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Impact of Multiple Pharmacy Use on Medication Adherence and Drug-drug Interactions in Older Adults with Medicare Part D

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Abstract

Objective—To assess the association between multiple pharmacy use and medication adherence and potential drug-drug interactions (DDIs) among older adults.

Design, Setting, and Participants—Cross-sectional propensity score-weighted analysis of 2009 claims data from a nationally representative sample of 926,956 Medicare Part D beneficiaries aged >65 continuously enrolled in fee-for-service Medicare and Part D that year, and filled >1 prescription at a community/retail or mail order pharmacy. Multiple pharmacy use was defined as concurrent (overlapping time periods) or sequential use (non-overlapping time periods) of >2 pharmacies in the year.

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Author Contributions

Drs. Marcum and Driessen had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Marcum, Driessen, Thorpe, Gellad, Donohue.

Acquisition of data: Donohue.

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Measurements—Medication adherence was calculated using a proportion of days covered 0.80 for eight therapeutic categories (β -blockers, renin angiotensin system antagonists, calcium channel blockers, statins, sulfonylureas, biguanides [i.e., metformin], thiazolidinediones, and dipeptidyl peptidase-IV inhibitors). Potential DDIs arising from use of certain drugs across a broad set of classes were defined as the concurrent filling of two interacting drugs.

Results—Overall, 38.1% of the sample used multiple pharmacies. Those using multiple pharmacies (both concurrently and sequentially) consistently had higher adjusted odds of non-adherence (ranging from 1.10 to 1.31, $p < 0.001$) across all chronic medication classes assessed after controlling for socio-demographic, health status and access to care factors, compared to single pharmacy users. The adjusted predicted probability of exposure to a DDI was also slightly higher for those using multiple pharmacies concurrently (3.6%) compared to single pharmacy users (3.2%, AOR 1.11, 95% CI 1.08–1.15) but lower in individuals using multiple pharmacies sequentially (2.8%, AOR 0.85, 95% CI 0.81–0.91).

Conclusions—Filling prescriptions at multiple pharmacies was associated with lower medication adherence across multiple chronic medications, and a small but statistically significant increase in DDIs among concurrent pharmacy users.

Keywords

pharmacy; medication adherence; drug interactions; Medicare

INTRODUCTION

Older adults account for 12% of the US population but consume over a third of prescription medications.^{1,2} The average community-dwelling older adult fills between 40 to 50 prescriptions per year and visits a community pharmacy nearly twice per month.^{3,4} Most older adults consistently fill all of their prescriptions at a single pharmacy, however, studies show that a minority of older adults use multiple pharmacies.^{3,4} Use of multiple pharmacies may stem in part from financial incentives. In what is an increasingly competitive industry, community pharmacies now offer patients steep discounts such as low or no cost generic fills as well as gift cards and coupons for new and transferred prescriptions.⁵

Little is known about the benefits and harms of multiple pharmacy use.^{3,4} On the one hand, use of multiple pharmacies may improve convenience to the consumer and may lower out of pocket costs, which may improve medication adherence.^{6,7} On the other hand, consistent use of a single pharmacy could enhance medication adherence by fostering regular communication with a pharmacist on drugs' uses, benefits and side effects; use of a single pharmacy may also lead to less confusion for the older adult with medication management. Surveys indicate that older adults have a high level of trust in their pharmacists to provide information on drug effectiveness and cost.^{8,9} Furthermore, pharmacists can improve adherence by issuing refill reminders, using motivational interviewing techniques and through medication therapy management (MTM).^{10,11} Pharmacists may also improve drug safety by avoiding dispensing of drugs causing potential drug-drug interactions (DDIs) by close monitoring of data on prescriptions filled.¹²

Using a nationally representative sample of Medicare Part D enrollees, we examined the extent of multiple pharmacy use and its association with medication adherence and potential DDIs in older adults. We hypothesized that adherence would be higher and that presence of DDIs would be lower in single pharmacy users.

METHODS

Study Population

We obtained 2009 Medicare claims (Parts A, B, and D) and enrollment data for individuals in the Chronic Conditions Warehouse 10% random sample of Part D beneficiaries who were continuously enrolled in a stand-alone prescription drug plan and alive throughout that year (n=1,529,825). We included beneficiaries if they were ≥65 years of age on January 1, 2009 and filled ≥1 prescription at a commercial/retail or mail order pharmacy during the study period (n=926,956). We excluded those who were missing any pharmacy identifying information (<1%) or filled any prescriptions at other pharmacy types (e.g., long-term care, home infusion, Indian Health Service, Department of Veterans Affairs, institutional, specialty, nuclear, and compounding; 15.8%). The study was approved by the University of Pittsburgh Institutional Review Board.

Study Variables

Outcome Measures—Medication adherence was measured using the proportion of days covered (PDC), defined as the number of days in a period ‘covered’ by a medication divided by number of days in the period.^{13,14} Compared to another commonly used measure of adherence via pharmacy claims (i.e., Medication Possession Ratio), the PDC avoids overestimating adherence when patients refill a medication before the previous prescription runs out.^{13,14} The PDC is a National Committee for Quality Assurance (NCQA)/National Quality Forum (NQF)-endorsed measure for medication adherence and is used in the Medicare Star Ratings.¹⁵ We defined the measurement period as starting with the beneficiary’s date of first fill of a medication in one of the classes of interest, and ending on December 31, 2009. The days’ supply for each prescription fill was captured from the “days’ supply” field in the PDE dataset (i.e., no calculations were required to determine days’ supply). Of note, the days’ supply with the terminal dispensing was truncated on the last day of observation and not included in the PDC calculation for any supply beyond that to avoid overestimating adherence. Consistent with the NQF quality measures, we constructed a dichotomous measure of medication adherence (PDC ≥0.80) in each of eight therapeutic classes widely used by older adults (β-blockers, renin angiotensin system antagonists (RASA), calcium channel blockers (CCB), statins, sulfonylureas, biguanides (i.e., metformin), thiazolidinediones (TZD), and dipeptidyl peptidase (DPP)-IV inhibitors).^{13,14}

Second, we constructed a dichotomous measure for presence of a potentially clinically significant DDI. Using an algorithm by Malone *et al* and information from medication package inserts, we identified beneficiaries filling two of several interacting medications (available upon request) during the same time period.^{16–18} Presence of a DDI was defined as

1 overlapping day in which the beneficiary possessed two interacting medications. Only oral, non-topical dosage forms were included in the DDI analysis.

Independent Variables—Multiple pharmacy use can be defined in several ways (see Box for operational definitions).^{3,4} One key issue is whether multiple pharmacy use is concurrent or sequential, as may be the case for ‘snowbirds’ who live part of the year in another state or who switch pharmacies at some point in the year. As such, we defined three non-overlapping groups: 1) single pharmacy use for the entire year, 2) sequential multiple pharmacy use in the year, or 3) at least one instance of concurrent multiple pharmacy use. Specifically, we first used the number of different pharmacy ID codes from the Part D pharmacy characteristics file to classify patients as using a single pharmacy or multiple pharmacies¹⁹ and then used the fill dates to further classify those who used multiple pharmacies as doing so sequentially versus concurrently. Sequential multiple pharmacy use was defined as filling at least one prescription at 2 pharmacies without overlapping fill dates throughout the year. Concurrent multiple pharmacy use was defined as filling at least one prescription at 2 pharmacies with at least some overlap in fill dates throughout the year. In addition, we defined a *primary pharmacy* for each beneficiary as the pharmacy where the plurality of prescriptions were filled in 2009.³

Box

Terminology Used for Pharmacy Use

Term	Operational Definition
Primary pharmacy	The pharmacy where a beneficiary filled the majority of their prescriptions during 2009
Concurrent pharmacy use	Filling at least one prescription at 2 pharmacies across overlapping time periods throughout the year For example, a beneficiary who filled a prescription at pharmacy A in February and April as well as a prescription at pharmacy B in March would be classified as concurrent multiple pharmacy use.
Sequential pharmacy use	Filling at least one prescription at 2 pharmacies without overlapping time periods throughout the year For example, a beneficiary who filled a prescription at pharmacy A in February, March, and April, and then filled a prescription at pharmacy B May through December (and never filled again at pharmacy A) would be classified as a sequential multiple pharmacy user.
Affiliated pharmacy	A pharmacy that has a chain or franchise relationship with another entity/pharmacy.
Unaffiliated pharmacy	A pharmacy that does not have a chain or franchise relationship with another entity/pharmacy.

Another key issue in defining multiple pharmacy use is whether it occurs within a pharmacy chain albeit different physical locations (affiliated), or across chains (unaffiliated).

Pharmacists operating at different locations within the same chain may not know the patient’s medication history in detail but may have access to complete electronic data on prescriptions filled. We used the ‘relationship type’ variable in the Part D pharmacy characteristics file to determine if the pharmacy had a chain or franchise relationship with another entity. We hypothesized that the effects of multiple pharmacy use might be different

for pharmacies with the same corporate parent than for pharmacies with different corporate parents.

Covariates—We grouped covariates into three main categories: socio-demographics (i.e., predisposing), access to care (i.e., enabling) and health status (i.e., medical need) factors.²⁰ Socio-demographics included age, sex, and race/ethnicity. Access to care variables included a composite indicator of low-income subsidy (LIS) and/or dual eligible status as well as presence of a national Part D plan (i.e., a plan that offers a benefit package in all 34 US Prescription Drug Plan [PDP] regions). We also assessed the impact of including fixed-effects for Part D plan as a covariate to adjust for any plan-level use of tools that may affect adherence (cost-sharing) or DDIs (medication monitoring). In addition, zip code was used to calculate beneficiaries' geographic location (rural vs. urban), and we calculated the total number of unique prescribers for each beneficiary during 2009.²¹ For health status, we included the beneficiary's total number of unique medications dispensed at all pharmacies in 2009, an indicator for end-stage renal disease, and nine chronic conditions captured in the Chronic Condition Data Warehouse (CCW) for which medication adherence and DDIs are important (i.e., diabetes, heart failure, hypertension, hyperlipidemia, asthma, chronic obstructive pulmonary disease, osteoporosis, osteoarthritis/rheumatoid arthritis, and depression).²² In addition, we created a Charlson Comorbidity Index score.²³ We also adjusted for whether the primary pharmacy was community/retail or mail order, and whether it was an independent, chain, or other. Finally, we created a dichotomous variable for any mail order use.

Statistical Analysis—We conducted analyses using Stata version 11.0 (Stata-Corp LP, College Station, TX). Descriptive statistics were examined for all variables, and t-tests and chi-square tests were used to assess differences according to single vs. multiple pharmacy use for continuous and categorical variables, respectively. To control for potential differences in health status between beneficiaries using single vs. multiple pharmacies, we used current best practices for multiple propensity score weighting in multinomial treatment analysis.^{24,25} As such, we estimated a multinomial logistic regression model to calculate the probabilities of an individual using a single pharmacy, multiple pharmacies sequentially, or multiple pharmacies concurrently, adjusted for all socio-demographic, access to care, and health status variables. Those probabilities were used to generate inverse probability of treatment (IPT) weights, which are the inverse of the probability an individual receives the 'treatment' (i.e., multiple concurrent, multiple sequential, or single pharmacy use).^{24,26} To assess the extent to which the propensity score weighting achieved balance of covariates, we examined differences in covariate values by the three groups of pharmacy users before and after applying the IPT weights using linear, logistic, and multinomial logistic regression depending on the nature of the covariate. The IPT weights were then used to weight the observations in two separate logistic regression models examining the effects of multiple pharmacy use on medication adherence and potential DDIs. Finally, we estimated adjusted predicted probabilities for both outcomes using Stata's "margins" command. The delta method was used to calculate 95% confidence intervals (CIs), which allows for correlation between observations. All regression models used robust estimates of variance.

In order to test for robustness, we conducted a series of sensitivity analyses. First, in our primary analysis we defined multiple pharmacy use based on different physical locations (even within the same chain or parent company). In a secondary analysis, we re-ran analyses using the more restrictive measure of multiple pharmacy use that defined multiple pharmacy use only as filling prescriptions at multiple physical locations with different parent companies. Second, we tested the effect of only assessing community/retail pharmacies (excluding mail order) on both outcomes. Third, we examined the PDC as a continuous variable and used different cut points (e.g., 0.60, 0.70) to assess robustness for the adherence outcome. We also examined the effect on the PDC of excluding those beneficiaries filling only one prescription, those who were hospitalized throughout the year, and those who were LIS beneficiaries. Fourth, we conducted an analysis on the DDI outcome using a more stringent definition of multiple pharmacy use that required the interacting medications to be filled at different pharmacies. In addition, we assessed more restrictive definitions of the presence of a DDI (i.e., 10 and 30 overlapping days of interacting drugs). The results of these sensitivity analyses were qualitatively similar in direction and magnitude to the main analyses.

RESULTS

Sample Characteristics

Table 1 displays sample characteristics overall and stratified by pharmacy use patterns. Overall, 38.1% of the sample used multiple pharmacies; among those using multiple pharmacies (n=352,964), 80.3% used multiple pharmacies concurrently. Overall health status appeared to be the worst for the group filling at multiple pharmacies concurrently. Compared to single pharmacy users, concurrent multiple pharmacy users obtained a greater number of unique medications (11.0 vs. 8.1; $p<0.001$), had higher prevalence of all chronic conditions assessed, had more prescribers (4.5 vs. 3.1; $p<0.001$), and were more likely to use a mail order pharmacy as the primary pharmacy (15.0% vs. 1.0%; $p<0.001$) (Table 1). Those filling at multiple pharmacies sequentially also had greater use of mail order pharmacy as the primary pharmacy (7.1% vs. 1.0%; $p<0.001$) compared to those filling at a single pharmacy. After multiple propensity score weighting and adjustment, most of the initial differences among the pharmacy use groups were insignificant while the remaining significant differences were reduced substantially in magnitude (Table 2).

Multiple Pharmacy Use

Compared to beneficiaries filling at multiple pharmacies sequentially, those filling at multiple pharmacies concurrently used significantly more pharmacies throughout the year (2.65 vs. 2.19; $p<0.001$) with a smaller proportion of the medications filled at their primary pharmacy (0.80 vs. 0.85; $p<0.001$).

Medication Non-Adherence

Overall, 26.1% of seniors taking CCBs to 41.5% of seniors taking TZDs were found to be non-adherent to the chronic medication classes assessed (data not shown). Those using multiple pharmacies (both concurrently and sequentially) consistently had higher unadjusted likelihood of non-adherence (Figure). The same patterns held after adjusting for various

socio-demographic, health status and access to care factors via propensity score analysis (Table 3). For example, the adjusted predicted probability of single pharmacy users being non-adherent to β -blockers was 29.8%, compared with 32.0% of individuals using multiple pharmacies concurrently (vs. single pharmacy use, AOR 1.11, 95% CI 1.09–1.13; Table 3) and 34.1% of individuals using multiple pharmacies sequentially (vs. single pharmacy use, AOR 1.22, 95% CI 1.18–1.26; Table 3).

Potential Drug-drug Interactions

Overall, 4.2% (n=38,953) were found to have at least one potential DDI (data not shown). Those using multiple pharmacies concurrently had the highest adjusted likelihood of a potential DDI (3.6%) compared to single pharmacy users (3.2%; AOR 1.11, 95% CI 1.08–1.15; Table 4). Conversely, the adjusted predicted probability of a potential DDI was lower in sequential multiple pharmacy users (2.8%) than in single pharmacy users (3.2%; AOR 0.85, 95% CI 0.81–0.91; Table 4). For those who used more than one pharmacy and had at least one potential DDI, 38.4% of the interactions involved medications filled at different pharmacies. Warfarin was implicated in eight of the 10 most frequent DDIs. In post-hoc analysis, we found that 42.4% of beneficiaries using warfarin were using multiple pharmacies.

DISCUSSION

This study examined medication adherence and drug interactions among older adults filling prescriptions at multiple pharmacies in Medicare Part D. We found that use of multiple pharmacies is common (38.1% of beneficiaries) and is associated with deleterious effects on medication adherence and potential safety concerns among older adults. Filling prescriptions at multiple pharmacies was associated with lower medication adherence across a range of chronic medications. In addition, multiple pharmacy use was associated with a small increase in DDIs among those with concurrent multiple pharmacy use and a small decrease among those with sequential multiple pharmacy use. To our knowledge, there have been no other published reports that examined the association between multiple pharmacy use and medication adherence and safety in Medicare beneficiaries.

We found that any use of multiple pharmacies was associated with a 10% to 31% increased odds of medication non-adherence compared to single pharmacy use across all chronic medication classes assessed. There are several potential mechanisms through which multiple pharmacy use could lead to worse medication adherence. For example, multiple pharmacy use may lead to incomplete or erroneous medication regimen documentation, and pharmacists may not be able to deliver the most effective counseling to improve adherence. In addition, multiple pharmacy use may hinder formation of a longitudinal relationship between the patient and the pharmacist. It may also lead to confusion for the older adult with managing their medications. Moreover, multiple pharmacy use may lead to poor communication between the patient and health care providers, including physicians, nurses, and pharmacists. In a recent study, poor communication with health care providers (as rated by patients) was found to be associated with objectively measured poor medication adherence to oral diabetes, lipid lowering, or antihypertensive medications.²⁷ More

consistent use of a single pharmacy (a ‘pharmacy home’) may in fact improve communication by establishing a consistent medication record and a longitudinal relationship between the patient and pharmacist.⁵ Furthermore, future study is needed to better identify those patients at risk for medication non-adherence, and multiple pharmacy use could be one such predictor.

Rates of potential DDIs in our study were consistent with previous studies.^{1,17} Our hypothesis that using multiple pharmacies concurrently is the highest-risk filling behavior for experiencing a potential DDI was supported by our findings. However, it is not entirely clear why sequential use of multiple pharmacies was associated with a lower rate of a potential DDI compared to single pharmacy use. It may be that these beneficiaries received a new review of their medication regimen when they switched to a new pharmacy, although we were not able to measure pharmacy-level activities in this study.

Pharmacists screen for DDIs using pharmacy software, and many Pharmacy Benefit Managers and claims processors conduct real-time reviews of medication regimens.^{16,17} If a potential DDI is detected, the pharmacist receives an alert; however, pharmacists are facing increasing workloads and may receive multiple alerts per submitted claim, leaving many DDI alerts overridden or overlooked.¹⁷ Furthermore, community pharmacists have reported a lack of confidence in having a complete medication history for patients using multiple pharmacies and thus may be even more likely to override DDI alerts for such patients.⁵ While some of the interacting drugs can be used safely together with adequate patient education and monitoring, DDIs can lead to serious patient harm and hospitalization.^{17,28} In one study, the interaction between warfarin and NSAIDs (involved in 5 of the top 10 most common DDIs in our analysis) was associated with a five-fold increase in risk for serious GI bleeding compared to those taking warfarin alone.²⁹

Our results have important implications. Although it may be impractical for all patients to use a single pharmacy, at the very least pharmacies should have access to all medication-related information for their patients.¹⁹ In the interim, as suggested by Polinski et al, pharmacists and pharmacy personnel could routinely ask questions such as, “What other medications are you taking that you do not fill here at our pharmacy?”; and “Does someone else fill prescriptions for you at a different pharmacy?”³ In addition, prescribers and pharmacists can encourage patients to use a single pharmacy for safety purposes, and pharmacies can work to help patients synchronize their refill dates.³⁰ These findings could also be used by Part D plans to better identify those beneficiaries who may need interventions regarding medication adherence and/or DDIs. Moreover, it is interesting to note that beneficiaries using multiple pharmacies concurrently were utilizing significantly more providers than those using a single pharmacy; use of multiple providers could lead to further confusion for the older adult with medication management and possibly increasing the risk of adherence and DDI issues. Likewise, those beneficiaries in the multiple pharmacy use groups used a mail order pharmacy significantly more often than those in the single pharmacy use group.

Our study has several limitations. First, we used pharmacy claims of fills to serve as a proxy for medication adherence. As such, we were only able to measure medication supply and not

actual adherence; however, this approach is commonly used in quality measurement for medication adherence. Second, although we accounted for several key socio-demographic, health status, and access to care factors that may have affected our outcomes, there may have been unmeasured differences in health status among our three groups of pharmacy use for which we were not able to control. Third, we drew our sample from older Medicare Part D beneficiaries enrolled in a stand-alone prescription drug plan, so the results may not be generalizable to other populations. Fourth, given that we only had one year of data available for this analysis, we were unable to employ a ‘run-in’ period to establish incident and prevalent medication users. However, we have no reason to suspect that the relative proportion of incident:prevalent medication users varied across pharmacy use groups. Fifth, we excluded those beneficiaries who filled prescriptions at long-term care and institutional pharmacies, which may include those at highest risk for non-adherence. Sixth, although we used a validated list of claims-based DDIs, there are additional DDIs that could have been included and their exclusion is not meant to represent lack of clinical importance. Finally, we were unable to account for non-Part D medication use; however, we believe that any resulting bias is likely quite small given the strong financial incentives to fill prescriptions in-network and because we limited our sample to individuals who filled at least one prescription in a network pharmacy.

CONCLUSION

In conclusion, we found that multiple pharmacy use was common, and was associated with reduced adherence and small increased risk of potential DDIs among some Part D beneficiaries. Clinicians and researchers should be aware of multiple pharmacy use in older adults, and identify ways to coordinate care across pharmacies to monitor the safety and quality of prescription drug use.

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Figure.

Unadjusted Rates of Medication Non-Adherence for 2009 Study Cohort (n=926,956)

Abbreviations: CCB, calcium channel blockers; DPP, dipeptidyl peptidase; RASA, renin angiotensin system antagonists

*Indicates significant difference ($p < 0.05$) compared to single pharmacy use group

Table 1
Characteristics of Individuals 65 Years Continuously Enrolled in Medicare Part D in 2009 by Pharmacy Use, n (%)

Variable	Overall	Use of single pharmacy	Multiple pharmacies, concurrently	P-value ^a	Multiple pharmacies, sequentially	P-value ^d
	n=926,956	n=573,992	n=283,418	--	n=69,546	--
<i>Socio-demographic</i>						
Age, mean (sd)	76.1 (7.5)	76.5 (7.6)	75.4 (7.2)	<0.001	75.6 (7.5)	<0.001
Women	597,542 (64.5)	371,098 (64.7)	182,635 (64.4)	0.05	43,809 (63.0)	<0.001
Race/ethnicity	--	--	--	<0.001	--	<0.001
White	777,049 (83.8)	481,817 (83.9)	237,649 (83.9)	--	57,583 (82.8)	--
Black	71,469 (7.7)	46,511 (8.1)	19,870 (7.0)	--	5,088 (7.3)	--
Asian/Pf	31,997 (3.5)	18,336 (3.2)	10,820 (3.8)	--	2,841 (4.1)	--
Hispanic	28,277 (3.1)	16,461 (2.9)	9,284 (3.3)	--	2,532 (3.6)	--
Other	18,164 (1.9)	10,867 (1.9)	5,795 (2.0)	--	1,502 (2.2)	--
<i>Access to care</i>	--	--	--	--	--	--
LIS/Dual eligible	294,824 (31.8)	193,033 (33.6)	79,929 (28.2)	<0.001	21,862 (31.4)	<0.001
National Part D plan	766,152 (82.7)	481,159 (83.8)	226,965 (80.1)	<0.001	58,028 (83.4)	0.01
Urban	676,193 (73.0)	406,606 (70.8)	216,790 (76.5)	<0.001	52,797 (75.9)	<0.001
No. of prescribers, mean (sd)	3.5 (2.3)	3.0 (2.0)	4.5 (2.6)	<0.001	3.2 (2.0)	<0.001
<i>Health status</i>	--	--	--	--	--	--
Medicare status	--	--	--	<0.001	--	0.15
Without ESRD	921,276 (99.4)	571,166 (99.5)	280,935 (99.1)	--	69,175 (99.5)	--
With ESRD	5,680 (0.6)	2,826 (0.5)	2,483 (0.9)	--	371 (0.5)	--
No. of medications in 2009, mean (sd)	8.9 (5.6)	8.1 (5.2)	11.0 (6.0)	<0.001	7.6 (5.0)	<0.001
Diabetes	302,393 (32.6)	178,622 (31.1)	103,297 (36.4)	<0.001	20,474 (29.4)	<0.001
Heart Failure	126,231 (13.6)	72,739 (12.7)	45,156 (15.9)	<0.001	8,336 (12.0)	<0.001
Hypertension	728,228 (78.6)	442,438 (77.1)	234,043 (82.6)	<0.001	51,747 (74.4)	<0.001
Hyperlipidemia	648,188 (69.9)	387,610 (67.5)	213,395 (75.3)	<0.001	47,183 (67.8)	0.09
Asthma	74,395 (8.0)	39,025 (6.8)	30,503 (10.8)	<0.001	4,867 (7.0)	0.05
COPD	177,917 (19.2)	101,542 (17.7)	64,198 (22.7)	<0.001	12,177 (17.5)	0.24

Variable	Overall	Use of single pharmacy	Multiple pharmacies, concurrently	P-value ^a	Multiple pharmacies, sequentially	P-value ^a
Osteoporosis	154,926 (16.7)	89,987 (15.7)	53,893 (19.0)	<0.001	11,046 (15.9)	0.16
OA/RA	334,746 (36.1)	191,070 (33.3)	120,359 (42.5)	<0.001	23,317 (33.5)	0.21
Depression	104,591 (11.3)	57,184 (10.0)	39,622 (14.0)	<0.001	7,785 (11.2)	<0.001
Charlson, mean (sd)	1.9 (2.3)	1.7 (2.1)	2.3 (2.5)	<0.001	1.7 (2.2)	0.11
Primary pharmacy	--	--	--	--	--	--
Primary dispenser type	--	--	--	<0.001	--	<0.001
Community/retail	873,835 (94.3)	568,280 (99.0)	240,965 (85.0)	--	64,590 (92.9)	--
Mail order	53,121 (5.7)	5,712 (1.0)	42,453 (15.0)	--	4,956 (7.1)	--
Dispenser class code	--	--	--	<0.001	--	<0.001
Independent	284,902 (30.7)	177,408 (30.9)	89,525 (31.6)	--	17,969 (25.8)	--
Chain	615,930 (66.5)	386,174 (67.3)	180,782 (63.8)	--	48,974 (70.4)	--
Other	26,124 (2.8)	10,410 (1.8)	13,111 (4.6)	--	2,603 (3.7)	--
Any mail order usage	85,438 (9.2)	5,712 (1.0)	71,473 (25.3)	<0.001	7,983 (11.5)	<0.001

^a Compared to 'Use of single pharmacy' group

Abbreviations: COPD: chronic obstructive pulmonary disease; sd: standard deviation; LIS: low-income subsidy; OA: osteoarthritis; PI: Pacific Islander; RA: rheumatoid arthritis

Balancing of Propensity Score Weighting for Characteristics of Individuals 65 Years Continuously Enrolled in Medicare Part D in 2009 by Type of Pharmacy Use, %

Table 2

	Before Propensity Score weighting					After Propensity Score weighting				
Variable	Use of single pharmacy	Multiple pharmacies, concurrently	P-value ^a	Multiple pharmacies, sequentially	P-value ^a	Use of single pharmacy	Multiple pharmacies, concurrently	P-value ^a	Multiple pharmacies, sequentially	P-value ^a
	n=573,992	n=283,418	--	n=69,546	--	n=573,992	n=283,418	--	n=69,546	--
<i>Socio-demographic</i>										
Age, mean	--	--	--	--	--	--	--	--	--	--
Women	76.5	75.4	<0.001	75.6	<0.001	76.1	76.1	<0.001	76.2	<0.001
Race/ethnicity	64.7	64.4	0.05	63.0	<0.001	64.7	64.8	0.32	64.9	0.23
White	--	--	<0.001	--	<0.001	--	--	0.01	--	0.22
Black	83.9	83.9	--	82.8	--	83.4	83.7	--	83.8	--
Asian/Pf	8.1	7.0	--	7.3	--	7.8	7.8	--	7.7	--
Hispanic	3.2	3.8	--	4.1	--	3.5	3.4	--	3.4	--
Other	2.9	3.3	--	3.6	--	3.2	3.1	--	3.2	--
<i>Access to care</i>	1.9	2.0	--	2.2	--	2.0	2.0	--	1.9	--
LIS/Dual eligible	--	--	--	--	--	--	--	--	--	--
National Part D plan	33.6	28.2	<0.001	31.4	<0.001	32.8	32.2	<0.001	32.8	0.69
Urban	83.8	80.1	<0.001	83.4	0.01	82.9	82.9	0.87	82.9	0.96
No. of prescribers, mean	70.8	76.5	<0.001	75.9	<0.001	73.2	73.2	0.96	72.8	0.07
<i>Health status</i>	3.0	4.5	<0.001	3.2	<0.001	3.7	3.7	0.06	3.6	0.001
Medicare status	--	--	--	--	--	--	--	--	--	--
Without ESRD	--	--	<0.001	--	0.15	--	--	0.53	--	0.18
With ESRD	99.5	99.1	--	99.5	--	99.3	99.3	--	99.4	--
No. of medications in 2009, mean	0.5	0.9	--	0.5	--	0.7	0.7	--	0.6	--
Diabetes	8.1	11.0	<0.001	7.6	<0.001	9.2	9.3	0.14	9.3	0.60
Heart Failure	31.1	36.4	<0.001	29.4	<0.001	33.2	33.8	<0.001	33.4	0.51
Hypertension	12.7	15.9	<0.001	12.0	<0.001	14.4	14.4	0.44	14.5	0.46
Hyperlipidemia	77.1	82.6	<0.001	74.4	<0.001	78.7	79.7	<0.001	79.1	0.02
Asthma	67.5	75.3	<0.001	67.8	0.09	70.1	70.9	<0.001	70.1	0.96
	6.8	10.8	<0.001	7.0	0.05	8.7	8.5	0.04	8.3	0.03

Variable	Before Propensity Score weighting					After Propensity Score weighting				
	Use of single pharmacy	Multiple pharmacies, concurrently	P-value ^a	Multiple pharmacies, sequentially	P-value ^a	Use of single pharmacy	Multiple pharmacies, concurrently	P-value ^a	Multiple pharmacies, sequentially	P-value ^a
COPD	17.7	22.7	<0.001	17.5	0.24	20.0	20.0	0.91	19.9	0.51
Osteoporosis	15.7	19.0	<0.001	15.9	0.16	17.1	17.1	0.62	17.1	0.88
OA/RA	33.3	42.5	<0.001	33.5	0.21	36.7	37.1	0.03	36.8	0.80
Depression	10.0	14.0	<0.001	11.2	<0.001	12.0	11.8	0.18	12.0	0.94
Charlson, mean	1.7	2.3	<0.001	1.7	0.14	2.0	2.0	0.08	2.0	0.62
<i>Primary pharmacy</i>	--	--	--	--	--	--	--	--	--	--
Primary dispenser type	--	--	<0.001	--	<0.001	--	--	<0.001	--	0.01
Community/retail	99.0	85.0	--	92.9	--	95.8	94.2	--	95.6	--
Mail order	1.0	15.0	--	7.1	--	4.2	5.8	--	4.4	--
Dispenser class code	--	--	<0.001	--	<0.001	--	--	<0.001	--	<0.001
Independent	30.9	31.6	--	25.8	--	30.1	30.2	--	30.8	--
Chain	67.3	63.8	--	70.4	--	67.6	67.0	--	66.8	--
Other	1.8	4.6	--	3.7	--	2.3	2.8	--	2.5	--
Any mail order usage	1.0	25.3	<0.001	11.5	<0.001	4.2	17.0	<0.001	8.5	<0.001

^a Compared to 'Use of single pharmacy' group

Abbreviations: COPD: chronic obstructive pulmonary disease; LIS: low-income subsidy; OA: osteoarthritis; PI: Pacific Islander; RA: rheumatoid arthritis

Table 3

Medication Non-Adherence Outcomes for 2009 Study Cohort by Type of Pharmacy Use (n=926,956)

Medication Class	Single Pharmacy Use n=573,992	Multiple pharmacy use, concurrently n=283,418		Multiple Pharmacy Use, sequentially n=69,546	
	Adjusted Predicted Probability, % (95% CI)	Adjusted Predicted Probability, % (95% CI)	Adjusted OR (vs single pharmacy use) (95% CI)	Adjusted Predicted Probability, % (95% CI)	Adjusted OR (vs single pharmacy use) (95% CI)
β blockers (n=381,435)	29.8 (29.5–30.0)	32.0 (31.7–32.3)	1.11 (1.09–1.13)	34.1 (33.4–34.7)	1.22 (1.18–1.26)
RASA (n=483,750)	26.5 (26.3–26.7)	28.4 (28.1–28.7)	1.10 (1.08–1.12)	31.9 (31.3–32.4)	1.30 (1.26–1.33)
CCBs (n=278,487)	24.9 (24.6–25.2)	26.9 (26.5–27.2)	1.11 (1.09–1.14)	30.2 (29.4–30.9)	1.31 (1.26–1.36)
Sulfonylureas (n=98,818)	31.8 (31.3–32.2)	34.2 (33.6–34.8)	1.12 (1.08–1.16)	37.4 (36.0–38.7)	1.28 (1.20–1.37)
Biguanides (n=121,867)	34.8 (34.3–35.2)	37.6 (37.1–38.2)	1.13 (1.10–1.17)	41.2 (40.0–42.4)	1.31 (1.25–1.38)
Thiazolidinediones (n=42,609)	40.4 (39.6–41.1)	43.2 (42.3–44.2)	1.13 (1.07–1.18)	46.5 (44.4–48.5)	1.28 (1.18–1.40)
DPP-IV Inhibitors (n=17,580)	38.0 (36.7–39.3)	41.2 (39.8–42.6)	1.14 (1.06–1.24)	43.3 (40.0–46.6)	1.25 (1.08–1.45)
Statins (n=466,795)	31.6 (31.4–31.9)	34.2 (33.9–34.5)	1.12 (1.11–1.14)	36.4 (35.8–37.0)	1.24 (1.20–1.27)

Abbreviations: CCB, calcium channel blockers; CI, confidence interval; DPP, dipeptidyl peptidase; OR, odds ratio; RASA, renin angiotensin system antagonists

Adjusted for age, gender, race, urban, Medicare status, number of medications, number of prescribers, Charlson index, low-income subsidy receipt, CCW indicators, national Part D plan, and primary pharmacy class and dispenser type

Table 4

Potential Drug-drug Interactions Outcomes for 2009 Study Cohort by Type of Pharmacy Use (n=926,956)^a

	Single pharmacy use N=573,992	Multiple pharmacy use, concurrently n=283,418	Multiple pharmacy use, sequentially n=69,546
Unadjusted prevalence of DDI, n (%)	21,647 (3.8)	15,228 (5.4)	2,078 (3.0)
Adjusted Predicted Probability, % (95% CI)	3.2 (3.2–3.3)	3.6 (3.5–3.7)	2.8 (2.7–2.9)
Adjusted OR (vs single pharmacy use) (95% CI)	1.00 (Reference)	1.11 (1.08–1.15)	0.85 (0.81–0.91)

Abbreviations: CI, confidence interval; DDI, drug-drug interaction; OR, odds ratio

Adjusted for age, gender, race, urban, Medicare status, number of non-interacting medications, number of prescribers, Charlson index, low-income subsidy receipt, CCW indicators, national Part D plan, and primary pharmacy class and dispenser type

^a 10 most common potential DDIs: 1) warfarin – levothyroxine (n=18,769); 2) simvastatin – gemfibrozil (n=3,338); 3) warfarin – celecoxib (n=3,262); 4) warfarin – fenofibrate (n=3,067); 5) simvastatin – clarithromycin (n=2,630); 6) warfarin – meloxicam (n=2,335); 7) warfarin – gemfibrozil (n=1,314); 8) warfarin – ibuprofen (n=1,187); 9) warfarin – naproxen (n=1,116); 10) warfarin – diclofenac (n=891)