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DOES THE NUMBER OF PHARMACIES A PATIENT FREQUENTS AFFECT ADHERENCE TO STATINS?

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Abstract

Background
We hypothesized that medication adherence is affected by the number of pharmacies a patient frequents.

Objective
The objective was to estimate the strength of association between the number of pharmacies a patient frequents and adherence to statins.

Methods
Using administrative data from the Nova Scotia Seniors' Pharmacare program, a retrospective cohort study was conducted among subjects aged 65 years and older first dispensed a statin between 1998 and 2008. The Usual Provider of Care (UPC), was defined as the number of dispensation days from the most frequented pharmacy divided by the total number of dispensation days. Adherence was defined as a Medication Possession Ratio of 80% or greater. Data were analyzed using hierarchical linear regression.

Results
The cohort of 25,641 subjects was 59% female with a mean age of 74 years. During follow-up, subjects filled prescriptions in a median of 2 (mean = 2; standard deviation = 0.88) pharmacies and visited pharmacies a median of 28 (mean = 30) times. During that time, 61% of patients used one pharmacy exclusively. Among subjects using 1 pharmacy, 59% were adherent while 58% using more than one pharmacy were adherent. However, upon adjustment for differences in distributions of age, sex, and other confounders, subjects who used more than one pharmacy had 10% decreased odds of statin adherence (odds ratio: 0.90, 95% confidence interval: 0.86–0.96). These results were robust in sensitivity analyses.

Conclusions
Among seniors newly starting statin therapy, using a single community pharmacy was modestly associated with adherence.

Keywords: *medication adherence, community pharmacy, continuity of care*

BACKGROUND

The problem of medication non-adherence is so large that the World Health Organization (WHO) concluded that increasing medication adherence would be more beneficial for population health than developing new treatments.[1] This view was based on multiple reports that show approximately 50% of persons prescribed long-term medication are adherent 1 year after initiating treatment.[1] Many interventions have attempted to improve medication adherence with limited success; many other studies seek to identify

the factors that promote or inhibit adherence, hoping to identify targets for future interventions.[1–4]

We hypothesized that medication adherence is affected by the number of pharmacies a patient frequents; defined as the extent to which a single pharmacy dispenses all medications to the patient. This definition is adapted from the definition of continuity of physician care.[5]

Use of a single pharmacy could influence medication adherence by modifying patient beliefs about adherence and fostering a strong provider-patient relationship, which then translates to increased information uptake and utilization, and subsequently improved adherence, while also reducing the risk for medication-related problems.[6–8] However, a literature review of Medline, 1960 to August 2015, identified only one study that directly assessed this association.[9] Five additional studies identified patient characteristics associated with the use of a single pharmacy.[8,10–13] There are currently no studies that show that the use of a single pharmacy influences clinical outcomes.

Statins were chose to study the association between adherence and pharmacy attendance because they are frequently prescribed and non-adherence has been linked to many negative health and economic outcomes.[14,15]

The objective was to estimate the strength of association between number of pharmacies a patient frequents and adherence to statins.

METHODS

Study Design

This was a retrospective cohort study of subjects enrolled in the Nova Scotia Seniors' Pharmacare Program (NSSPP). Ethics review was obtained from the Dalhousie University Health Sciences Research Ethics Board in May, 2013 (Reference number: 2013–2971).

Data Sources

Data were obtained from Health Data Nova Scotia (HDNS) at Dalhousie University.[16] HDNS housed anonymously coded records from the NSSPP database, the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD), and the Medical Services Insurance (MSI) database. The NSSPP database contained patient level information as well as information on medications claimed for coverage. Enrollees in the NSSPP were seniors aged 65 years and older, who were residents of Nova Scotia with a valid Nova Scotia health card.[17] Seniors could not register in the program if they had any other public or private health insurance that covered most prescriptions.[18] The plan required enrolled seniors to pay a yearly premium as well as a co-payment for their prescriptions. At the beginning of this study, in the 1998–1999 fiscal year, 88% of seniors in the province were enrolled in the program.[19] Ten years later, in the 2007–2008 year 70% of eligible seniors in NS were enrolled in the program, receiving a total of 3,255,724 prescriptions.[20] Of residents enrolled in the program in the 2007–2008 year, 99% claimed a medication for reimbursement.[20] The program did not cover medications provided in hospital, outpatient clinics or corrections facilities. As with other Canadian public medication reimbursement program databases, the quality of the data contained in the NSSPP is thought to be high.[21–23] The CIHI-DAD contained a discharge summary of the demographic, administrative and clinical information from all hospital separations from acute care, same day surgery, rehabilitation or psychiatric facilities in Nova Scotia. The MSI database contained dates and records of insured physician services that were paid for by the Nova Scotia provincial health system.

Study Population

Subjects were included in this study if they were a member of the NSSPP at any time between January 1, 1996 and April 30, 2008 and had received a first (index) prescription for a statin medication after January 1st 1998 and at least one year after enrolment in the program. Patients were identified in the NSSPP by WHO ATC codes C10AA01- C10AA05 and C10AA07.[24] These codes correspond to the statins available in Canada. Subjects were excluded if they had; a statin prescription in the 2 years prior to January 1, 1998; not been enrolled on the NSSPP for at least one year prior to the first statin prescription; a WHO ATC code for cerivastatin (C10AA06), a diagnosis or procedure for dialysis or kidney transplant; or a prescription for a non-statin cholesterol lowering medication within the 365 days prior to the first statin prescription. Subjects were also excluded if they had only one dispensation date for any medication,

hereafter referred to as a pharmacy visit, prior to the first (index) statin.

Exposure

We determined single pharmacy use by calculating the UPC index.[5] The UPC was calculated as the number of dispensation days from the most used pharmacy divided by the total number of pharmacy dispensation days. The UPC was assessed at least one year but not more than 2 years prior to the first statin dispensation (Figure 1). All dispensations successfully submitted to the NSSPP that occurred during that time, regardless of medication class, were used to calculate the UPC. This period was chosen because, in Nova Scotia, medications are commonly filled at 30 to 90 day intervals, resulting in a minimum of 4 prescriptions fills for chronic medications each year. Shorter pre-statin periods could inflate the values of continuity for those subjects.[25] Subjects who redeemed multiple medications on the same fill date were considered to have received one dispensation on that date in order to accurately reflect the number of visits to each pharmacy.

The UPC was analyzed as a dichotomous variable; a score of 1.0 indicated that the subject had only used a single pharmacy, and scores less than 1.0 indicated that more than one pharmacy was used. The UPC has been referred to as "pharmacy loyalty" or the "fidelity coefficient" in previous studies.[10,13]

Outcome

Adherence was approximated by the Medication Possession Ratio (MPR), which is the ratio of the number of days of medication supplied during the adherence assessment period to the number of days in the adherence assessment period.[26] In this study, the MPR was calculated for the 365 days immediately following the first statin prescription (see Figure 1). Subjects were considered to be adherent if their MPR was ≥ 0.80, which is the usual cut-point for signifying adherence to cardiovascular medications.[21,27,28] The MPR was calculated for the statin medication class, not for individual statins within the class.

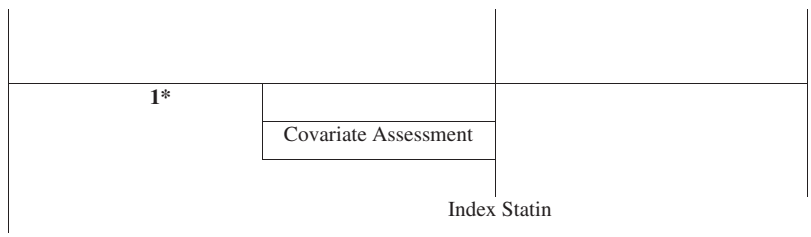
Covariates

Ten potential confounders that may have influenced the exposure-outcome relationship were determined *a priori*, based on the current literature, biological/social plausibility and the ability to calculate them.[2,5,29–38] Covariates were collected at the time of the first statin prescription, and were gathered from the preceding one year. Demographic variables included: subject age, sex, hypertension diagnosis, average 2001 household income by census enumeration area, and urban or rural place of residence. A binary variable indicated the use of greater than 4 distinct prescribed medications dispensed at the WHO ATC code level, hospitalization in the year prior to index, and having greater than 4 physician visits in the year prior to index. Statin dose (low or high) was determined using the definition published by Law and colleagues in the *British Medical Journal*.[39] The number of unique physicians who prescribed a statin was measured during the 365 days after the first statin dispensation.

Analysis

Statistical analysis was completed using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA). The statistical significance for all tests was set to $\alpha = 0.05$. The unit of analysis was the person to whom the statin was dispensed. Hierarchical linear regression, clustered by index pharmacy was used to estimate the strength of

FIG 1. Study timeline.



association between the UPC index and adherence to statins, measured by the MPR. Clustering was used to take into account the variability at both the pharmacy and subject levels, while allowing the pharmacy effect to be analyzed.[40,41] A binomial distribution of the MPR was used in the model. In addition to the UPC, the final model was designed to contain the 10 selected patient level covariates. Sensitivity analyses were conducted by changing the adherence level to a MPR of 0.75 and 0.90, restricting the study population to subjects living in urban areas or to subjects who had been hospitalized in the year prior to their index statin because these populations may have had altered adherence and/or continuity behaviour. Additional sensitivity analysis, restricting the study population to subjects who had filled thirteen or fewer statin prescriptions during the adherence assessment period was also conducted.

RESULTS

A total of 31,592 subjects with a first statin prescription between January 1, 1998 and April 30, 2008 met inclusion criteria. These subjects were dispensed a total of 1,532,464 prescriptions in the 2 years prior to their index statin, a mean of 48.5 per person. After exclusions (details in Figure 2), 25,641 (81.2%) of the original subjects remained in the dataset.

Demographic characteristics of the study population are found in Table 1. The cohort comprised of 25,641 subjects, was 59% female had a mean age of 74 years. Subjects filled prescriptions in a median 2 (mean = 2; standard deviation = 0.88) pharmacies, visited pharmacies a median of 28 (mean = 30) times and received a median of 44 (mean = 51.6; standard deviation = 47.8) dispensations. Median annual household income was $44,800 (mean = $46,500; standard deviation =$16,000). Most subjects received a low-dose statin as their index prescription. During the adherence assessment period, subjects were dispensed a statin a median of 5 (mean = 6.0; standard deviation = 3.8) times.

Pharmacy use was skewed toward 1.0, with 60.9% of subjects having a UPC equal to 1.0, indicating exclusive use of one pharmacy. The mean UPC was 0.92 (standard deviation: 0.15). The median UPC was 0.89 and the interquartile range was 0.50. Among the 39.1% of patients with a UPC less than 1.0, the mean UPC was 0.79 (standard deviation: 0.17). The mean MPR for the study population was 0.73 (standard deviation: 0.31), and was skewed toward 1.0 with 58.9% of subjects having an MPR greater than or equal to 0.80. The median UPC was 1.0 and the interquartile range was 0.10. Adherence was observed in 59% of subjects who used a single pharmacy and in 58% who used more than one pharmacy.

Table 2 shows the patient characteristics associated with single pharmacy use. Female sex was associated with lower odds of single pharmacy use, while those

FIG 2. Summary of subject selection.

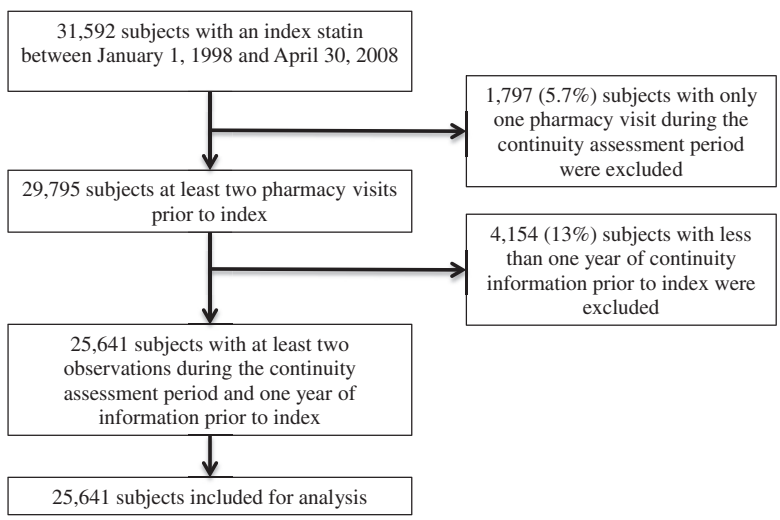


TABLE 1A Demographic and clinical characteristics of subjects who met inclusion criteria[a] (Categorical Variables)

(*N*) = 25,641		% (*N*)
Sex	Male	41.4 (10,614)
	Female	58.6 (15,027)
Age, years	65-69	29.6 (7,600)
	70-74	29.5 (7,555)
	75-79	21.8 (5.576)
	≥ 80	19.2 (4,910)
Income tertile[b]	High	32.1 (8,246)
	Moderate	32.1 (8,249)
	Low	32.1 (8,236)
	Unknown	03.6 (910)
Place of residence	Urban	58.6 (15,024)
	Rural	41.4 (10,611)
	Unknown	0.02 (6)
Use of greater than four medications[c]	Yes	79.6 (20,401)
	No	20.4 (5,240)
Hospitalized[c]	Yes	38.0 (9,756)
	No	62.0 (15,885)
Greater than four physician visits[c]	Yes	91.4 (23,444)
	No	08.6 (2,197)
Statin dose[d]	High	33.4 (8,559)
	Low	66.6 (17,082)
Hypertension	Yes	56.5 (14,496)
	No	43.5 (11,145)

[a]Dispensed first statin at least one year after enrolling in the Nova Scotia Seniors' Pharmacare program; at least two dispensation dates for any medication prior to the first statin. No dispensation for cerivastatin; or any other cholesterol lowering medication; no diagnosis of renal dialysis or renal transplant in the year prior to the first statin.
[b]Average 2001 household income in thousands of dollars, by census enumeration area.
[c]During continuity assessment period.
[d]Low dose: atorvastatin < 20 mg, simvastatin < 40 mg, rosuvastatin < 10 mg or any dose of pravastatin, lovastatin or fluvastatin. High dose: all other molecules and strengths.

who took less than 4 medications, those who saw a physician less than four times during the year prior to index, and those who had not been hospitalized in the year prior to the index statin had increased odds of single pharmacy use. After adjustment, urban or rural place of residence was not associated with increased odds of using a single pharmacy.

The unadjusted model indicated that subjects who frequented multiple pharmacies had slightly reduced odds of adherence compared to subjects who used a single pharmacy (odds ratio: 0.96, 95% confidence interval: 0.91–1.01). After adjustment, subjects who used multiple pharmacies had 10% decreased odds of adherence compared to subjects who used a single

TABLE 1B Demographic and Clinical Characteristics of Subjects Who Met Inclusion Criteria[a] (Continuous Variables)

(*N*) = 25,641	Mean	SD	Mean (One Pharmacy)	Mean (>1 Pharmacy)	*p*-value
Age	73.91	6.13	73.64	74.33	<0.001
Income[b]	46,525.33	15,991.48	46,304.54	46,873.17	0.006
Pharmacies used[c]	1.57	0.88	1.00	2.46	<0.001
Pharmacy visits[c]	30.40	22.53	28.52	33.32	<0.001
Dispensations[c]	51.6	47.8	48.05	57.20	<0.001

[a]Dispensed first statin at least one year after enrolling in the Nova Scotia Seniors' Pharmacare program; at least two dispensation dates for any medication prior to the first statin. No dispensation for cerivastan or any other cholesterol lowering medication; no diagnosis of renal dialysis or renal transplant in the year prior to the first statin.
[b]Average 2001 household income in thousands of dollars, by census enumeration area.
[c]During continuity assessment period.

TABLE 2 Unadjusted and Adjusted Odds Ratios of the Relationship Between Single Pharmacy Use and Sociodemographic and Clinical Variables in Nova Scotia Seniors' Pharmacare Beneficiaries Meeting Inclusion Criteria[a]

n=25,641		Unadjusted		Adjusted	
		OR	95% CI	OR	95% CI
Sex	Male	1.00		1.00	
	Female	0.88	0.83–0.92	0.89	0.84–0.94
Age (years)	≥80	1.00		1.00	
	75–79	1.17	1.09–1.27	1.11	1.02–1.20
	70–74	1.17	1.09–1.26	1.05	0.97–1.13
	65–69	1.38	1.28–1.48	1.18	1.10–1.28
Income tertile[b]	High	1.00		1.00	
	Mod	1.13	1.06–1.21	1.13	1.06–1.21
	Low	1.10	1.03–1.17	1.11	1.04–1.19
	Unknown	0.77	0.67–0.88	0.78	0.67–0.89
Place of residence	Urban	1.00		1.00	
	Rural	0.95	0.90–1.00	1.02	0.97–1.08
	Unknown	0.77	0.14–4.18	1.75	0.31–9.62
Use of greater than four medications[c]	Yes	1.00		1.00	
	No	1.80	1.69–.92	1.56	1.45–1.67
Hospitalized[c]	Yes	1.00		1.00	
	No	1.46	1.39–1.54	1.30	1.23–1.37
Greater than four physician visits[c]	Yes	1.00		1.00	
	No	1.82	1.65–2.00	1.36	1.22–1.50
Hypertension	Yes	1.00		1.00	
	No	0.97	0.92–1.02	0.96	0.91–1.01

[a]Dispensed first statin at least one year after enrolling in the Nova Scotia Seniors' Pharmacare program; at least 2 dispensation dates for any medication prior to the first statin. No dispensation for cerivastatin; or any other cholesterol lowering medication; no diagnosis of renal dialysis or renal transplant in the year prior to the first statin.
[b]Average 2001 household income, by census enumeration area.
[c]During the continuity assessment period.

TABLE 3 Adjusted Relationship between Single Pharmacy Use and Statin Adherence among Subjects Who Met Inclusion Criteria[a]

		Unadjusted		Adjusted	
		OR	**95% CI**	**OR**	**95% CI**
UPC[b]	1.0	1.0	1.00	1.00	
	<1.0	0.96	0.91–1.01	0.90	0.85–0.95
Sex	Male	1.0		1.00	
	Female	0.91	0.86–0.95	0.94	0.89–0.99
Age (years)	≥ 80	1.0		1.00	
	75–79	1.10	1.02–1.19	1.13	1.05–1.23
	70–74	1.10	1.02–1.18	1.18	1.09–1.27
	65–69	1.01	0.94–1.09	1.13	1.04–1.22
Income tertile[c]	High	1.0		1.00	
	Mod	0.90	0.84–0.96	0.91	0.85–0.97
	Low	0.85	0.80–0.91	0.85	0.80–0.91
	Unknown	1.00	0.86–1.15	0.98	0.85–1.14
Place of residence	Urban	1.0		1.00	
	Rural	0.94	0.89–1.00	0.96	0.90–1.02
Use of greater than four medications[d]	Yes	1.0		1.00	
	No	0.82	0.77–0.87	0.97	0.90–1.04
Hospitalized[d]	Yes	1.0		1.00	
	No	0.76	0.75–0.81	0.96	0.90–1.01
Greater than four physician visits[d]	Yes	1.0		1.00	
	No	0.81	0.74–0.88	0.97	0.88–1.07
Statin dose[e]	High	1.0		1.00	
	Low	0.953	0.93–1.01	1.02	0.97–1.08
Hypertension	Yes	1.0		1.00	
	No	0.83	0.79–0.87	0.85	0.80–0.89
Number of prescribers[f]	1	1.0		1.00	
	>1	2.50	2.35–2.67	2.46	2.30–2.62

[a]*Dispensed first statin at least one year after enrolling in the Nova Scotia Seniors' Pharmacare program; at least two dispensation dates for any medication prior to the first statin. No dispensation for cerivastatin; or any other cholesterol lowering medication; no diagnosis of renal dialysis or renal transplant in the year prior to the first statin.*
[b]*Usual provider of care index.*
[c]*Average 2001 household income, by census enumeration area.*
[d]*During the continuity assessment period.*
[e]*Low dose: atorvastatin < 20 mg, simvastatin < 40 mg, rosuvastatin < 10 mg or any dose of pravastatin, lovastatin, or fluvastatin. High dose: all other molecules and strengths.*
[f]*During the adherence assessment period.*

pharmacy (odds ratio 0.90, 95% confidence interval: 0.86–0.96). The results of the adjusted relationship are found in Table 3. Women, subjects using 4 or less medications, subjects without hypertension and subjects with lower income had decreased odds of adherence. Subjects younger than age 80 years and subjects with more than one statin prescriber had increased odds of adherence compared to subjects with only one statin prescriber. Place of residence (urban/rural) had no apparent impact on adherence.

Altering the levels of MPR to 0.75 and 0.90 and restricting the study population to subjects residing in urban areas at the time of the index statin dispensation, to subjects who had been admitted to hospital during

the year prior to their index statin dispensation or to those who received 13 or fewer statin dispensations did not change the direction of the result (see Table 3).

DISCUSSION

This study showed that NSSPP beneficiaries who frequented multiple pharmacies have a 10% decreased odds of adherence compared to subjects who frequented a single pharmacy for their medications (odds ratio: 0.90, 95% confidence interval: 0.86–0.96). This finding has never been reported among users of a long-term cardiovascular medication. However, after a literature search, one abstract was found that showed that among adult patients with schizophrenia, those who used a single pharmacy for all of their dispensations had a 30% increased odds of adherence to antipsychotic medications compared to subjects using more than one pharmacy.[9]

The level of adherence and single pharmacy use obtained in this study were similar to those reported in prior research. In this study, 58.9% of subjects had a MPR of 0.80 or above and were classified as adherent to their statin over the one-year follow-up period. This is similar to previous studies assessing statin adherence, which reported adherence rates close to 50% after one year.[29,42,43] In this study 60.9% of subjects attended a single pharmacy during the pre-statin period. This is similar to the 57.8% who used a single pharmacy in a previous study of adult patients with schizophrenia.[13] However, our result is much lower than that of a study in the Netherlands, where 89% of subjects used a single pharmacy for all of their prescriptions, and lower than a recent CIHI report which found that 69% of seniors in Canada used only one pharmacy during a one year period.[8,12] Three previous studies have detailed patient characteristics associated with exclusive pharmacy attendance. Similar to previous work, we found that increasing age is associated with increased single pharmacy use and that female sex and the use of greater than 4 medications is associated with the use of multiple pharmacies.[8,13] We observed that hospitalization was associated with multiple pharmacy use. It is not known if this behaviour occurred prior to hospitalization because patients were sicker, or if it occurred after hospitalization when they may have been prescribed new medications.

We hypothesized that single pharmacy use promoted adherence because it resulted in a complete record of all medications at a single pharmacy which allowed the pharmacist to identify non-adherence. Also, single pharmacy use may have promoted a strong pharmacy-patient relationship, which allowed the pharmacist to better work with patients to improve adherence.[7] However, it is possible that patients more likely to be adherent were also more likely to use a single pharmacy. Although this study indicated that single pharmacy use was associated with increased medication adherence, the association will need to be shown in different study populations, for different classes of medication and over longer time periods. If the association persists, we have provided a good description of which subjects are more likely to use a single pharmacy. If the findings are consistent, among these populations, patient behaviour and system design needs to be arranged so that the use of a single pharmacy is encouraged.

Limitations

There are some limitations of this study that may that may impact the validity of the results. The use of an administrative database limited us to the data that is contained on the NSSPP standard collection form. This introduced potential confounding due to lack of optimal information. We attempted to minimize this confounding by clustering patients at their most used pharmacy and by controlling for confounders that have been detailed in previous studies. However, we were unable to adjust the model for other confounders that could influence the relationship such as frailty, life expectancy, statin adverse effects and pharmacy effects such as prescription volume, number of pharmacy staff and pharmacist years of practice.

Enrolment into the NSSPP is not mandatory and approximately 30% of Nova Scotian seniors were not enrolled in the program at the end of the study period.[20] It is likely that these persons were not missing at random: seniors not enrolled have been found to have a higher income, be taking less medications, have lower medication costs and/or to be in good health compared to program enrollees; all characteristics that may have predisposed them to higher adherence.[30,32,46] Persons with fewer medications and higher income may be

more likely to use a single pharmacy.[13] Therefore, the result may only strictly be generalized to seniors with medication coverage.

In this study we assessed the relationship between adherence to a single class of medications and the number of pharmacies used, however it is likely that participants are taking medications in addition to their statin. It is unclear if the found relationship between adherence and single pharmacy use is consistent among participants taking multiple medications. Subjects with a higher cardiovascular risk will be taking many medications in addition to their statin. Without a measure of cardiovascular risk in this study, we do not know if participants exhibiting poor adherence fit into a higher risk group than participants with low adherence. It is possible that cardiovascular risk is an effect modifier to the relationship between single pharmacy use and adherence.

CONCLUSIONS

Among seniors newly starting statin therapy, using a single community pharmacy was modestly associated with adherence. Further research will be needed to investigate whether pharmacy-based interventions might improve adherence and clinical outcomes.

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