 24, 2017. Accepted: January 2, 2018. Published: January 15, 2018.

ABSTRACT

Background
In 2007, a drug benefit plan for seniors (SDP) was launched in Saskatchewan, Canada. SDP capped out-of-pocket costs at $15 per prescription for individuals aged 65 and older.

Objectives
To quantify the impact of the SDP on chronic medication adherence.

Methods
A retrospective cohort study was conducted for participants aged 65 or older who were eligible to the SPD, controlled by a younger group aged 40 to 64 who were ineligible. Adherence was measured over 365 days using medication possession ratio (MPR). MPRs were compared between age groups, and between pre- and post SDP-launch periods. The odds ratio of optimal adherence (i.e., MPR≥80%) was estimated using logistic regression models with generalized estimating equations (GEE).

Results
Between 2005 and 2009, 353,568 adherence observations were observed from 188,109 unique patients. Comparing the post-SDP period vs before, the increase in the odds of optimal medication adherence was significant (OR = 1.08, 95% CI: 1.04 to 1.11) and was stronger after excluding patients already receiving medication benefits from other government programs (OR = 1.21, 95% CI: 1.16 to 1.26). The SDP was

associated with improved adherence among the subgroup of prevalent medication users (OR = 1.08, 95% CI: 1.04 to 1.12), but not incident users (OR = 1.05, 95% CI: 0.98 to 1.13).

Conclusion

Reducing out-of-pocket medication costs for seniors was associated with small improvements in medication adherence across the population.

Poor medication adherence continues to be a major challenge in today's health care system. Although many factors likely contribute to poor adherence, studies have suggested that out-of-pocket (OOP) cost might be highly influential.[1–5] OOP cost has been identified as a barrier to the use of blood-pressure-lowering regimens and statins,[2,3,5–10] resulting in poor disease control and unfavourable clinical outcomes.[2,7–10] In fact, it has been suggested that increasing OOP costs result in higher overall health care spending through higher physician visits, emergency department visits, and hospitalizations.[2,6,7,9]As a result, a reasonable strategy to combat rising health care costs might be to increase spending on drug insurance plans to help improve medication adherence among their beneficiaries.

Several observational studies have linked lower OOP costs with higher medication adherence and reduced spending on health care services.[11–15] Chernew and colleagues reported that reduced OOP costs increased adherence up to 14% following a reduction in OOP costs by 50–100%,[16] whereas smaller improvements in adherence (4–6%) were observed in a randomized trial testing the benefits of providing cardiac medications free of charge.[4] In the latter study, significant reductions in total major vascular events or revascularizations was found among subjects receiving free medications during a follow-up period of three years following a myocardial infarction.[4] These studies suggest that investing in medication costs has positive benefits;[4] however, previous research has produced highly variable estimates about the impact of reducing OOP cost at the population level.[4,16]

On July 1st, 2007, the Saskatchewan government launched the Senior's Drug Plan benefit (SDP) to reduce seniors' OOP costs to a maximum of $15 per prescription for all medications listed in the provincial drug formulary. This province-wide intervention represented another opportunity to study the impact of OOP cost reduction at the population level. The purpose of this study was to estimate the impact of the SDP on medication adherence for major chronic conditions in Saskatchewan.

METHODS

Data Source

The Saskatchewan Ministry of Health maintains several databases including a person registry, a prescription database, a Hospital Discharge Abstract Database (DAD), and a physician services claims database. These databases can be linked by the unique identification number derived from each individual's encrypted health service number.[17,18]

The prescription database captures all outpatient dispensations to beneficiaries for medications listed in an extensive benefit list. Over 90% of the population are registered beneficiaries, excluding individuals receiving drug benefits from the federal government (e.g., First Nations or Canadian Armed Forces). The prescription database does not capture information for prescriptions excluded from the benefit list, physician samples, over-the-counter (OTC) drugs, or medications used during hospitalization.[17] The physician services database contains all claims by physicians providing service under a fee-for-service model; each claim contains a 3-digit ICD-9 diagnostic code. The hospital discharge abstract database records information on every discharge, transfer, or death of an inpatient. Diagnoses are recorded using the ICD-10-CA classification system since 2001[18-20] and each hospital discharge record can record up to 25 diagnoses[18,21] and up to 20 procedures.[18,22] Overall, Saskatchewan health-administrative databases have been used frequently in health services research and provide valid information on diagnoses and drug use.[17,23–26]

Subjects

We created a retrospective cohort study of patients receiving four major classes of chronic medications

in Saskatchewan between 2005 and 2009 (blood-pressure-lowering, cholesterol-lowering [i.e., statins], oral glucose-lowering, or anti-depressants). Four cohorts were identified: the pre-SDP cohort consisting of seniors ≥ 65 years of age receiving eligible medications before implementation of the SDP; the post-SDP cohort consisting of seniors ≥ 65 years of age receiving eligible medications after the SDP; and the two parallel control cohorts consisting of patients between 40 and 64 years receiving eligible medications in the pre- or post-SDP period but did not receive the benefit in the post-SDP period due to age.

The pre-SDP cohort consisted of individuals receiving at least one target medication between July 1st, 2005 and June 30, 2007, while the post-SDP cohort received eligible medications between July 1st, 2007 and June 30th, 2009. For subjects receiving more than one eligible medication (e.g., cholesterol-lowering agent and blood-pressure lowering agent), pharmacy claims of each medication type were followed up as separate observations. Patients were excluded if they were not continuous drug-plan beneficiaries for at least one-year before and one-year after the earliest dispensation for a target medication during the study period.

Previous studies have clearly demonstrated that adherence levels decline much faster among incident users[27,28]; therefore, separate analyses were carried out for incident and prevalent users of chronic medications. Incident users were defined by no dispensations within the same therapeutic category during 365 days prior to the index date.

Adherence Outcome Measures:

Medication adherence was estimated using the Medication Possession Ratio (MPR) with the exception that 'days supplied' was not available to investigators so it had to be estimated.[29] For statin, ACE inhibitors/angiotensin receptor blockers (ACEI/ARB), and antidepressants, the number of days supplied for each dispensation was fixed at 34 days corresponding to the typical refill duration by Saskatchewan pharmacies.[30] This approach has been used previously to assess medication adherence with good consistency with other measures.[29] For the oral blood-glucose-lowering agents (metformin, and glyburide), the number of days supplied was defined according to an algorithm based on the dispensed quantity (Appendix 1) because the maintenance drug schedule of the Saskatchewan drug plan formulary allows up to 100-day supplies to be dispensed for these agents.[31]

The MPR was calculated as the total of all days-supplied between the index date and the following 365 days, divided by 365 to obtain an adherence percentage. Hospitalized days were subtracted from the denominator because medication use cannot be captured for inpatients.[32,33] Adherence values were truncated to 100% but values exceeding 120% were manually examined to identify possible misclassification. Individuals switching within the same medication class were considered continuous users.

Data Analyses

Generalized estimating equations (GEE) with an exchangeable working correlation structure were constructed to test the impact of the SDP on the endpoint of optimal adherence (i.e., MPR ≥ 80%) at one year. This definition is the most frequently applied criteria in medication adherence studies.[34,36] Covariates (Appendix 2) were identified according to a framework of adherence determinants by the World Health Organization,[24,37–42] and all were included in the multivariable model to minimize the risk of confounding in the comparison of adherence between the pre-SDP and post-SDP cohorts. To quantify the impact of the SDP, an interaction term was created between TIME (i.e., before/after the SDP) and age category (i.e., <65/≥65) because only those ≥65 were exposed to the SDP in the 'after period'. The null hypothesis asserted that the impact of TIME (before vs after) was not impacted by one's age (≥65 versus <65), whereas the alternative hypothesis is that the impact of TIME would depend on a person's age because only those ≥65 received the SDP in the post-period. The odds ratios (OR) and 95% confidence intervals for the impact of the SDP were determined from the equation e^{β} where β represents the coefficient for the interaction term.

Subgroup analyses were conducted based on type of medication, sex, age, hospitalization (0 vs. ≥ 1 hospitalized days during the observation period), and medication cost (<$15, $15-30 and >$30) using the

same modelling approach described above. In addition, several sensitivity analyses were carried out on the estimation of MPR. Specifically, the number of days supplied for each dispensation was estimated using alternative methods to determine if the specific approach impacted the results. For example, statins are most commonly prescribed as one tablet/capsule per day; thus, the number of days supplied of each statin dispensation was estimated by using the quantity dispensed instead of the fixed estimate of 34 days per each dispensation.[43] However, the risk for bias originating from any of the MPR calculations was felt to be low because the approach was consistently applied to all cohorts in each model. SAS statistical software, version 9.3, (SAS Institute Inc., Cary, NC, USA) was used to conduct all analyses.[44]

RESULTS

Among 1.9 million individuals registered in the provincial health care database between July 2005 and June 2009, 236,906 seniors received at least one eligible medication for a total of 535,490 adherence observations. We further excluded 50,285 observations because of insufficient follow-up, and 131,637 observations derived from 48,797 unique patients for missing data to estimate residency and income, leaving 353,568 observations in the final cohort of 188,109 patients (Figure 1).

Population adherence rates were measured before versus after the implementation of the SDP (i.e., pre- versus post-SDP). In addition, patients <65 years of age who did not receive SDP benefits in either period (pre or post) were included in the analysis to control for the effect of time. Within both subgroups of patients (≥65 and <65) baseline differences between the pre-SDP period and the post-SDP period were rarely of clinical importance (Table 1). ACEI and ARBs were the most frequently used medications in both age groups (≥65 and <65), followed by statins (see Table 1). On average, patients ≥65 received five different medications within the first three months of observation. In terms of adherence, a weighted mean improvement of 2.59% was observed in the senior's group before versus after the implementation of the SDP (unadjusted) compared to 0.75% among those <65 years over the same period (Table 2).

After multivariate adjustment, the SDP program was associated with a small but statistically significant

FIG. 1 Patient Flow Diagram for the Retrospective Cohort Study Examining the Impact of the Seniors' Drug Plan (SDP) in Saskatchewan on Medication Adherence.

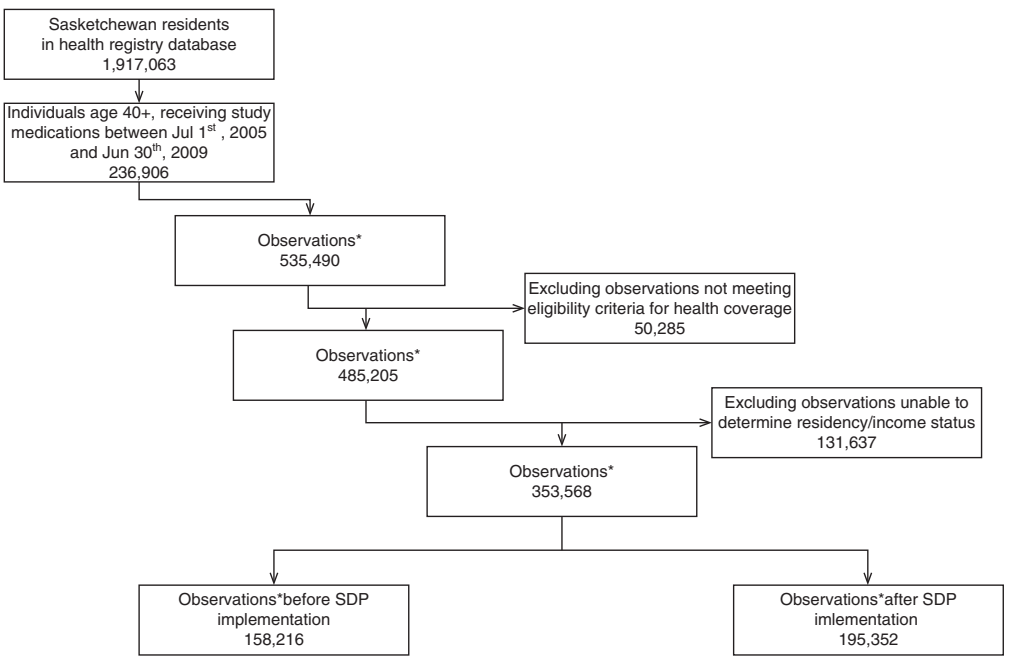


TABLE 1A Baseline Characteristics Stratified by Age and Temporal Association with the Implementation of the Seniors' Drug Plan (SDP)

		Age 65+		**Age 40-64**	
		Pre-SDP	**Post-SDP**	**Pre-SDP**	**Post-SDP**
		***N*=62,759**	***N*=83,950**	***N*=95,457**	***N*=111,402**
Gender					
	Females	35,786 (57.0%)	46,752 (55.7%)	47,508 (49.8%)	54,454 (48.9%)
Age at index date		73.3±5.9	74.0±6.3	53.5±6.6	53.9±6.5
	40-64	N/A	N/A	95,457 (100%)	111,402 (100%)
	65-69	19,786 (31.5%)	24,644 (29.4%)	N/A	N/A
	70-74	18,219 (29.0%)	22,538 (26.8%)	N/A	N/A
	75-79	14,667	19,359	N/A	N/A
		(23.4%)	(23.1%)		
	≥80	10,087	17,389	N/A	N/A
		(16.1%)	(20.7%)		
Residency type					
	Urban	40,214 (64.1%)	54,592 (65.0%)	64,322 (67.4%)	75,606 (67.9%)
	Rural	22,545 (35.9%)	29,358 (35.0%)	31,135 (32.6%)	35,796 (32.1%)
Medication class					
	Statin	18,877 (30.1%)	26,772 (31.9%)	25,022 (26.2%)	31,284 (28.1%)
	ACEI/ARB*	28,120 (44.8%)	36,113 (43.0%)	34,228 (35.9%)	39,326 (35.3%)
	CCB*	734 (1.2%)	814 (1.0%)	459 (0.5%)	429 (0.4%)
	Metformin	6,578 (10.8%)	9,361 (11.2%)	9,790 (10.3%)	11,863 (10.7%)
	Glyburide	3,045 (4.9%)	3,344 (4.0%)	3,697 (3.9%)	3,439 (3.1%)
	SSRI*	3,891 (6.2%)	5,570 (6.6%)	14,504 (15.2%)	16,092 (14.4%)

TABLE 1A Baseline Characteristics Stratified by Age and Temporal Association with the Implementation of the Seniors' Drug Plan (SDP) *(Continued)*

		Age 65+		Age 40-64	
		Pre-SDP	**Post-SDP**	**Pre-SDP**	**Post-SDP**
		***N*=62,759**	***N*=83,950**	***N*=95,457**	***N*=111,402**
	SNRI*	1,334 (2.1%)	1,976 (2.4%)	7,757 (8.1%)	8,969 (8.1%)
Type of user					
Incident Users		10,626 (16.9%)	13,748 (16.4%)	22,320 (23.4%)	24,178 (21.7%)
Prevalent Users		52,133 (83.1%)	70,202 (83.6%)	73,137 (76.6%)	87,224 (78.3%)

**Pre-SDP = observation period before the launch of the SDP on Jul 1st, 2007; Post-SDP = observation period after the launch of the SDP*

TABLE 1B Baseline Characteristics Stratified by Age and Temporal Association with the Implementation of the Seniors' Drug Plan (SDP)

		Age 65+		Age 40-64	
		Pre-SDP	**Post-SDP**	**Pre-SDP**	**Post-SDP**
		***N*=62,759**	***N*=83,950**	***N*=95,457**	***N*=111,402**
Prescriber type					
Family Physician		59,435 (94.7%)	79,919 (95.2%)	90,528 (94.8%)	106,490 (95.6%)
Specialist		3,324 (5.3%)	4,031 (4.8%)	4,929 (5.2%)	4,912 (4.4%)
Hyperlipidemia					
		13,816 (22.0%)	17,736 (21.1%)	24,131 (25.3%)	27,551 (24.7%)
Hypertension					
		46,051 (73.4%)	59,145 (70.5%)	54,266 (56.9%)	61,774 (55.5%)
Coronary Heart Disease (CHD)					
		15,918 (25.4%)	21,684 (25.8%)	16,733 (17.5%)	19,891 (17.9%)
Stroke					
		5,302 (8.5%)	8,808 (10.5%)	8,585 (9.0%)	11,567 (10.4%)

TABLE 1B Baseline Characteristics Stratified by Age and Temporal Association with the Implementation of the Seniors' Drug Plan (SDP) *(Continued)*

		Age 65+		**Age 40-64**	
		Pre-SDP	**Post-SDP**	**Pre-SDP**	**Post-SDP**
		***N*=62,759**	***N*=83,950**	***N*=95,457**	***N*=111,402**
Diabetes					
		22,539 (35.9%)	32,921 (39.2%)	34,327 (36.0%)	42,549 (38.2%)
Depression					
		5,821 (9.3%)	7,988 (9.5%)	21,273 (22.3%)	24,046 (21.6%)
Medication class					
	Statin	18,877 (30.1%)	26,772 (31.9%)	25,022 (26.2%)	31,284 (28.1%)
	ACEI/ARB*	28,120 (44.8%)	36,113 (43.0%)	34,228 (35.9%)	39,326 (35.3%)
	CCB*	734 (1.2%)	814 (1.0%)	459 (0.5%)	429 (0.4%)
	Metformin	6,578 (10.8%)	9,361 (11.2%)	9,790 (10.3%)	11,863 (10.7%)
	Glyburide	3,045 (4.9%)	3,344 (4.0%)	3,697 (3.9%)	3,439 (3.1%)
	SSRI*	3,891 (6.2%)	5,570 (6.6%)	14,504 (15.2%)	16,092 (14.4%)
	SNRI*	1,334 (2.1%)	1,976 (2.4%)	7,757 (8.1%)	8,969 (8.1%)
Type of user					
	Incident Users	10,626 (16.9%)	13,748 (16.4%)	22,320 (23.4%)	24,178 (21.7%)
	Prevalent Users	52,133 (83.1%)	70,202 (83.6%)	73,137 (76.6%)	87,224 (78.3%)

**ACEI = angiotensin-converting-enzyme inhibitor; ARB= angiotensin receptor blocker; CCB=calcium channel blocker; SSRI=selective serotonin reuptake; SNRI= serotonin-norepinephrine reuptake inhibitors*

TABLE 1C Baseline Characteristics Stratified by Age and Temporal Association with the Implementation of the Seniors' Drug Plan (SDP).

		Age 65+		Age 40-64	
		Pre-SDP	**Post-SDP**	**Pre-SDP**	**Post-SDP**
Group	**Category**	***N*=62,759**	***N*=83,950**	***N*=95,457**	***N*=111,402**
Income Level (+000 $)		24.7± 7.0	24.8 ± 7.0	25.9 ± 7.5	26.0 ± 7.6
	Quintile 1: 3.2-19	13,798(22.0%)	18,246(21.7%)	17,467(18.3%)	20,254(18.2%)
	Quintile 2: 19.1-$22	13,717(21.9%)	18,145(21.6%)	17,326(18.2%)	19,748(17.7%)
	Quintile 3: $22.1-$26	12,902(20.6%)	17,292(20.6%)	18,804(19.7%)	21,940(19.7%)
	Quintile 4: $26.1-$31	11,492(18.3%)	15,607(18.6%)	20,218(21.2%)	23,866(21.4%)
	Quintile 5: ≥$31	10,850(17.3%)	14,660(17.5%)	21,642(22.7%)	25,594(23.0%)
Number of visits to prescribers during the observation period		10.6 ± 10.5	11.3 ± 11.4	7.9 ± 8.5	7.9 ± 8.6
	Quintile 1 : 0-3	11,352(18.1%)	14,017(16.7%)	27,713(29.0%)	32,773(29.4%)
	Quintile 2 : 4-5	9,736(15.5%)	12,491(14.9%)	18,402(19.3%)	21,725(19.5%)
	Quintile 3 : 6-8	13,294(21.2%)	17,469(20.8%)	20,101(21.1%)	22,960(20.6%)
	Quintile 4 : 9-14	14,726(23.5%)	20,079(23.9%)	16,956(17.8%)	19,729(17.7%)
	Quintile 5 : ≥15	13,651(21.8%)	19,894(23.7%)	12,285(12.9%)	14,215(12.8%)
Number of non-prescriber physicians visited during the observation period		4.1 ± 3.9	3.9 ± 3.8	3.5 ± 3.6	3.3 ± 3.5
	Quintile 1 : 0	7,238(11.5%)	9,538(11.4%)	14,481(15.2%)	17,510(15.7%)
	Quintile 2 : 1-2	19,868(31.7%)	27,379(32.6%)	33,387(35.0%)	40,310(36.2%)
	Quintile 3 : 3	8,341(13.3%)	11,208(13.4%)	12,280(12.9%)	14,343(12.9%)
	Quintile 4 : 4-6	15,182(24.2%)	20,440(24.4%)	21,113(22.1%)	23,924(21.5%)
	Quintile 5 : ≥7	12,130(19.3%)	15,385(18.3%)	14,196(14.9%)	15,315(13.8%)
Charlson Comorbidity Index (CCI) score		4.1 ± 1.1	4.3 ± 1.4	2.1 ± 1.0	2.1 ± 1.1
	Quintile 1: 1	0(0.0%)	0(0.0%)	26,648(27.9%)	28,302(25.4%)
	Quintile 2: 2	0(0.0%)	0(0.0%)	43,460(45.5%)	50,715(45.5%)
	Quintile 3: 3	17,675(28.2%)	21,723(25.9%)	21,876(22.9%)	27,361(24.6%)
	Quintile 4: 4	29,929(47.7%)	37,350(44.5%)	1,867(2.0%)	2,332(2.1%)
	Quintile 5: ≥5	15,155(24.2%)	24,877(29.6%)	1,606(1.7%)	2,692(2.4%)

TABLE 1C Baseline Characteristics Stratified by Age and Temporal Association with the Implementation of the Seniors' Drug Plan (SDP). *(Continued)*

		Age 65+		Age 40-64	
		Pre-SDP	**Post-SDP**	**Pre-SDP**	**Post-SDP**
Group	**Category**	***N*=62,759**	***N*=83,950**	***N*=95,457**	***N*=111,402**
Number of nights in hospital during the observation period		2.1 ± 7.0	2.1 ± 7.5	1.1 ± 5.4	1.1 ± 5.6
	Subgroup1: =0	42,255(67.3%)	57,317(68.3%)	74,540(78.1%)	87,998(79.0%)
	Subgroup2: >0	20,504(32.7%)	26,633(31.7%)	20,917(21.9%)	23,404(21.0%)
Number of dispensations of target medication within 365 days prior to the index date among prevalent users		6.5 ± 4.4	6.7 ± 4.5	5.8 ± 4.6	6.0 ± 4.7
	Quintile 1: 0	10,626(16.9%)	13,748(16.4%)	22,320(23.4%)	24,178(21.7%)
	Quintile 2: 1-4	11,948(19.0%)	15,742(18.8%)	18,700(19.6%)	21,923(19.7%)
	Quintile 3: 5-8	11,990(19.1%)	15,416(18.4%)	18,855(19.8%)	21,503(19.3%)
	Quintile 4: 9-10	18,151(28.9%)	25,062(29.9%)	23,040(24.1%)	28,523(25.6%)
	Quintile 5: ≥11	10,044(16.0%)	13,982(16.7%)	12,542(13.1%)	15,275(13.7%)
Number of distinct medications received within first 3 months of the observation period		4.7 ± 2.6	5.0 ± 2.6	3.8 ± 2.5	4.0 ± 2.5
	Quintile 1 : 1-2	12,435(19.8%)	13,525(16.1%)	33,031(34.6%)	36,302(32.6%)
	Quintile 2 : 3	10,739(17.1%)	12,799(15.3%)	17,854(18.7%)	20,746(18.6%)
	Quintile 3 : 4	10,549(16.8%)	13,861(16.5%)	14,418(15.1%)	17,243(15.5%)
	Quintile 4 : 5-6	15,816(25.2%)	22,641(27.0%)	17,621(18.5%)	21,170(19.0%)
	Quintile 5 : ≥7	13,220(21.1%)	21,124(25.2%)	12,533(13.1%)	15,941(14.3%)
Number of hospitalizations 3 months prior to the index date		0.2 ± 0.4	0.1 ± 0.4	0.1 ± 0.3	0.1 ± 0.3
	Subgroup1: =0	54,627(87.0%)	73,561(87.6%)	87,440(91.6%)	102,628(92.1%)
	Subgroup2: >0	8,132(13.0%)	10,389(12.4%)	8,017(8.4%)	8,774(7.9%)

increase in the odds of optimal adherence for seniors ≥65 years of age receiving their medications in the post-SDP period (OR = 1.08, 95% CI: 1.04 to 1.11) compared to the pre-SDP period. The association between the SDP benefit and higher adherence was strengthened by the results of several subgroup analyses. First, a slight *reduction* in the odds of optimal adherence was observed in the cohort of patients <65 years of age who did not receive SDP benefits (OR = 0.96, 95% CI: 0.94 to 0.98). Also, no impact of the

TABLE 2 Percentage of Patients Achieving Optimal Adherence (≥80%) Estimated using the Medication Possession Ratio before Implementation of the Senior's Drug Plan (Pre-SDP) versus After (Post-SDP)

	Age 65+			Age 40-64		
	Pre-SDP	**Post-SDP**	**p-value***	**Pre-SDP**	**Post-SDP**	**p-value***
Statin	63.3%	66.8%	<0.01	58.1%	59.6%	<0.01
ACEI/ARB*	75.1%	76.9%	<0.01	71.8%	72.1%	0.37
CCB*	77.7%	76.8%	0.72	71.9%	73.9%	0.55
Metformin	66.8%	68.9%	0.01	65.0%	64.6%	0.53
Glyburide	60.9%	60.8%	0.98	58.4%	55.0%	<0.01
SSRI*	56.1%	59.9%	<0.01	50.9%	51.8%	0.11
SNRI*	63.0%	67.7%	0.01	60.1%	63.2%	<0.01
All classes	68.5%	70.8%	<0.01	62.9%	63.6%	<0.01

**ACEI = angiotensin-converting-enzyme inhibitor; ARB= angiotensin receptor blocker; CCB=calcium channel blocker; SSRI=selective serotonin reuptake inhibitors; SNRI= serotonin-norepinephrine reuptake inhibitors; p-value by crude chi-square test.*

SDP was observed among patients with medications costing less than $15 (OR = 0.97, 95% CI: 0.86 to 1.11) or those receiving discounted dispensations due to another government plan with self-payment less than $15 (OR = 0.94, 95% CI: 0.89 to 1.01). In contrast, the impact of the SDP on adherence was consistently demonstrated in subgroups of patients receiving medications costing between $16 and $30 (OR = 1.24, 95% CI: 1.08 to 1.41) as well as those costing ≥ $30 (OR = 1.21, 95% CI: 1.16 to 1.26). After excluding individuals who were already receiving medication benefits from other government programs, the odds of achieving optimal adherence increased by 21% following SDP implementation (OR = 1.21, 95% CI: 1.16 to 1.26, Figure 2) Finally, the SDP was significantly associated with higher odds of achieving good adherence for prevalent users of chronic medications (OR of prevalent users = 1.08, 95% CI: 1.04 to 1.12), but not for incident users (OR of incident users = 1.05, 95% CI: 0.98 to 1.13).

When cohorts were stratified by medication class, blood-cholesterol-lowering agents (i.e., statin), blood-pressure-lowering medications (i.e., ACEI/ARB), the blood-glucose-lowering agent metformin, and the SSRIs were significantly impacted by the SDP (Figure 3). Although all OR values were higher than one, the odds of achieving optimal adherence for the other medication classes did not reach statistical significance.

Several sensitivity analyses were conducted to ensure that the primary results were not influenced by methodologic approaches. Consistent results were obtained with alternative estimation on supply days (by dispensation quantity), and different thresholds of optimal adherence (MPR of 50% to 100%) Also, the results were consistent when the original cohort was expanded by 131,637 observations of 48,797 unique patients who were originally excluded due to missing residency and income information.

DISCUSSION

This retrospective study examined the impact of a drug benefit program for seniors in Saskatchewan, Canada where OOP costs for most prescription medications were capped at $15. A statistically significant improvement in medication adherence was observed following the implementation of the SDP benefit in Saskatchewan (OR 1.08; 95% CI 1.04 to 1.11). The impact of SDP on adherence was larger in patients with higher drug costs and in patients who had previously received the same drug without the SDP benefit (i.e., prevalent users). In absolute terms, the improvement in medication adherence following SDP implementation was small. However, these findings are consistent

FIG. 2 Adjusted Odds Ratio of Achieving Optimal Adherence* Following Implementation of the Seniors' Drug Plan (SDP) Stratified by Retail Cost of Medication (left) or Presence of Another Copayment Benefit (right).

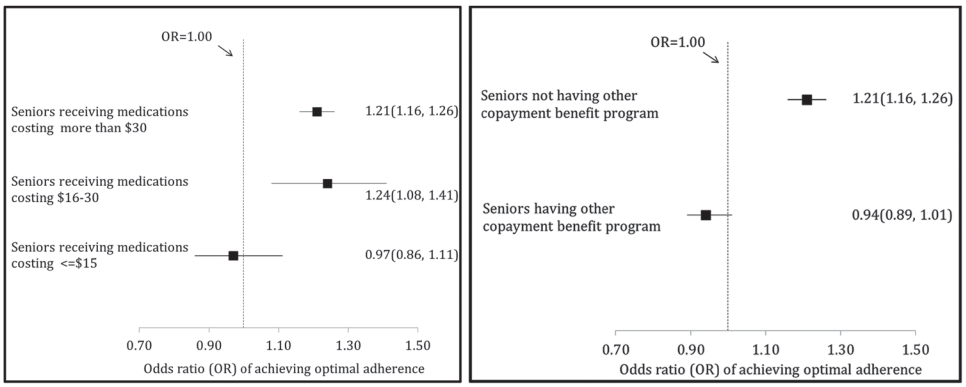
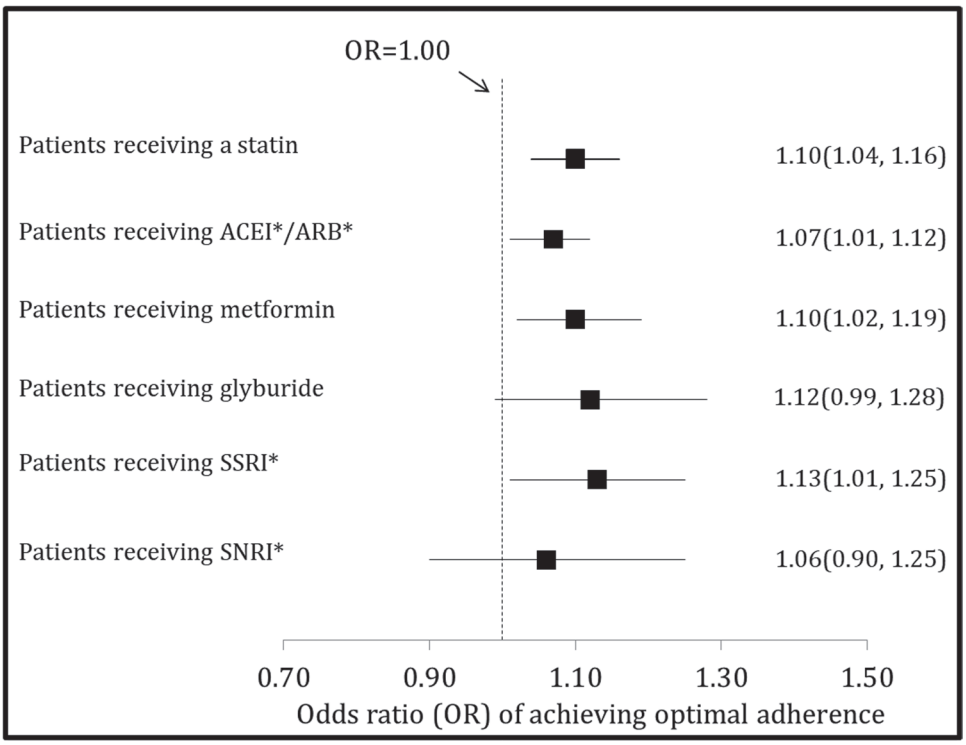


FIG. 3 Adjusted Odds Ratio of Achieving Optimal Adherence† Following Implementation of the Seniors' Drug Plan (SDP), Stratified by Medication Class.



with current paradigms describing non-adherence as a multifactorial problem. In other words, simply reducing one single factor (such as cost) does not drastically impact overall adherence levels.[45] A similar finding was reported by Choudhry and colleagues who found that full coverage for medications resulted in a 5% increase in the percentage of patients with optimal adherence (i.e., from 39% to 44%).[4]

The SDP affected prevalent medication users but not incident users. Several possible reasons for these results can be theorized. First, adherence levels decline much faster among incident users.[28] Thus, it is

possible that the relative importance of cost may be diluted in the early phases of therapy when numerous other adherence barriers such as tolerability, attitudes, beliefs, and knowledge may be more impactful. On the other hand, prevalent users witnessed a direct reduction in the cost of their medications following the SDP launch. Perhaps this obvious cost reduction motivated a slight improvement in adherence for the following year. Most importantly, this study was restricted to a one-year period of adherence assessment so it is not known whether these small increases in adherence were sustained over the long term.

The evaluation of the SDP used comprehensive population based databases and produced results that were verified in sensitivity analyses. However, several limitations must be recognized. First, the presence of private medication coverage is not captured in Saskatchewan's health-administrative databases. Thus, we cannot be certain of the OOP costs paid by beneficiaries. However, rates of private insurance were not likely to have changed between seniors starting medications before versus after the SDP. Further, considering all individuals are over the age of 65, drug coverage from private insurance through employment is expected to be low. Secondly, the indicators of medication use are based on electronic refill databases, which are indirect measures of drug consumption. However, studies suggest that refill claims are highly concordant to actual intake.[49] Thirdly, only a one-year period of adherence was examined for individuals taking chronic medications. It is not clear whether the small impacts of the SDP would be sustained over a long-term follow-up period. Fourth, the impact of the SDP on medication adherence was restricted to a few classes of chronic medications only. Measurement of adherence to all types of medication classes would not be feasible. Moreover, many medication classes such as antibiotics and pain medications are not meant to be taken chronically. However, the medications examined in this study represented the most commonly used chronic medications in Canada and corresponded to the diseases of highest prevalence in elderly patients. Lastly, we did not control for each individual's overall medication cost. Hypothetically, the benefit of the SDP may have been greater among seniors receiving multiple medications because of greater savings on total medication costs. It would be interesting to conduct further analyses in this regard.

In conclusion, the SDP was associated with a statistically significant improvement in medication adherence for specific chronic medications; however, it remains unknown if these small improvements have translated into health benefits and/or economic savings for downstream health care services. Regardless, cost reduction for seniors in Saskatchewan must have provided substantial relief independent of the impact on adherence and utilization.

ACKNOWLEDGEMENT

We would like to thank the Saskatchewan Health Quality Council, which has provided critical training, resources, and technical support for us to extract and prepare data from the health administrative databases. We would also like to thank Drug Plan and Extended Benefits Branch of Saskatchewan Ministry of Health from whom we received funding for this study.

FUNDING

Drug Plan and Extended Benefits Branch, Saskatchewan Ministry of Health

CONFLICT OF INTEREST

David Blackburn is the Chair in Patient Adherence to Drug Therapy within the College of Pharmacy and Nutrition, University of Saskatchewan. This position was created through unrestricted financial support from AstraZeneca Canada, Merck Canada, Pfizer Canada, and the Province of Saskatchewan's Ministry of Health.

DISCLOSURE

This study is based in part on de-identified data provided by the Saskatchewan Ministry of Health. The interpretation and conclusions contained herein do not necessarily represent those of the government of Saskatchewan or the Saskatchewan Ministry of Health.

REFERENCES

1. Rubin RJ, Mendelson DN. A framework for cost-sharing policy analysis. Pharmacoeconomics 1996;10 Suppl 2:56–67.
2. Goldman DP, Joyce GF, Zheng Y. Prescription drug cost sharing: associations with medication and medical

utilization and spending and health. JAMA 2007 Jul 4;298(1):61–9.
3. Rezayatmand R, Pavlova M, Groot W. The impact of out-of-pocket payments on prevention and health-related lifestyle: a systematic literature review. Eur J Public Health 2013 Feb;23(1):74–9.
4. Choudhry NK, Avorn J, Glynn RJ, et al. Full coverage for preventive medications after myocardial infarction. N Engl J Med 2011 Dec 1;365(22):2088–97.
5. Briesacher BA, Gurwitz JH, Soumerai SB. Patients at-risk for cost-related medication nonadherence: a review of the literature. J Gen Intern Med 2007 Jun;22(6):864–71.
6. Austvoll-Dahlgren A, Aaserud M, Vist G, et al. Pharmaceutical policies: effects of cap and co-payment on rational drug use. Cochrane Database Syst Rev 2008 Jan 23;(1):CD007017.
7. Remler DK, Greene J. Cost-sharing: a blunt instrument. Annu Rev Public Health 2009;30:293–311.
8. Gibson TB, Ozminkowski RJ, Goetzel RZ. The effects of prescription drug cost sharing: a review of the evidence. Am J Manag Care 2005 Nov;11(11):730–40.
9. Choudhry NK. Copayment levels and medication adherence: less is more. Circulation 2009 Jan 27;119(3):365–7.
10. Eaddy MT, Cook CL, O'Day K, et al. How patient cost-sharing trends affect adherence and outcomes: a literature review. P T 2012 Jan;37(1):45–55.
11. Donohue JM, Zhang Y, Aiju M, et al. Impact of Medicare Part D on antidepressant treatment, medication choice, and adherence among older adults with depression. Am J Geriatr Psychiatr 2011 Dec;19(12):989–97.
12. Zhang Y, Donohue JM, Lave JR, et al. The impact of Medicare Part D on medication treatment of hypertension. Health Serv Res 2011 Feb;46(1 Pt 1):185–98.
13. Zhang Y, Lave JR, Donohue JM, et al. The impact of Medicare Part D on medication adherence among older adults enrolled in Medicare-Advantage products. Med Care 2010 May;48(5):409–17.
14. Zhang Y, Donohue JM, Lave JR, et al. The effect of Medicare Part D on drug and medical spending. N Engl J Med 2009 Jul 2;361(1):52–61.
15. Donohue JM, Zhang Y, Lave JR, et al. The Medicare drug benefit (Part D) and treatment of heart failure in older adults. Am Heart J 2010 Jul;160(1):159–65.
16. Chernew ME, Shah MR, Wegh A, et al. Impact of decreasing copayments on medication adherence within a disease management environment. Health Aff (Millwood) 2008 Jan-Feb;27(1):103–12.
17. Edited by Strom BL, Kimmel SE. Textbook of Pharmacoepidemiology. John Wiley & Sons Ltd, West Sussex, England; 2006.
18. Health Quality Council. Saskatchewan MOH Data Warehouse Overview (HQC Internal Document). Saskatoon, SK; 2013.
19. Centers for Disease Control and Prevention, USA. International Classification of Diseases, Ninth Revision (ICD-9). Atlanta, GA; 1998-2011, USA.
20. Canadian Institute for Health Information. Canadian Coding Standards for Version 2015 ICD-10-CA and CCI. Canadian Institute for Health Information, Ottawa, Toronto, Victoria; 2015.
21. Quail JM, Lix LM, Osman BA, et al. Comparing comorbidity measures for predicting mortality and hospitalization in three population-based cohorts. BMC Health Serv Res 2011 Jun 10;11:146.
22. Canadian Institute for Health Information. Discharge Abstract Database (DAD). Data Elements 2010-2011, 2010; 1–8.
23. Tulloch J, Evans B. Evaluation of the accuracy of the saskatchewan health pharmaceutical information program for determining a patient's medication use immediately before admission. Can J Hosp Pharm 2009 Jan;62(1):21–7.
24. Varas-Lorenzo C, Castellsague J, Stang MR, et al. Positive predictive value of ICD-9 codes 410 and 411 in the identification of cases of acute coronary syndromes in the Saskatchewan Hospital automated database. Pharmacoepidemiol Drug Saf 2008 Aug;17(8):842–52.
25. Rawson NS, D'Arcy C. Assessing the validity of diagnostic information in administrative health care utilization data: experience in Saskatchewan. Pharmacoepidemiol Drug Saf 1998 Nov;7(6):389–98.
26. West SL, Richter A, Melfi CA, et al. Assessing the Saskatchewan database for outcomes research studies of depression and its treatment. J Clin Epidemiol 2000 Aug;53(8):823–31.
27. Ho PM, Rumsfeld JS, Masoudi FA, et al. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. Arch Intern Med. 2006 Sep 25;166(17):1836–41.
28. Lemstra M, Blackburn D. Nonadherence to statin therapy: discontinuation after a single fill. Can J Cardiol 2012 Sep-Oct;28(5):567–73.
29. Blackburn DF, Dobson RT, Blackburn JL, et al. Adherence to statins, beta-blockers and angiotensin-converting

enzyme inhibitors following a first cardiovascular event: a retrospective cohort study. Can J Cardiol 2005 May 1;21(6):485–8.
30. Saskatchewan Health. Drug Plan Formulary V62. Regina, SK; 2013.
31. Saskatchewan Health. Saskatchewan Drug Plan Formulary v62 Supplement Maintenance drug schedule. Regina, SK; 2013.
32. Strom BL. Pharmacoepidemiology, 4th Edition. John Wiley & Sons Ltd, West Sussex, England; 2005.
33. Donnelly LA, Morris AD, Pearson ER. Adherence in patients transferred from immediate release metformin to a sustained release formulation: a population-based study. Diabetes Obes Metab 2009 Apr;11(4):338–42.
34. Sackett DL. The hypertensive patient: 5. Compliance with therapy. Can Med Assoc J 1979 Aug 4;121(3):259–61.
35. Insull W. The problem of compliance to cholesterol altering therapy. J Intern Med 1997 Apr;241(4):317–25.
36. Avorn J, Monette J, Lacour A, et al. Persistence of use of lipid-lowering medications: a cross-national study. JAMA 1998 May 13;279(18):1458–62.
37. World Health Organization. Adherence to long-term therapies Evidence for action. World Health Organization, Geneva, Switzerland; 2003.
38. Yeaw J, Benner JS, Walt JG, et al. Comparing adherence and persistence across 6 chronic medication classes. J Manag Care Pharm 2009 Nov-Dec;15(9):728–40.
39. Wang CC, Wei D, Farley JF. Impact of monthly prescription cap on medication persistence among patients with hypertension, hyperlipidemia, or diabetes. J Manag Care Pharm 2013 Apr;19(3):258–68.
40. Petersen LA, Wright S, Normand SL, et al. Positive predictive value of the diagnosis of acute myocardial infarction in an administrative database. J Gen Intern Med 1999 Sep;14(9):555–8.
41. Lee DS, Stitt A, Wang X, et al. Administrative hospitalization database validation of cardiac procedure codes. Med Care 2013 Apr;51(4):e22–6.
42. Gurevich Y, McFarlane A, Morris K, et al. Estimating the number of coronary artery bypass graft and percutaneous coronary intervention procedures in Canada: a comparison of cardiac registry and Canadian Institute for Health Information data sources. Can J Cardiol 2010 Aug-Sep;26(7):e249–53.
43. Larsen J, Andersen M, Kragstrup J, et al. High persistence of statin use in a Danish population: compliance study 1993-1998. Br J Clin Pharmacol 2002 Apr;53(4):375–8.
44. SAS Institute INC. SAS for Windows version 9.3. Cary, NC, USA; 2011.
45. Brown M, Bussell J. Medication Adherence: WHO Cares? Mayo Clin Proc. 2011 Apr; 86(4):304–14.
46. Shalev V, Goldshtein I, Halpern Y, et al. Association between persistence with statin therapy and reduction in low-density lipoprotein cholesterol level: analysis of real-life data from community settings. Pharmacotherapy 2014 Jan;34(1):1–8.
47. Dragomir A, Côté R, Roy L, et al. Impact of adherence to antihypertensive agents on clinical outcomes and hospitalization costs. Med Care 2010 May;48(5):418–25.
48. Perreault S, Ellia L, Dragomir A, et al. Effect of statin adherence on cerebrovascular disease in primary prevention. Am J Me. 2009 Jul;122(7):647–55.
49. Grymonpre R, Cheang M, Fraser M, et al. Validity of a prescription claims database to estimate medication adherence in older persons. Med Care 2006 May;44(5):471–7.

APPENDICES

Appendix 1 Algorithm to estimate supply days

Type of medication	Algorithm to estimate supply days
Statin	34 days per refill
Angiotensin converting enzyme inhibitors (ACE inhibitor), or angiotensin-receptor blocker (ARB)	34 days per refill
Oral blood-glucose-lowering agents (metformin, and glyburide)	When dispensation quantity ≤ 34: supply days = dispensation quantity; When dispensation quantity between 35 and 68: supply days = dispensation quantity / 2; When dispensation quantity between 69 and 102: supply days = dispensation quantity / 3; When dispensation quantity between 103 and 136: supply days = dispensation quantity / 4; When dispensation quantity higher than 136: supply days = 100.*

* Extensive sensitivity testing and descriptive analyses were conducted on the specific strategies used to estimate the number of days supplied.

Appendix 2 Variables Included in Regression Models to Control for Confounding in the Evaluation of Adherence before versus After the Implementation of the Seniors' Drug Plan (SDP) in Saskatchewan

Category	Variables	Variable categories
Social and demographic factors	• Age at index date • Sex • Inflation adjusted income level quintile imputed from residential neighborhood • Rural/Urban residence	• 0 for age 40-46, 1 for age 65-59, 2 for 70-74, 3 for 75-79, 4 for age 80 and above • 0 for males, 1 for females • Quintiles of 5 levels • 0=rural, 1=urban
Health system-related factors	• Specialty of the prescriber based on index dispensation date • Receipt of other health plan benefit • Number of physician visits with 'prescriber' during observation year • Number of distinct physicians providing service during observation year besides prescriber	• 0=family physician, 1= Specialist • 0=no dispensations with OOP < $15 in observation period, otherwise =1 • Quintiles of 5 levels • Quintiles of 5 l

Appendix 2 Variables Included in Regression Models to Control for Confounding in the Evaluation of Adherence before versus After the Implementation of the Seniors' Drug Plan (SDP) in Saskatchewan *(Continued)*

Category	Variables	Variable categories
Condition-related factors	• Charlson Comorbidity Index (CCI) Score • Presence of a target chronic diseases* • Number of nights spent in hospital during observation year • Previous hospitalization of at least one day for any reason within 3 months prior to the index date	• Quintiles of 5 levels • 0 = not diseased, 1=diseased • zero nights in hospital=0, one or more nights in hospital = 1 • 0 for no hospitalizations, 1 for at least one hospitalization
Therapy-related factors	• The specific target medication initiated • Number of dispensations of the target medication in previous year *(for prevalent users only)* • Pill burden. Number of distinct medications received within the first 3 months of the observation period by AHFS class • Dispensation cost • Prevalent user	• 1 for statin, 2 for ACEI/ARB, 3 for CCB, 4 for metformin, 5 for glyburide, 6 for SSRI, 7 for SNRI. • Quintiles of 5 levels • Quintiles of 5 levels • 1=receiving at least one dispensation of studied medication with total cost <$15 during the observation period, otherwise=0 • 1=receiving at least one dispensation of studied medication within 365 days prior to the initial date of observation, otherwise=0

**Target chronic diseases: Hypertensive disease (ICD9:401-405 ;ICD10CA: I10-I13, I15), Coronary Heart Disease (ICD9:410-414 ;ICD10CA: I20-I25), Stroke(ICD9:430-438 ;ICD10CA: I60-69), Diabetes Mellitus(ICD9:250 ;ICD10CA: E10-E14), Hyperlipidemia(272 ;ICD10CA: E78), Depression(ICD9:311 ;F32). Cases were identified by at least two outpatients or one hospital diagnosis occurring during a two year period starting one-year before the index dispensation.*

Appendix 3 Number of Observations in Stratified Analysis

Stratification	Subgroups	Pre-SDP*	Post-SDP*
By age group	Age 65 and above	62,759	83,950
	Age 40-64	95,457	111,402
By cost of medication	≤$15 (a)*	8,294	8,706
	$16-30 (b)*	8,307	13,180
	>$30 (c)*	93,498	102,876
	Covered by other benefit plans (d) (excluded in this stratified analysis)*	*48,117*	*70,590*

Appendix 3 Number of Observations in Stratified Analysis *(Continued)*

Stratification	Subgroups	Pre-SDP*	Post-SDP*
By coverage of other benefit plans	Not covered by other benefit plans (i)*	101,805	116,056
	Covered by other benefit plans (ii)*	4,437	66,369
	Cost per dispensation ≤$15(iii) (excluded in this stratified analysis)*	*51,974*	*12,927*
By medication class	Statin	43,899	58,056
	ACEI/ARB*	62,348	75,439
	*CCB (excluded in this stratified analysis)**	*1,193*	*1,243*
	Metformin	16,548	21,224
	Glyburide	6,742	6,783
	SSRI*	18,395	21,662
	SNRI*	9,091	10,945
By user type	Incident users	31,072	36,052
	Prevalent users	125,270	157,426
	Incident users that appeared in both periods (excluded in this stratified analysis)	*1,874*	*1,874*
By age level	Age 40-64	95,457	111,402
	Age 65-69	19,786	24,664
	Age 70-74	18,219	22,538
	Age 75-79	14,667	19,359
	Age 80 and above	10,087	17,389
By sex	Male	74,922	94,146
	Female	83,294	101,206

**SDP=seniors' Drug Plan; Subgroup (a)= observations not in subgroup (d), and with at least one dispensation of total cost ≤$15;Subgroup (b), observations exclusive in subgroup (a), (c), and (d); Subgroup(c)=observations not in subgroup(a), or (d), and with at least one dispensation of total cost > $30; Subgroup (d) = observations with at least one dispensation of which patient self-payment <$15; Subgroup (i)=observations exclusive in subgroup (ii) and (iii); Subgroup (ii)=observations not in subgroup (iii), and with at least one dispensation of which patient self-payment <$15; Subgroup (iii) = observations with at least one dispensation of total cost ≤$15; ACEI = angiotensin-converting-enzyme inhibitor; ARB= angiotensin receptor blocker; CCB=calcium channel blocker; SSRI=selective serotonin reuptake; SNRI= serotonin-norepinephrine reuptake inhibitors.*