Dispensing Channel and Medication Adherence: Evidence Across 3 Therapy Classes

Reethi Iyengar, PhD, MBA, MHM; Rochelle Henderson, PhD, MPA; Jay Visaria, PhD, MPH; and Sharon Glave Frazee, PhD, MPH

Objectives: To examine the association of mail order versus retail pharmacy dispensing channels with medication adherence for patients on diabetes, hypertension, or high blood cholesterol medications, controlling for prior adherence behavior (PAB) and days of supply.

Study Design: Retrospective analysis using de-identified pharmacy claims data from a large national pharmacy benefits manager between April 2009 and December 2011.

Methods: Continuously eligible patients with an antidiabetic, antihypertensive, or antihyperlipidemic prescription claim between October and December 2009 were identified and followed over a 2-year period. Multivariate logistic regression was used to evaluate the impact of dispensing channel on medication adherence, controlling for differences in demographics, disease burden, and drug use pattern. Patients with a medication possession ratio of 80% or greater were considered adherent. The analysis controlled for PAB by using patients' adherence status in 2010.

Results: Overall, patients using the mail order channel had higher adherence rates than their retail counterparts across all 3 therapeutic classes. In 2011, the likelihood of a mail order patient being adherent was approximately 1.15 times higher than that of a retail patient for antidiabetics, 1.11 times higher for antihypertensives, and 1.19 times higher for antihyperlipidemics. PAB was the strongest contributor to the odds of a patient being adherent across all 3 therapy classes: odds ratios ranged from 5.87 to 9.49.

Conclusions: After adjusting for PAB, differential days of supply, and differences in demographics and disease burden, patients who use mail order have a greater likelihood of being adherent than patients who use a retail pharmacy.

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For author information and disclosures, see end of text.

Medication adherence, defined as taking medications as prescribed, is a key component in controlling disease progression and managing chronic illnesses.[1,2] The clinical benefits of medication adherence have been well established in the scientific literature. Previous studies have indicated that medication adherence is associated with reducing disease morbidity,[3] reducing healthcare resource utilization,[4] decreasing hospitalization,[5] improving effectiveness of treatment,[6] and increasing likelihood of survival.[7]

In addition to worse health outcomes, medication nonadherence is linked to increased healthcare costs. Nonadherence across just 3 chronic therapy classes (antidiabetics, antihypertensives, and antihyperlipidemics) resulted in an estimated $105.8 billion in direct costs in the United States during 2010 alone.[8] Nevertheless, this cost burden can be reduced. Previous studies have found that adherence rates of 80% or greater were associated with significant decreases in total medical costs for diabetes, hypertension, and high blood cholesterol.[4]

Studies have indicated that obtaining medication through the mail is one option for improved medication adherence.[9-11] Compared with retail pharmacies, mail order has been touted as more cost-effective[12] and convenient.[13] In contrast, retail pharmacies are perceived to add value in terms of pharmacist face-to-face interaction.[14-16] Proponents of mail order contend that medication adherence is greater among patients who secure medications via mail order, while proponents of retail attribute any improved adherence to the increased days of supply per prescription in mail order.[14]

Many patients who intend to take their medications as prescribed fail to get medications refilled due to various factors such as inability to visit a pharmacy, their schedule, forgetfulness, or procrastination. Mail order provides a convenient and effective alternative for continued access to medications. Inadequate access[17] and financial concerns[18] are 2 factors identified as impediments to adherence.[19] The impact of access and cost is reduced for many patients by the use of mail order, because prescriptions are delivered to one's home and the total patient out-of-pocket (OPP) costs are frequently less. Hence, we hypothesized that use of the mail order channel is associated with higher adherence rates than use of the retail channel.

A common limitation in adherence studies is the failure to

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control for underlying factors that affect adherence and selection of delivery channel. For example, it is quite possible that health-conscious individuals are more likely to have other healthy behaviors such as exercise, good diet, and preventive screenings. Hence, they may be more likely to engage proactively in activities that improve their adherence—sometimes referred to as the "healthy adherer" effect.[20,21] Mail order generally provides more days of supply, regular refill reminders, and convenient reordering for members, mitigating the potential to procrastinate on medication refills, which can adversely affect adherence. Health-conscious individuals may choose the mail order channel to ensure continuity in their medication regimens. Thus, better medication adherence with mail order may reflect healthier patients' predisposition to self-select the mail order option. To accurately attribute the impact of dispensing channel on adherence, it is important to control for bias from a patient's predisposition to be adherent.

To our knowledge, previously published channel-adherence studies have not controlled for this potential confounder.[13-15] A part of this effect, prior adherence behavior (PAB), can be controlled for by using a proxy measure—prior adherence, calculated based on pharmacy claims data. Also, most channel-adherence studies either have not fully controlled for differences in the days of supply between the 2 channels or have not taken patients' choice of channel into account. This study aims to address the aforementioned biases and limitations, and tease out the effect of dispensing channel on adherence to medications to treat diabetes, hypertension, and high blood cholesterol.

Take-Away Points

The dispensing channel is an important contributor to improving maintenance medication adherence among patients. Given that patients' prior adherence behavior might confound the relationship between channel and adherence, it is important to control for this effect in any channel-adherence analysis.

- Our study demonstrated that adherence is better with mail order than with retail pharmacies and is not just an artifact of increased days of supply.
- Prior adherence behavior is an important confounder in channel-adherence studies, and our study provides a reasonable proxy measure based on pharmacy claims data to lessen the impact of this confounder.

METHODS

Study Population

This study used prescription claims data from a nationally representative sample of commercially insured members whose pharmacy benefits were managed by a large pharmacy benefit management company. Inclusion was limited to patients who were continuously enrolled for pharmacy benefits from April 1, 2009, until December 31, 2011, who were between the ages of 18 and 64 years, and who had any prescription claim for antidiabetics, antihypertensives, or antihyperlipidemics during the index period, which was from October 1, 2009, to December 31, 2009. Patients whose pharmacy benefit design required the use of mail order exclusively for maintenance medications or did not allow access to mail order (mandatory retail) at any time during the entire study period were excluded from analysis. That is, only those patients who were free to choose either channel at any time during the study to fill their maintenance prescriptions were selected. Under provisions of the Health Insurance Portability and Accountability Act of 1996, all data specific to individual patients were removed to maintain the privacy of protected health information from internal analytical data sets. All prescription claims were adjusted to 30-day equivalents.

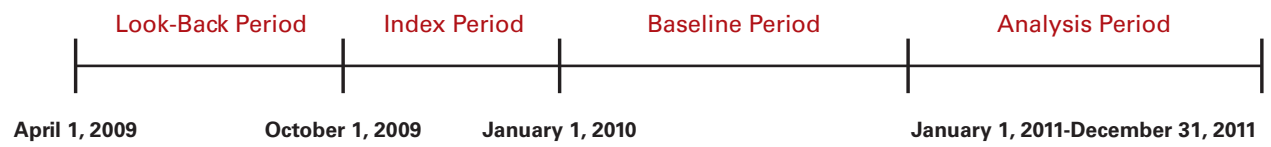
Research Design

A retrospective claims analysis over a 3-year period divided into 4 distinct phases (**Figure**) was conducted. A 6-month look-back period from April to September 2009 was used to assess whether the patients were new or continuing users of the medications identified. Patients having a claim within the same therapy class under study in the look-back period were categorized as continuing users and those without claims as new users. This indicator attempted to capture any differences in adherence that resulted from the longevity of treatment. The analysis period for this study was from January 1, 2011, to December 31, 2011. As previous adherence may be indicative of a health-conscious personality and a measure of better health-seeking behavior,[22] a patient's prior adherence was used as a proxy control for self-selection bias due to the PAB effect in the multivariate model. Prior adherence was based on the patient's medication possession ratio (MPR) in the year 2010, termed as the baseline period.

Study Variables

The primary outcome measure was patient adherence to diabetes, hypertension, or high blood cholesterol medications, defined as an MPR of 80% or greater[23] in the analysis period. Patients' MPR was calculated as the total days of supply divided by 365 days, capping it at 100%. At the drug group level, the combination of 8-digit Generic Product Identifier (GPI) codes and clinically appropriate drug groups was used to calculate the MPR, which then was averaged to the therapy class level for

Figure. Schematic of Study Timeline



each patient (eAppendix A, available at **www.ajmc.com**). Drug groups were based on clinically accepted drug subclasses within each therapy class. Only the numbers of medication units actually meant to be taken during the study periods were included in calculations. That is, the parts of any claim that were in possession before the key periods (2010 for baseline and 2011 for analysis) and any excess in possession after the ends of the periods were excluded from the adherence calculations.

Based on a literature review, independent variables to be included in the model were identified. In addition to dispensing channel, other independent variables included prior adherence, age, sex, OOP costs for 30-day adjusted prescriptions, disease burden, severity of illness, location (urbanicity) of the patient, and average days of supply per claim. Channel was assigned to individuals based on where they obtained at least two-thirds (66.7%) of their 30-day adjusted prescriptions. Those who did not receive at least 66.7% of their 30-day adjusted prescriptions from either mail order or retail were assigned to a mixed channel group. Prior adherence was included in the model to control for the PAB effect, as past health behavior has been known to be a good marker for predicting future health behavior.[24] A similar method was used in a 2011 study examining the association between statin use and outcomes that used prior adherence to control for the healthy-adherer effect.[22] The MPR for 2010 was calculated for each patient to establish prior adherence, and patients with an MPR of 80% or greater were classified as adherent.[13,23,25]

Patient demographics have been known to be significant confounders in assessing the relationship between dispensing channel and medication adherence.[26] Age as of December 31, 2009, was used in the analysis. The OOP costs for 30-day adjusted prescriptions were calculated by dividing total OOP pharmacy costs (for each therapeutic class) for the patient in 2011 by that patient's total number of 30-day adjusted prescriptions. In addition, proxy covariates controlled for patient disease burden and severity of illness. A patient's overall disease burden was defined as the number of unique 2-digit GPIs, which indicate drug therapy classes used by the patient. The number of unique drug groups for which the patient had a prescription claim in 2011 defined severity of illness for diabetes and hypertension. For high blood cholesterol, only adherence to statins was analyzed and hence involved only 1 drug group. The location variable (urbanicity) was based on the core-based statistical area used by the US Census Bureau to ascertain the urban core of metropolitan and micropolitan statistical areas.[27] Average days of supply per claim were used to control for the differences in days of supply of prescriptions between retail and mail order channels. The adherence rate was defined as the percentage of patients in each cohort (mail order/retail/mixed) who had an MPR of 80% or greater over the study period.

Analysis

From a random sample of 4 million members, 109,794 diabetes patients, 467,054 hypertension patients, and 296,594 high blood cholesterol patients were identified between October and December 2009. eAppendix B (available at **www.ajmc.com**) presents the sample selection methodology for the study, which resulted in final analytical samples of data for 37,639 diabetes, 152,819 hypertension, and 103,333 high blood cholesterol patients.

Descriptive statistics were estimated and bivariate differences between groups were tested using analysis of variance for all continuous variables and χ^2 tests for categorical variables. Multivariate logistic regression analyses were performed to estimate the association of aforementioned covariates with the odds of being adherent. In order to address the suggestion that better adherence with mail order is an artifact of more days of supply,[15] average days of supply per claim was used as a proxy measure.

Additionally, an analysis on a subsample of patients filling exclusively 90-day prescriptions evaluated the impact of channel on adherence. Inclusion was limited to patients who filled all their prescriptions through 1 channel only (either retail or mail order). The final analytical subanalysis sample consisted of data for 7253 diabetes, 35,797 hypertension, and 32,391 high blood cholesterol patients. All analyses were conducted using SAS version 9.3 (SAS Institute Inc, Cary, North Carolina).

RESULTS

Descriptive Findings

Generally, patients using mail order tended to be older and included a lower proportion of females than retail or mixed channels. Mail order patients had lower OOP costs per 30-day adjusted prescriptions, more average days of supply per claim, lower average disease burden, and marginally higher mean

Table 1. Percentage of Adherent Patients by Therapy Class and Channel[a]

Therapy Class	Mail Order, %	Retail, %	Mixed, %	Difference Between Mail Order and Retail, %	Difference Between Mail Order and Mixed, %
Diabetes	65.0	44.7	43.1	20.3	22.1
Hypertension	77.1	59.6	54.6	17.5	22.5
High blood cholesterol	75.2	58.3	54.9	16.9	20.3
Mean difference				18.2	21.6

[a]Diabetes sample size was 10,919 for mail order, 25,690 for retail, and 1170 for mixed (n = 37,779). Hypertension sample size was 46,301 for mail order, 102,547 for retail, and 4499 for mixed (n = 153,347). High blood cholesterol sample size was 36,251 for mail order, 64,750 for retail, and 2518 for mixed (n = 103,519).

severity of illness (for diabetes and hypertension) than retail-patients. However, patients in the mixed group were more severely ill compared with mail order or retail patients. Across all 3 classes, prior adherence was significantly higher in mail order than in retail or mixed channels, reflecting the importance of using a proxy measure to control for PAB in the model in order to obtain less biased estimates of the effect of dispensing channel on adherence (**eAppendix C**, available at **www.ajmc.com**).

On average, mail order had 18.2% more adherent patients than retail and 21.6% more adherent patients than mixed channels across the 3 therapy classes. Unadjusted adherence rates for those using mail order were consistently higher than those for patients using retail, with percentage point differences ranging from 16.9% for high blood cholesterol medications to 20.3% for antidiabetic agents (**Table 1**).

Subanalysis comparing 90-day retail patients with 90-day mail order patients also indicated that adherence rates were significantly higher in mail order compared with retail for users of hypertension (80.9% vs 76.3%; $P < .001$) and high blood cholesterol medication (76.9% vs 73.9%; $P < .001$). There was no significant difference in adherence rates for diabetes medication users among mail order and retail channel users (69.0% vs 67.3%; $P = .1996$).

Multivariate Findings

The results presented in **Table 2** indicate the significance of controlling for the PAB effect. Model 1 presents the odds of a patient being adherent without controlling for prior adherence behavior. Model 2 presented the odds of a patient being adherent controlling for the PAB effect. Prior adherence behavior had a significant impact on the results, as observed from the corresponding odds ratio (OR). It was the strongest contributor to the odds of a patient being adherent across all 3 therapy classes. ORs ranged from 5.87 to 9.49.

After controlling for relevant population differences (age, sex, and patient OOP cost per 30-day adjusted prescription) and key covariates (PAB, average days of supply per claim, disease burden, severity of illness, and urbanicity), the differences follow the same pattern as shown in model 1 (Table 2, model 2). In 2011, the likelihood of a mail order patient being adherent was approximately 1.15 times higher than that of a retail patient for antidiabetics, 1.11 times higher for antihypertensives, and 1.19 times higher for antihyperlipidemics. The odds of being adherent for a patient using mixed channels were approximately 20% to 30% lower than the odds for a retail patient for antidiabetics, antihypertensives, and antihyperlipidemics.

On average, mail order had 3.2% more adherent patients than retail and 10.2% more adherent patients than mixed channels across the 3 therapy classes. Adjusted adherence rates for those using mail order were consistently higher than those for patients using retail, with percentage point differences ranging from 2.3 for high blood pressure medications to 3.8 for antihyperlipidemics. The adjusted adherence rate for antidiabetics was 3.5% higher for patients using the mail order channel compared with patients using the retail channel.

Additional sensitivity analysis examining patients filling only 90-day prescriptions concluded that the adjusted odds of being adherent were significantly higher in mail order compared with retail for hypertension patients (OR = 1.19, 95% CI, 1.12-1.26) and high blood cholesterol patients (OR = 1.10, 95% CI, 1.03-1.18), indicating that mail order patients using antihypertensives and antihyperlipidemics were almost 19% and 10% more likely, respectively, to be adherent than their respective retail counterparts, even after equalizing the days of supply differential. There was no significant difference in the adjusted odds of being adherent between dispensing channels for diabetes patients (OR = 1.02, 95% CI, 0.90-1.16).

DISCUSSION

Mail order patients were significantly more adherent than their retail counterparts after controlling for demographics, drug use patterns, differences in days of supply, and the PAB effect. Although sensitivity analysis revealed no statistically

Table 2. Odds Ratio of Adherence by Therapy Class, Key Findings[a]

	Model 1 (n = 37,690)		Model 2 (n = 37,639)	
Therapy Class	**OR**	**95% CI**	**OR**	**95% CI**
Diabetes				
Mail order versus retail	1.278[b]	1.190-1.371	1.149[b]	1.064-1.241
Mixed versus retail	0.817[c]	0.722-0.925	0.807[c]	0.705-0.924
Age	1.036[b]	1.034-1.039	1.027[b]	1.024-1.030
Female vs male	0.820[b]	0.785-0.856	0.852[b]	0.812-0.893
OOP costs 30-day adjusted	0.993[b]	0.991-0.995	0.994[b]	0.992-0.996
Disease burden	1.007[c]	1.002-1.012	1.003	0.997-1.008
Severity of illness	0.624[b]	0.603-0.646	0.608[b]	0.586-0.631
Urbanicity	0.829[b]	0.768-0.893	0.873[c]	0.804-0.948
Average days of supply per claim	1.013[b]	1.012-1.014	1.009[b]	1.008-1.011
Prior adherence	NA	NA	5.868[b]	5.599-6.149
Hypertension	**Model 1 (n = 153,034)**		**Model 2 (n = 152,819)**	
Mail order versus retail	1.229[b]	1.183-1.276	1.112[b]	1.068-1.159
Mixed versus retail	0.721[b]	0.677-0.768	0.691[b]	0.644-0.740
Age	1.033[b]	1.032-1.034	1.024[b]	1.023-1.026
Female versus male	0.905[b]	0.885-0.925	0.926[b]	0.904-0.950
OOP costs 30-day adjusted	0.998[c]	0.997-0.999	0.999	0.997-1.000
Disease burden	0.998	0.995-1.001	1.000	0.997-1.003
Severity of illness	0.546[b]	0.535-0.556	0.559[b]	0.547-0.571
Urbanicity	0.904[b]	0.869-0.940	0.943[c]	0.903-0.985
Average days of supply per claim	1.013[b]	1.013-1.014	1.010[b]	1.009-1.011
Prior adherence	NA	NA	7.018[b]	6.847-7.194
High blood cholesterol	**Model 1 (n = 103,334)**		**Model 2 (n = 103,333)**	
Mail order versus retail	1.312[b]	1.256-1.371	1.188[b]	1.131-1.247
Mixed versus retail	0.754[b]	0.695-0.819	0.737[b]	0.671-0.810
Age	1.039[b]	1.037-1.041	1.027[b]	1.025-1.029
Female versus male	0.819[b]	0.797-0.842	0.874[b]	0.847-0.901
OOP costs 30-day adjusted	0.995[b]	0.994-0.996	0.996[b]	0.995-0.997
Disease burden	1.004[d]	1.001-1.007	0.997	0.993-1.001
Severity of illness	NA	NA	NA	NA
Urbanicity	0.960	0.912-1.010	1.005	0.948-1.064
Average days of supply per claim	1.010[b]	1.009-1.011	1.006[b]	1.005-1.007
Prior adherence	NA	NA	9.488[b]	9.199-9.787

CI indicates confidence interval; NA, not applicable; OOP, out-of-pocket; OR, odds ratio.
[a]Model 1 presents the results of the analysis without controlling for prior adherence behavior. Model 2 presents the results of the analysis controlling for prior adherence behavior.
[b]Significant at $P < .001$.
[c]Significant at $P < .01$.
[d]Significant at $P < .05$.

significant difference for patients on diabetes medications, the findings from the main model were consistent across the 3 studied therapy classes. For hypertension and high blood cholesterol, patients classified as using a mixed channel had significantly lower adherence rates compared with patients who received 66.7% or more of their prescriptions from either retail or mail order. Controlling for the PAB effect, adjusting for the difference in days of supply in all models, and including only those patients who could exercise their choice of channel, the results offer strong evidence that mail order

leads to greater odds of being adherent. The multivariate adjusted coefficients on age, sex, and OOP costs are consistent with previous research.[13] As this study used prior adherence to identify and control for the PAB effect, estimates of adherence behavior with respect to dispensing channel are less likely to be biased than those in any of the previous channel adherence studies.

This study makes an important methodologic contribution in the area by controlling for an important confounder—the PAB effect—which no previously published channel adherence studies took into account. Therefore, some results might have misattributed the impact of channel on adherence. Although 1 study on statins did address adherence and used prior adherence to identify healthy adherers in the context of outcomes, the study did not examine dispensing channel.[22] To our knowledge, this study is the first to address the concern of researchers who stressed the need to find a measure that controls for the confounding of patients' predisposition to be adherent and to caution researchers to interpret the results of previous studies in light of this important limitation.[21,22,28]

Limitations

The results of this study should be interpreted in the context of its limitations. First, the study analyzed pharmacy administrative claims data, using medication possession as a proxy for medication-taking behavior. It assumed that a pill in hand is a pill taken, which is not always the case. However, the use of medication possession as a proxy for medication use has been well documented in previous studies.[13,23,26,28] Further, claims data cannot help distinguish between nonadherence and prescriber-recommended discontinuation. Second, because the study sample was limited to commercially insured patients aged 18 to 64 years, the results of the analyses may not be generalizable to other populations. Third, our ability to control for the confounding effects of covariates in the relationship between dispensing channel and adherence was limited by the reliability and validity of these proxy measures. We had access only to pharmaceutical claims data, and lack of medical information is a limitation of this study. Further studies should look into medical covariates to strengthen the proxy variables. Lastly, we also were limited by our study design, because we included patients on medication for at least 2 years. Thus, patients who did not fill at least 1 prescription in each of the distinct time periods of the study were excluded from the analysis.

CONCLUSION

We found that patients receiving their medications via mail order had greater adherence than those receiving the medications via retail, even after accounting for differences in days of supply. Until now, to our best knowledge, channel adherence evaluations neither addressed the effect of prior adherence behaviors nor controlled for the difference in days of supply between channels. Thus, this study provides empirically sound evidence that mail order is an important alternative to retail pharmacies for helping patients reach optimal adherence. By accounting for the biases resulting from the effect of prior adherence behavior and differential days of supply, this study demonstrates that the mail order channel is associated with improved adherence rates that are not simply a by-product of self-selection or increased days of supply.

Our study evaluated the overall impact of dispensing channel on adherence to medications in 3 widely used chronic therapy classes. Although 45% of US adults have at least 1 of the 3 studied conditions,[29] studies across additional maintenance therapy classes would create a more comprehensive perspective on the relationship between channel and adherence. Future research should use a similar approach (using past measures as a proxy for future effects) to control for individual-specific characteristics. Also intriguing was the finding that adherence was better in both the mail order and retail cohorts compared with the mixed cohort. Further studies could examine the mixed cohort in greater detail, including medical claims data wherever possible. Our study presents mail order as a viable alternative strategy to address medication nonadherence and provides evidence to health plan sponsors and managed care organizations who want to encourage use of more cost-effective and efficient dispensing channels.

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Author Affiliations: Express Scripts (RI, RH, JV, SGF), St. Louis, MO.

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Address correspondence to: Reethi Iyengar, PhD, MBA, MHM, Research and New Solutions, Express Scripts, 4600 N Hanley Rd, PTIC08, St Louis, MO 63134. E-mail: rniyengar@express-scripts.com.

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eAppendix A. List of Drugs Used in Calculation of Medication Possession Ratio for the Study

The Generic Product Identifier, from Medi-Span, is a hierarchical identifier comprising 7 subsets of 2 digits each that provide progressively more detailed information about a drug, specific to treatment indication.

Diabetes

- Sulfonylureas: 27-20-00-20, 27-20-00-27, 27-20-00-30, 27-20-00-40, 27-20-00-50, 27-20-00-60, 27-99-78-02
- Biguanides: 27-25-00-50, 27-99-25-02, 27-99-50-02, 27-99-70-02, 27-99-80-02
- Meglitinide analogues: 27-28-00-40, 27-28-00-60
- Alpha-glucosidase inhibitors: 27-50-00-10, 27-50-00-50
- Insulin-sensitizing agents: 27-60-70-50, 27-60-70-60

Hypertension

- Selective aldosterone receptor antagonist: 36-25-00-30
- Beta-blockers: 33-10-00-10, 33-10-00-25, 33-10-00-30, 33-10-00-40, 33-10-00-50, 33-20-00-10, 33-20-00-20, 33-20-00-21, 33-20-00-22, 33-20-00-30, 33-20-00-40, 33-30-00-07, 33-30-00-10, 36-99-20-02
- Calcium channel blockers: 34-00-00-03, 34-00-00-10, 34-00-00-13, 34-00-00-15, 34-00-00-18, 34-00-00-20, 34-00-00-24, 34-00-00-30
- Angiotensin-converting enzyme inhibitors/angiotensin receptor blockers/direct renin inhibitors: 36-10-00-05, 36-10-00-10, 36-10-00-20, 36-10-00-27, 36-10-00-30, 36-10-00-33, 36-10-00-35, 36-10-00-40, 36-10-00-50, 36-10-00-60, 36-15-00-10, 36-15-00-20, 36-15-00-24, 36-15-00-30, 36-15-00-40, 36-15-00-55, 36-15-00-70, 36-15-00-80, 36-17-00-10, 36-99-15-02, 36-99-18-02, 36-99-30-02, 36-99-40-02, 36-99-45-03, 36-99-60-02, 36-99-65-02

High blood cholesterol

- HMG-CoA reductase inhibitors (statins): 39-40-00-10, 39-40-00-30, 39-40-00-50, 39-40-00-58, 39-40-00-60, 39-40-00-65, 39-40-00-75, 39-40-99-02

eAppendix B. Sample Selection Methodology and Description of Sample Size (Percent Retained)

Study Selection Criterion	Diabetes	Hypertension	High Blood Cholesterol
Random sample of patients in the study period	109,794	467,054	296,598
Patients not enrolled in exclusive mail order or retail programs during study period	98,474 (89.7%)	417,831 (89.5%)	265,977 (89.7%)
Patients continuously enrolled for the entire study period	57,562 (58.5%)	246,662 (59.0%)	157,657 (59.3%)
Patients with at least 1 claim in all distinct periods of the study timeline	50,907 (88.4%)	227,646 (92.3%)	140,994 (89.4%)
Patients aged 18 to 64 years	42,120 (82.7%)	184,271 (80.9%)	113,199 (80.3%)
Patients with claims for the drugs listed in eAppendix A	41,528 (98.6%)	182,210 (98.9%)	112,997 (99.8%)
Patients with no outlier claims	37,779 (91.0%)	153,347 (84.2%)	103,519 (91.6%)
Patients with no missing values for key covariates	37,639 (99.6%)	152,819 (99.7%)	103,333 (99.8%)

eAppendix C. Baseline Characteristics Across Channels

Characteristics	Mail Order	Retail	Mixed
Diabetes			
No.	10,919	25,690	1170
Age in years, mean (SD)	53.9 (7.3)[a]	51.9 (8.3)[a]	52.7 (7.7)[a]
OOP costs per 30-day adjusted prescriptions, mean (SD)	$8.30 ($9.19)[a]	$10.29 ($11.84)[b]	$10.84 ($10.72)[b]
Disease burden proxy, mean (SD)	7.84 (4.19)[c]	7.85 (4.46)[c]	8.33 (4.37)[a]
Severity of illness proxy, mean (SD)	1.52 (0.66)[a]	1.46 (0.63)[a]	1.66 (0.68)[a]
Average days of supply per claim, mean (SD)	84.59 (10.84)[a]	39.92 (20.55)[a]	55.87 (22.43)[a]
Baseline adherent patients, (%)	7544 (68.8)	12,139 (47.1)[b]	590 (50.2)[b]
Female, (%)	4804 (43.8)	12,235 (47.4)[b]	553 (46.9)[b]
Urbanicity, (%)	10,296 (94.0)	23,210 (90.1)[a]	1100 (93.5)
Hypertension			
No.	46,301	102,547	4499
Age in years, mean (SD)	53.8 (7.3)[a]	51.5 (8.3)[a]	52.1 (8.0)[a]
OOP costs per 30-day adjusted prescriptions, mean (SD)	$7.56 ($7.35)[a]	$10.49 ($10.25)[a]	$9.47 ($8.35)[a]
Disease burden proxy, mean (SD)	5.71 (3.85)[a]	5.80 (4.09)[a]	6.36 (4.18)[a]
Severity of illness proxy, mean (SD)	1.38 (0.58)[a]	1.36 (0.57)[a]	1.53 (0.65)[a]
Average days of supply per claim, mean (SD)	85.32 (10.33)[a]	40.91 (21.37)[a]	56.17 (23.08)[a]
Baseline adherent patients, n (%)	36,631 (79.1)[a]	62,933 (61.4)[a]	2836 (63.1)[a]
Female, n (%)	21,410 (46.2)[a]	50,317 (49.0)[b]	2214 (49.2)[b]
Urbanicity, n (%)	43,625 (94.3)	92,381 (90.1)[a]	4238 (94.2)
High blood cholesterol			
No.	36,251	64,750	2518
Age in years, mean (SD)	54.5 (6.8)[a]	53.1 (7.2)[b]	52.8 (7.4)[b]
OOP costs per 30-day adjusted prescriptions, mean (SD)	$11.37 ($10.47)[a]	$14.93 ($13.83)[b]	$14.36 ($11.98)[b]
Disease burden proxy, mean (SD)	6.05 (3.98)[a]	6.30 (4.24)[a]	6.54 (4.37)[a]
Average days of supply per claim, mean (SD)	87.11 (8.95)[a]	41.80 (22.33)[a]	56.78 (24.83)[a]
Baseline adherent patients, n (%)	28,856 (79.6)[a]	40,185 (62.1)[b]	1591 (63.2)[b]
Female, n (%)	15,143 (41.8)	27,824 (43.0)[b]	1062 (42.2)
Urbanicity, n (%)	34,510 (95.3)	59,061 (91.4)[a]	2381 (94.8)

OOP indicates out-of-pocket; SD, standard deviation.
[a]Significantly different at $P = .05$ from both other groups.
[b]Significantly different at $P = .05$ from mail order only.
[c]Significantly different at $P = .05$ from mixed channels only.