Effect of Prescription Drug Coupons on Statin Utilization and Expenditures: A Retrospective Cohort Study

By: Matthew Daubresse, Martin Andersen, Kevin R. Riggs, G. Caleb Alexander

This is the peer reviewed version of the following article:

Daubresse, M., Andersen, M., Riggs, K. R., & Alexander, G. C. (2017). Effect of prescription drug coupons on statin utilization and expenditures: a retrospective cohort study. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 37(1), 12–24. DOI: 10.1002/phar.1802

which has been published in final form at https://doi.org/10.1002/phar.1802.

Abstract:

Importance Drug coupons are widely used, but their effects are not well understood.

Objective To quantify the effect of coupons on statin use and expenditures.

Design Retrospective cohort analysis of IMS Health LRx LifeLink database.

Setting U.S. retail pharmacy transactions.

Participants Incident statin users who initiated branded atorvastatin or rosuvastatin between June 2006 and February 2013.

Main Outcomes and Measures Monthly statin utilization (pill-days of therapy), switching (filling a different statin), termination (failure to refill statin for 6 mo), and out-of-pocket and total costs.

Results Of 1.1 million incident atorvastatin and rosuvastatin users, 2% used a coupon for at least one statin fill. At 1 year, compared with noncoupon users, those who used a statin coupon on their first fill were dispensed an equal number of monthly pill-days (23.7 vs 23.8), were less likely to switch statins (14.4% vs 16.3%), and were less likely to have terminated statin therapy (31.3% vs 39.2%). At 4 years, coupon users were more likely to have switched (45.5% vs 40.8%) and less likely to have terminated statin therapy (50.6% vs 61.1%) compared with noncoupon users. Those who used greater numbers of coupons were substantially less likely to switch and terminate statin therapies. Monthly out-of-pocket costs were lower among coupon than noncoupon users at 1 year ($9.7 vs $15.1), but total monthly costs were qualitatively similar ($115.5 vs $116.9). At 4 years, monthly out-of-pocket costs among coupon users remained lower ($14.3 vs $16.6) compared with noncoupon users. Sensitivity analyses supported the main results.

Conclusions Coupons for branded statins are associated with higher utilization and lower rates of discontinuation and short-term switching to other statin products.

Keywords: copay | coupons | statins utilization | costs

Article:

Although 86% of prescriptions filled in the United States in 2013 were generics, payers and patients spent $232 billion on branded medications, accounting for 71% of all prescription drug costs.1 Pharmaceutical companies employ a variety of promotional strategies to encourage the use of these single-source branded medications. One such strategy is the use of drug coupons, widely available at physicians' offices and on the Internet. These coupons can be used to decrease patient copays for certain medications.2, 3 Between 2009 and 2011, the number of coupons offered in the United States increased 260% and ~11–13% of branded prescriptions were associated with a copay coupon.4

Debate surrounding the appropriateness and "moral hazard"5 of coupons mirrors that of other promotional activities, such as direct-to-consumer advertising6, 7 and the use of free samples.8 Proponents argue that coupons lower patients' out-of-pocket costs, reduce cost-related nonadherence, and provide a safer alternative to drug samples by requiring dispensing through licensed pharmacists.3, 9 Opponents argue that coupons incentivize patients to initiate and adhere to expensive branded therapies, increasing out-of-pocket and third-party spending that ultimately drives higher premiums for coupon users and nonusers alike.6, 9-11

Despite their increasing prevalence, remarkably little evidence regarding the effect of coupons on prescription drug utilization or expenditures is available. One retrospective cohort study used commercial pharmacy claims from incident statin patients to examine the impact of coupons on brand-name statin utilization and spending. The authors found that coupon users had higher rates of adherence and substantially higher total statin costs than those who initiated generic statins.3, 9 Despite these insights, the authors only examined prescription fills, restricted their follow-up to a single observation at 12 months, and used a cross-sectional study design that limited causal inference.

We conducted a retrospective cohort study comparing the effect of coupon use on utilization and expenditures among incident statin users. We focused on statins because the indications for statin use consist of prevalent and costly chronic conditions, and because multiple statins are on the market, some of which have been heavily marketed and promoted with drug coupons.

Methods

We examined data used from the IMS Health LifeLink LRx Anonymized Longitudinal Prescription database, consisting of prescriptions from retail, food store, independent, and mass merchandiser pharmacies, all of which represent approximately two-thirds of retail prescriptions dispensed in the United States.12 These data include detailed information about the quantity, form, and dose of medications dispensed as well as annual flags to indicate individuals who utilized a mail-order pharmacy. The data are generated daily at pharmacies and then automatically transmitted to IMS Health through weekly feeds. The prescription data are also linked to the previously noted database using a patented algorithm based on 16 different fields such as the

patient's first name, last name, and date of birth. Each prescription claim contains information about the retail transaction (days supply, number of refills), patient (year of birth, sex), product (National Drug Code), and the payer and prescription drug plan. We used payer and plan variables to identify statin claims associated with copay coupons.

Setting and Participants

We derived a closed cohort of incident statin users from a larger extract that contained all prescriptions from January 2006 through August 2013 for any patient who filled two or more prescriptions for an opioid in one of 11 states over any 1-year period during that time. This extract, derived for a separate study, consisted of 5.3 billion retail transactions from more than 50 million patients, 1.5 million prescribers, and 52,000 pharmacies.

Participants were incident statin users, defined by evidence of no prior statin use for at least a 6-month period with evidence of other prescription claims activity, who initiated branded atorvastatin or rosuvastatin. Medicare and Medicaid prohibit coupon use, so we excluded individuals older than age 65 or who otherwise used Medicaid or Medicare. We categorized patients into four mutually exclusive groups: coupon used on first statin fill (initial coupon users); coupon used on statin fill, but not the first (subsequent coupon users); coupon used on nonstatin fills (other coupon users); or no coupons used (noncoupon users). Our final data set included ~700,000 coupons for atorvastatin (82%) or rosuvastatin (18%), which together accounted for 87% of all statin coupons observed.

To account for potential differences between early and late coupon adopters, we excluded individuals who used a coupon for either statin before coupons were widely available for that drug, which we defined as the use of a coupon for at least 0.1% of all commercial claims for a given drug during a particular month. For our primary analyses, we included only individuals who used pharmacies that consistently reported data to IMS throughout the study period and who filled at least one prescription for any drug within the first and last 6 months of the study period.

Measures

We examined three measures of utilization and two measures of cost. First, we calculated the quantity of a prescription medicine sufficient for 1 day of therapy (pill-day) and then examined the average monthly number of pill-days supplied. We allowed for unlimited “stockpiling”13 and thus accounted for inherent differences in prescription quantity across different pharmacy claims. Second, we calculated switching as the probability of switching statins from 1 month to the next. Third, we calculated the proportion of people who terminated therapy, defined as a 6-month period without any statin utilization. Fourth, we calculated the average monthly out-of-pocket costs for statins, reflecting the amount of coinsurance the payer determined is owed by the patient for the transaction, based on an individual's benefit design. These values represent the patient's out-of-pocket costs after any discount from a coupon was applied. Finally, we quantified patients’ total costs for statins (the copay plus the amount billed to insurance, i.e., what the pharmacy is paid from all sources). We excluded claims with missing cost information from our analyses that examined out-of-pocket and total costs.

In some cases, individuals had multiple statin transactions during a given month that made it difficult to easily assign patients to a particular statin therapy. In our main analyses, we dropped individuals who could not be assigned to a single statin therapy based on either the plurality of

their claims in a given month or by comparison of their current month's use with their use during the prior or subsequent month.

Statistical Analysis

We used generalized estimating equations (GEE) models, accounting for within-subject correlations over time to calculate the predicted and marginal effects of coupon use between coupon users in each group and their counterfactual noncoupon counterparts. We used the number of months contributed by each person included in the cohort (i.e., person-months) as our unit of analysis. We controlled for the age and sex of individual respondents and included flexible specifications for time on drug, measured in months, and controlled for the year and month that therapy was initiated. Our data did not include diagnoses, so we controlled for differences in patient comorbidities using the Chronic Disease Score, a method of quantifying comorbid burden using automated pharmacy claims that has been validated as a measure of hospitalizations, expenditures, and mortality.14 To allow the effect of time on drug to vary with initial coupon status, we included interactions between a cubic spline with five knots in time on drug and coupon utilization of the individual.15 To calculate the effect of coupons, we included dummy variables for coupon utilization that indicate whether a coupon was used that month.

We modeled the number of pills dispensed in a given month using a negative binomial specification; out-of-pocket costs, pharmacy costs, and monthly pill utilization were modeled using a Poisson distribution. In most analyses, we estimated GEE models with exchangeable correlation matrices. However, in our constant store sample it was necessary to assume independence between observations for the model to converge. We used GEE logistic regression that allows for within-subject correlation over time to examine the effects of drug coupons on switching and termination. To interpret the results of our models, we used “recycled predictions” to construct a synthetic comparison group for each of our three coupon categories15, 16 and computed the predicted value for each person-month in each group. This approach provides a method of standardizing the average predicted values over the distribution of other covariates. We then computed average marginal differences as the average difference between the coupon group predicted values and the comparison group predicted values. We computed standard errors for average predicted values and marginal differences using the delta method from cluster-robust variance matrices.17 All models were estimated using Stata v.13.1 (StataCorp, College Station, TX).

Sensitivity Analyses

We conducted several sensitivity analyses. First, because we limited our primary analyses to a closed cohort of individuals, we repeated our analyses, allowing subjects to enter and leave the cohort. Second, since our data do not capture mail-order medications, we repeated our analyses excluding individuals who filled any prescriptions by mail order during the analysis period. Third, because our original extract oversampled opioid users, we repeated our analyses after limiting them to individuals who had no opioid prescription fills from incident statin use until termination or censoring. Fourth, we varied rules that allowed for unlimited stockpiling, allowing patients to stockpile fewer pills from one prescription to a subsequent prescription. Fifth, we varied our definition of statin termination to include those with no statin fills for 3 months or 9 months.

Results

Characteristics of Coupon and Noncoupon Users

Our final sample consisted of ~1.1 million incident atorvastatin (66%) and rosuvastatin (34%) users. Of these, 7839 (0.7%) used a coupon on their first statin fill, 12,864 (1.2%) used a coupon on a subsequent statin fill, 11,473 (1.1%) used a coupon for a nonstatin product, and ~1 million patients (97%) filled a prescription for an incident statin without any associated coupon use (Table 1).

Overall, coupon and noncoupon users had similar demographic characteristics, prescription drug utilization, and comorbid conditions. Coupon users were significantly more likely to fill claims through an insurer (96% initial coupon users vs 89% noncoupon users; $p<0.05$), and other coupon users had significantly higher median copays ($110 vs $88; $p<0.05$) and total pharmacy costs ($2354 vs $1698; $p<0.05$) than noncoupon users.

Figure A1 depicts trends in branded and generic atorvastatin dispensing during the study period among coupon users and nonusers. In January 2007, there were ~223,000 branded prescription transactions without a coupon and a negligible number of branded sales where a coupon was used. Branded sales remained relatively flat until May 2012 when generic atorvastatin was released. This was associated with a reduction of ~95% in branded sales and a 75% reduction in coupon use over the ensuing 15 months as the generic product took hold. A similar trend for rosuvastatin is shown in Figure A2, although a generic formulation of the product was not introduced during the study period.

Effect of Coupons on Statin Utilization, Switching, and Termination

Table 2 depicts differences in utilization, switching, and termination between coupon users on atorvastatin or rosuvastatin and their counterfactual noncoupon counterparts within each group (initial, subsequent, nonstatin). Overall, coupon users had similar levels of statin utilization and switching compared with their noncoupon users. At 1 year, initial coupon users were dispensed 0.1 fewer average pill-days/month, were 1.9% less likely to switch statins (16.6% vs 18.9%; $p<0.05$), and were 6.9% less likely to terminate statin therapy (31.3% vs 39.2%; $p<0.001$) than noncoupon users. Differences in termination amplified over time; at 4 years, initial coupon users were 11.1% less likely to terminate statin therapy than noncoupon users (50.6% vs 60.7%; $p<0.0001$; Table 2).

Compared with initial coupon users, the association between coupon use and statin utilization and switching was similar for subsequent and other coupon users. However, both subsequent and other coupon users were less likely to terminate statin therapy than initial coupon users: at 2 years, subsequent coupon users were 35.2% less likely to terminate statin therapy than nonusers (15.1% vs 50.8%; $p<0.0001$), whereas initial coupon users were 8.7% less likely to terminate treatment (41.8% vs 50.8%; $p<0.0001$). These patterns continued to persist through 4 years of follow-up.

The cumulative probability of statin termination over time among the four groups is shown in Figure A3. Rates of discontinuation were greatest for noncoupon users. The length of time until a discontinuation rate of 25% was 10 months for initial coupon users (95% confidence interval [CI] 9–10 mo), 35 months for subsequent statin coupon users (95% CI 33–37 mo), 23 months for other coupon users (95% CI 23–24), and 7 months for noncoupon users (95% CI 7–7).

Table 1. Characteristics of Coupon Users and NonUsers Prior to Initiating Atorvastatin or Rosuvastatin Therapy[a]

	Coupon Users			Nonusers
	Incident statin coupon	Subsequent statin coupon	Incident nonstatin coupon	No coupon use
Female, %	55	54	54	57
Age, yrs, mean, median (IQR)	49, 51 (11)	50, 52 (11)	48, 49 (12)	50, 51 (11)
Insurance status, %				
Commercially insured	96	96	94	89
None/cash	4	4	6	11
Number of unique prescribers,b mean, median (IQR)	4, 3 (3)	4, 3 (3)	5, 4 (4)	4, 3 (3)
Number of unique pharmacies,b mean, median (IQR)	2, 1 (1)	2, 1 (1)	2,1 (2)	2, 1 (1)
Drug utilization				
Prescriptions,b mean, median (IQR)	22, 18 (18)	27, 22 (24)	30, 23 (27)	26, 21 (24)
Coupon use				
Coupons used prior to first statin,b mean, median (IQR)	1, 0 (0)	0, 0 (0)	1, 0 (1)	–
Unique therapeutic classes,b mean, median (IQR)	8, 7 (6)	9, 8 (7)	10, 8 (8)	9, 8 (7)
Chronic disease score,b mean, median (IQR)	2, 2 (2)	2, 2 (2)	2, 2 (2)	2, 2 (2)
Costs				
Total copay,b mean, median (IQR)	249, 86 (345)	227, 96 (285)	2134, 110 (354)	246, 88 (283)
Total cost,b mean, median (IQR)	2422, 1530 (2302)	2905, 1876 (2824)	3760, 2354 (3773)	2864, 1698 (2859)
Total patients, N	7839	12,864	11,473	1,018,739

a Values represent column percentages unless otherwise noted.
b Based on claims filled 6 mo prior to incident statin fill date. Source: IMS Health LifeLink LRx Data, 2007–2013.

Table 2. Differences in Average Monthly Atorvastatin and Rosuvastatin Utilization Among Coupon Users and Nonusers[a]

	Time				
Time following incident statin fill	1 Mo	1 Yr	2 Yrs	3 Yrs	4 Yrs
Statin utilization (average pill-days dispensed)					
No coupons					
Predicted level, pill-days (SE)	29.1 (0.0)	23.7 (0.0)	24.5 (0.0)	24.7 (0.0)	25.4 (−0.1)
Other coupon					
Predicted level, pill-days (SE)	28.3 (−0.1)	23.7 (−1.2)	24.7 (−2.8)	24.9 (−4.4)	25.2 (−6.1)
Difference from counterfactual[b]	−0.7 (−0.1)	0.1 (−1.2)	0.2 (−2.8)	0.2 (−4.4)	−0.1 (−6.1)
Initial statin coupon					
Predicted level, pill-days (SE)	28.4 (−0.2)	23.8 (−3.0)	24.3 (−6.7)	24.7 (−10.5)	24.7 (−14.3)
Difference from counterfactual	−0.8 (−0.2)	−0.1 (−3.0)	−0.4 (−6.7)	0.0 (−10.5)	−0.6 (−14.3)
Subsequent statin coupon					
Predicted level, pill-days (SE)	26.7 (−0.1)	24.0 (−2.1)	24.5 (−4.6)	24.8 (−7.2)	25.1 (−9.9)
Difference from counterfactual	−2.2 (−0.1)	0.3 (−2.1)	−0.2 (−4.6)	0.0 (−7.2)	−0.4 (−9.9)
Statin switching (cumulative probability of switching from one statin to another)					
No coupons					
Predicted level, % switching (SE)	1.5 (0.0)	16.6 (−0.1)	27.4 (−0.2)	35.6 (−0.3)	42.8 (−0.4)
Other coupon					
Predicted level, % switching (SE)	1.9 (−0.1)	18.9 (−0.4)	31.5 (−0.7)	42.3 (−1.0)	51.4 (−1.2)
Difference from counterfactual	0.3 (−0.1)	1.9 (−0.5)	3.6 (−0.7)	5.9 (−1.0)	7.7 (−1.3)
Initial statin coupon					
Predicted level, % switching (SE)	1.4 (−0.2)	14.4 (−0.9)	25.5 (−1.8)	36.0 (−3.5)	45.5 (−5.6)
Difference from counterfactual	−0.1 (−0.2)	−1.9 (−1.0)	−1.1 (−1.8)	1.8 (−3.5)	4.7 (−5.6)
Subsequent statin coupon					
Predicted level, % switching (SE)	1.4 (−0.2)	15.6 (−0.8)	28.3 (−1.1)	39.3 (−1.4)	48.8 (−1.6)
Difference from counterfactual	−0.2 (−0.2)	−1.4 (−0.8)	0.6 (−1.1)	3.4 (−1.4)	5.6 (−1.7)
Statin termination (cumulative probability of failure to refill for period of at least 6 mo)					
No coupons					
Predicted level, % terminating (SE)	12.0 (−0.1)	39.2 (−0.1)	50.8 (−0.2)	56.3 (−0.2)	60.7 (−0.2)
Other coupon					
Predicted level, % terminating (SE)	2.3 (−0.1)	14.9 (−0.3)	24.1 (−0.4)	30.2 (−0.5)	35.9 (−0.6)
Difference from counterfactual	−9.9 (−0.1)	−25.1 (−0.4)	−27.6 (−0.5)	−27.0 (−0.5)	−25.7 (−0.6)
Initial statin coupon					
Predicted level, % terminating (SE)	8.2 (−0.5)	31.3 (−1.0)	41.8 (−1.3)	46.3 (−1.6)	50.6 (−2.1)
Difference from counterfactual	−3.5 (−0.5)	−6.9 (−1.1)	−8.7 (−1.3)	−9.9 (−1.6)	−10.5 (−2.1)
Subsequent statin coupon					
Predicted level, % terminating (SE)	0.4 (−0.1)	8.3 (−0.5)	15.1 (−0.6)	20.7 (−0.8)	25.9 (−1.0)
Difference from counterfactual	−11.6 (−0.1)	−30.6 (−0.5)	−35.2 (−0.7)	−34.9 (−0.8)	−33.9 (−1.0)

a Values represent 12-mo averages at varying duration of follow-up.

b Difference from counterfactual represents the difference in average predicted values between coupon users and their counterfactual noncoupon using counterparts within each group (initial, subsequent, nonstatin). Source: IMS Health LifeLink LRx Data, 2007–2013.

Compared with initial coupon users, the association between coupon use and statin utilization and switching was similar for subsequent and other coupon users. However, both subsequent and other coupon users were less likely to terminate statin therapy than initial coupon users: at 2 years, subsequent coupon users were 35.2% less likely to terminate statin therapy than nonusers (15.1% vs 50.8%; $p<0.0001$), whereas initial coupon users were 8.7% less likely to terminate treatment (41.8% vs 50.8%; $p<0.0001$). These patterns continued to persist through 4 years of follow-up.

The cumulative probability of statin termination over time among the four groups is shown in Figure A3. Rates of discontinuation were greatest for noncoupon users. The length of time until a discontinuation rate of 25% was 10 months for initial coupon users (95% confidence interval [CI] 9–10 mo), 35 months for subsequent statin coupon users (95% CI 33–37 mo), 23 months for other coupon users (95% CI 23–24), and 7 months for noncoupon users (95% CI 7–7).

Effect of Varying Levels of Coupon Utilization

Higher levels of coupon use resulted in higher utilization and a lower probability of switching and termination (Table 3). For example, at 3 years, initial coupon users were 5.2% more likely to switch and 0.6% more likely to terminate than noncoupon users. However, at 3 years, incident statin users who used coupons for five or more fills were 16% less likely to switch and 28% less likely to terminate than noncoupon users.

Effect of Coupon Use on Out-of-Pocket and Total Costs

All coupon users had consistently lower out-of-pocket costs than noncoupon users (Table 4). At 1 year, average monthly out-of-pocket costs for statins appeared $5 lower for initial coupon users than for noncoupon users; however, this difference was not statistically significant ($9.7 vs $15.9, not significant). Between 2 and 4 years of follow-up, this difference persisted, ranging from $2 to $6.

The association between coupon use and total costs differed from those for out-of-pocket costs. Overall, only negligible differences in monthly average total costs were found between coupon users and noncoupon users. At 1 month, total costs were ~$7 higher for initial coupon users compared with their noncoupon users ($143.3 vs $136.5; $p<0.001$). However, for longer periods of follow-up, this difference decreased, and total costs for initial coupon users were very similar to that of noncoupon users.

Sensitivity Analyses

Repeating our analyses stratified by atorvastatin and rosuvastatin (Tables A1 and A2) with an open cohort of statin patients, patients with no use of mail-order prescription services and patients with limited opioid use (Table A3) did not substantively impact the results from our main analyses. Similarly, allowing for unlimited stockpiling, varying the time period defining termination, and using an alternative method for comorbidity adjustment had little impact on our main results.

Table 3. Association Between Coupons and Utilization Among Incident Statin Coupon Users

	Time				
Time following incident statin fill	1 mo	1 Yr**	2 Yrs**	3Yrs**	4 Yrs**
Statin utilization (average pill-days dispensed)					
No coupons					
Predicted level, pill-days (SE)	26.5 (0.0)	23.7 (0.0)	24.5 (0.0)	24.7 (0.0)	25.4 (−0.1)
Coupon use on first fill only					
Predicted level, pill-days (SE)	24.0 (−0.2)	23.0 (−4.0)	23.4 (−8.9)	23.6 (−13.8)	24.6 (−19.5)
Difference from counterfactual[a]	−2.5 (−0.3)	−0.9 (−4.0)	−1.1 (−8.9)	−1.0 (−13.8)	−0.6 (−19.5)
Coupon use for two fills					
Predicted level, pill-days (SE)	26.3 (−0.3)	24.5 (−6.6)	24.3 (−14.0)	24.1 (−21.4)	24.3 (−29.5)
Difference from counterfactual	−0.6 (−0.3)	0.4 (−6.6)	−0.3 (−14.0)	−0.5 (−21.4)	−0.8 (−29.5)
Coupon use for three or four fills					
Predicted level, pill-days (SE)	29.1 (−0.2)	23.6 (−3.8)	23.6 (−8.1)	25.7 (−13.8)	30.5 (−22.9)
Difference from counterfactual	2.1 (−0.2)	−0.6 (−3.9)	−1.2 (−8.1)	0.8 (−13.8)	4.2 (−22.9)
Coupon use for five or more fills					
Predicted level, pill-days (SE)	30.1 (−0.1)	25.7 (−3.3)	26.8 (−7.2)	27.1 (−11.3)	26.3 (−14.9)
Difference from counterfactual	3.1 (−0.1)	1.5 (−3.3)	1.8 (−7.2)	2.2 (−11.3)	0.9 (−14.9)
Statin switching (cumulative probability of switching from one statin to another)					
No coupons					
Predicted level, % switching (SE)	3.0 (0.0)	16.7 (−0.1)	27.4 (−0.2)	35.8 (−0.3)	43.0 (−0.4)
Coupon use on first fill only					
Predicted level, % switching (SE)	5.2 (−0.6)	18.8 (−1.5)	30.6 (−2.7)	39.8 (−5.0)	48.3 (−7.5)
Difference from counterfactual	2.2 (−0.6)	2.5 (−1.5)	3.8 (−2.7)	5.2 (−5.0)	7.1 (−7.5)
Coupon use for two fills					
Predicted level, % switching (SE)	2.3 (−0.8)	11.7 (−2.5)	20.8 (−4.3)	35.5 (−6.2)	38.0 (−7.2)
Difference from counterfactual	−0.7 (−0.8)	−4.5 (−2.5)	−5.6 (−4.3)	1.9 (−6.2)	−2.4 (−7.2)
Coupon use for three or four fills					
Predicted level, % switching (SE)	0.7 (−0.3)	14.2 (−2.2)	26.4 (−4.2)	40.4 (−7.1)	46.9 (−12.2)
Difference from counterfactual	−2.3 (−0.3)	−2.2 (−2.2)	−0.6 (−4.3)	6.5 (−7.1)	8.8 (−12.1)
Coupon use for five or more fills					
Predicted level, % switching (SE)	0.0 (0.0)	4.7 (−1.3)	13.5 (−2.8)	18.2 (−4.2)	18.3 (−4.3)
Difference from counterfactual	−2.9 (−0.1)	−11.3 (−1.3)	−13.1 (−2.8)	−15.5 (−4.2)	−22.2 (−4.3)
Statin termination (cumulative probability of failure to refill for period of at least 6 mo)					
No coupons					
Predicted level, % terminating (SE	19.1 (−0.1)	39.2 (−0.1)	50.9 (−0.2)	56.4 (−0.2)	60.9 (−0.2)
Coupon use on first fill only					
Predicted level, % terminating (S	19.9 (−1.1)	39.6 (−1.4)	51.9 (−1.7)	57.0 (−1.9)	62.2 (−2.2)
Difference from counterfactual	1.1 (−1.1)	1.0 (−1.5)	1.0 (−1.7)	0.6 (−1.9)	0.9 (−2.2)
Coupon use for two fills					
Predicted level, % switching (SE)	8.9 (−1.4)	33.9 (−3.1)	45.7 (−3.9)	52.9 (−5.0)	61.2 (−6.2)
Difference from counterfactual	−9.5 (−1.4)	−3.9 (−3.1)	−4.8 (−3.9)	−3.7 (−5.0)	−0.2 (−6.2)
Coupon use for three or four fills					
Predicted level, % switching (SE)	2.9 (−0.6)	24.6 (−2.5)	35.4 (−3.4)	45.3 (−5.1)	54.0 (−14.7)
Difference from counterfactual	−15.3 (−0.6)	−13.1 (−2.5)	−15.0 (−3.4)	−10.6 (−5.1)	−0.3 (−14.7)
Coupon use for five or more fills					
Predicted level, % switching (SE)	0.0 (0.0)	10.4 (−1.7)	20.4 (−2.8)	27.2 (−4.3)	30.2 (−5.9)
Difference from counterfactual	−17.9 (−0.1)	−26.8 (−1.7)	−28.7 (−2.8)	−27.9 (−4.3)	−29.2 (−5.9)

[a] Difference from counterfactual represents the difference in average predicted values between coupon users and their counterfactual noncoupon using counterparts within each group (initial, subsequent, nonstatin). Source: IMS Health LifeLink LRx Data, 2007–2013.

Table 4. Differences in Average Monthly Atorvastatin and Rosuvastatin Expenditures Between Coupon and Noncoupon Users

	Time				
Time following incident statin fill	1 mo	1 Yr**	2 Yrs**	3Yrs**	4 Yrs**
Average copayment, $					
No coupons					
Predicted level (SE)	19.4 (−0.1)	15.9 (−0.1)	17.0 (−0.1)	16.1 (−0.1)	15.2 (−0.2)
Other coupon					
Predicted level (SE)	16.1 (−0.2)	13.0 (−3.0)	13.4 (−6.7)	12.6 (−9.7)	12.1 (−12.6)
Difference from counterfactual[a]	−3.4 (−0.1)	−2.9 (−3.0)	−3.6 (−6.7)	−3.4 (−9.7)	−3.1 (−12.6)
Initial statin coupon					
Predicted level (SE)	16.4 (−1.7)	9.7 (−10.2)	11.0 (−25.8)	14.3 (−51.6)	14.3 (−70.0)
Difference from counterfactual	−2.9 (−1.7)	−5.4 (−10.2)	−6.1 (−25.8)	−2.8 (−51.6)	−2.3 (−70.0)
Subsequent statin coupon					
Predicted level (SE)	12.9 (−0.3)	14.7 (−11.0)	15.6 (−25.3)	14.6 (−36.6)	12.2 (−41.6)
Difference from counterfactual	−7.6 (−0.3)	−1.3 (−11.0)	−1.4 (−25.3)	−1.6 (−36.6)	−3.1 (−41.6)
Average total cost, $					
No coupons					
Predicted level (SE)	128.4 (−0.1)	104.6 (−0.2)	112.4 (−0.2)	115.9 (−0.2)	121.4 (−0.4)
Other coupon					
Predicted level (SE)	127.3 (−0.3)	106.7 (−6.2)	114.9 (−14.5)	118.2 (−23.0)	121.6 (−32.0)
Difference from counterfactual	−2.5 (−0.3)	1.3 (−6.2)	1.7 (−14.5)	1.9 (−23.0)	0.0 (−32.0)
Initial statin coupon					
Predicted level (SE)	143.3 (−1.3)	115.5 (−14.9)	117.3 (−32.7)	121.8 (−52.5)	123.7 (−72.3)
Difference from counterfactual	6.8 (−1.2)	1.4 (−14.9)	−2.6 (−32.7)	0.5 (−52.5)	−1.5 (−72.3)
Subsequent statin coupon					
Predicted level (SE)	118.1 (−0.4)	109.6 (−10.1)	115.6 (−23.3)	121.1 (−37.6)	125.1 (−52.5)
Difference from counterfactual	−9.9 (−0.3)	3.6 (−10.1)	1.6 (−23.3)	3.7 (−37.6)	2.6 (−52.5)

a Difference from counterfactual represents the difference in average predicted values between coupon users and their counterfactual noncoupon using counterparts within each group (initial, subsequent, nonstatin). Source: IMS Health LifeLink LRx Data, 2007–2013.

Discussion

In this longitudinal study of statin users among commercially insured incident statin users, those who used a coupon on their first fill were dispensed a similar quantity of pills than noncoupon users over 1 year, but they were less likely to have switched statins or to have terminated treatment altogether after 12 months of follow-up. There was a dose-response association present, and these effects increased modestly over time. At 1 year, coupon users had out-of-pocket costs that were ~$1–$5/month lower than noncoupon users but had similar total costs. These results are important because the use of drug coupons is increasing, and little is known about the effects of these coupons on patients' utilization, out-of-pocket costs, and total costs.

Our study contributes to a growing evidence base regarding the effect of drug coupons on drug utilization and expenditures. One prior report used a hypothetical insurance program and publicly available retail prices for statins to suggest that coupons may lead to lower out-of-pocket costs among patients but significantly higher costs for insurers due to a reduction in the use of generic products.3 A second study using commercial pharmacy claims from incident statin patients suggested that coupon users had more statin fills 1 year after statin initiation and both higher out-of-pocket and total statin prescription costs compared with generic statin initiators and noncoupon users of branded statins.9 In contrast to these studies, we found that statin coupons were associated with similar levels of utilization and total pharmacy costs. Important differences between our approach and these prior studies may account for these differences including our use of longitudinal GEE models that account for within-subject correlations over time, as well as our analytic approach that increased comparability across the groups of coupon users and nonusers.18

Manufacturers' use of drug coupons remains a controversial area of pharmaceutical policy. In addition to historic concerns that are similar to those regarding direct-to-consumer advertising6 and the distribution of free medication samples,8 particular provisions in payment policy preclude the use of coupons for services covered by nearly all federal health care programs.19 Despite safeguards to prevent unauthorized use, a survey commissioned by the National Coalition on Health Care found that 6% of Medicare beneficiaries enrolled in Part D were using coupons,19 an issue under study in 2014 by the Office of the Inspector General.20 The practice of providing drug coupons has also been challenged by groups outside of the federal government. For example, in 2012, a group of trade union health plans sued eight large drug manufacturers claiming that drug coupon programs violate federal bribery laws.21 Massachusetts has prohibited drug coupons since 1988, which made it the only state with a complete ban on coupons. However, in 2013, the Massachusetts legislature created an exception to the law that allowed the use of coupons for branded drugs with no generic equivalent.22

The rapid growth of specialty drug utilization in the United States, which totaled ~$87 billion in 2012, are projected to reach $400 billion by 2020.23 This also lends added urgency to the issue of drug coupons. In one analysis examining the use of coupons for biological antiinflammatory or multiple sclerosis medications among the commercially insured, coupons offset more than 60% of patients' out-of-pocket costs. Although this substantially reduced patients' cost sharing, it also circumvented payer efforts to constrain rising health care costs through the use of pharmacy benefits management.24 The use of coupons in this setting may be increasingly common as payers attempt to manage specialty costs through higher deductibles as well as changes to pharmacy benefit design, such as the use of higher cost-sharing tiers in lieu of the standard three-tier design as well as step therapy or fail-first programs that steer physicians and patients toward lower cost therapies.

Our analyses had several limitations. First, we were unable to determine the dollar amount of the coupon used and therefore the savings to the consumer, after accounting for coupons. Second, our analysis was limited to individuals filling prescriptions through retail pharmacies because our data did not include individual-level claims data for transactions filled through mail-order services. Third, we assumed that the availability of a drug coupon only affects individuals who choose to use such a coupon, even though it is possible that the availability of a coupon affects the broader equilibrium prescription drug prices, formulary assignment, and out-of-pocket costs. Fourth, our analyses were not designed to account for additional market complexities, such as atorvastatin's patent expiry and potential switching from statin to nonstatin lipid-lowering therapies that may also have been relevant to the primary associations of interest. Fifth, these data capture only prescriptions paid for and given to an individual patient; therefore, we were unable to account for prescriptions that were filled but never picked up. Sixth, we derived our analytic cohort from a larger cohort of opioid recipients, which may have diminished the generalizability of our findings. However, restricting our analyses to patients with no opioid fills after their incident statin fill had no substantive impact on our main results. Finally, our analyses do not allow determination of whether drug coupons result in lower utilization of generic medications.

Conclusions

Despite their increasing use, relatively little is known regarding the effect of drug coupons on consumer behavior. In the case of statins, we found that drug coupons are associated with greater utilization and lower rates of statin discontinuation and short-term switching. It is unclear whether coupons have a similar effect when applied in other therapeutic contexts, and these associations may be of particular interest and importance in the coming decade as manufacturers continue to design programs that buffer patients from high cost sharing that simultaneously reduce patient's potential cost burden while preserving demand for higher cost, branded products.

Appendix

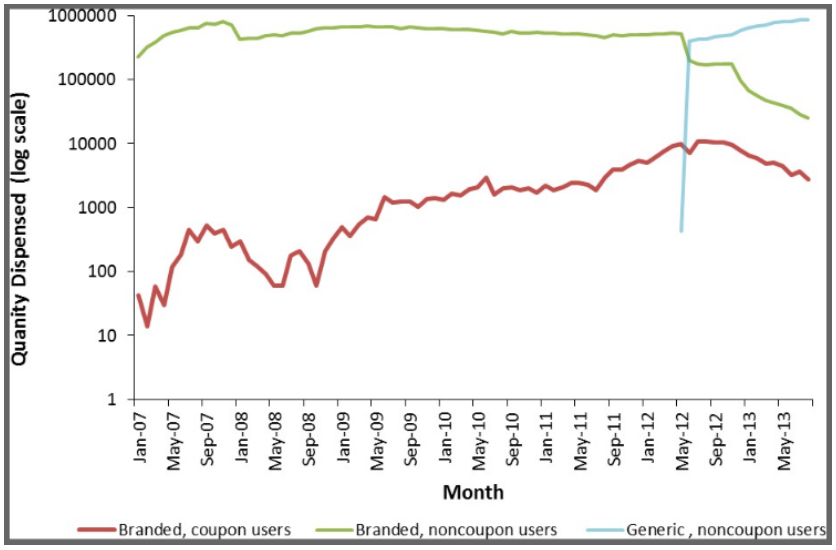

Figure A1. Monthly retail sales of atorvastatin, 2007-2013.
Source: IMS Health LifeLink LRx Data, 2007-2013.

Figure A2. Pharmacy sales of rosuvastatin, 2007–2013.
Source: IMS Health LifeLink LRx Data, 2007–2013

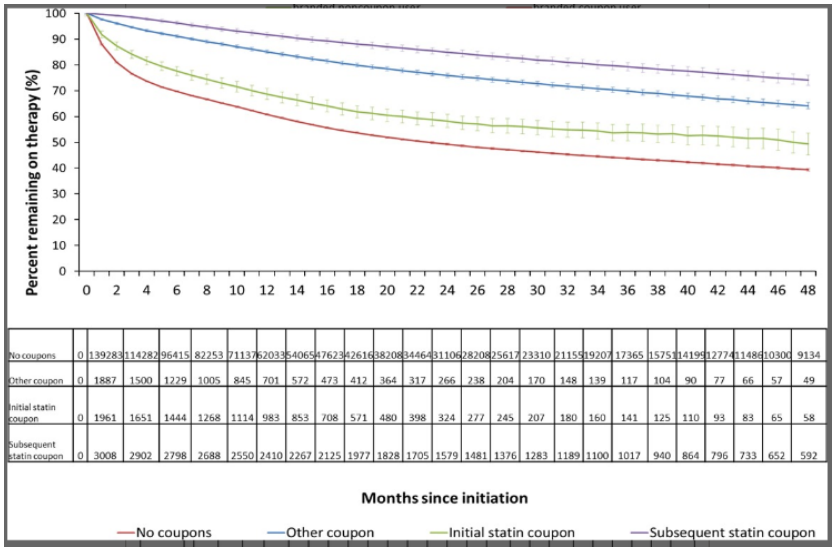

Figure A3. Cumulative termination of atorvastatin and rosuvastatin therapy stratified by coupon use.
Source: IMS Health LifeLink LRx Data, 2007–2013

Table A1. Differences in Average Monthly Utilization Stratified by Type of Statin

	Time following first coupon				
Time following incident statin fill	1 mo	1 Yr	2 Yrs	3 Yrs	4 Yrs
Atorvastatin (average pill-days dispensed)					
No coupons					
Predicted level (SE)	29.4 (0.0)	23.8 (0.0)	24.7 (0.0)	24.8 (−0.1)	25.5 (−0.1)
Other coupon					
Predicted level (SE)	28.8 (−0.1)	23.8 (−1.8)	24.9 (−4.0)	25.1 (−6.2)	25.3 (−8.5)
Difference from counterfactual[a]	−0.6 (−0.1)	0.0 (−1.8)	0.2 (−4.0)	0.3 (−6.2)	−0.2 (−8.5)
Initial statin coupon					
Predicted level (SE)	30.3 (−0.3)	24.5 (−3.8)	24.3 (−8.1)	25.1 (−12.9)	25.0 (−17.4)
Difference from counterfactual	0.5 (−0.3)	0.1 (−3.8)	−0.8 (−8.1)	−0.1 (−12.9)	−1.0 (−17.4)
Subsequent statin coupon					
Predicted level (SE)	26.7 (−0.1)	24.4 (−2.6)	24.5 (−5.7)	24.9 (−8.8)	25.2 (−12.1)
Difference from counterfactual	−2.5 (−0.1)	0.5 (−2.6)	−0.3 (−5.7)	−0.1 (−8.8)	−0.4 (−12.1)
Rosuvastatin (average pill-days dispensed)					
No coupons					
Predicted level (SE)	28.6 (0.0)	23.5 (0.0)	24.3 (−0.1)	24.5 (−0.1)	25.2 (−0.1)
Other coupon					
Predicted level (SE)	27.8 (−0.1)	23.6 (−1.8)	24.4 (−4.0)	24.6 (−6.3)	25.2 (−8.7)
Difference from counterfactual	−0.8 (−0.1)	0.2 (−1.8)	0.2 (−4.0)	0.2 (−6.3)	0.0 (−8.7)
Initial statin coupon					
Predicted level (SE)	24.4 (−0.3)	22.7 (−5.2)	24.0 (−12.0)	24.8 (−19.1)	24.7 (−25.8)
Difference from counterfactual	−4.2 (−0.3)	−0.8 (−5.2)	−0.3 (−12.0)	0.3 (−19.1)	−0.5 (−25.8)
Subsequent statin coupon					
Predicted level (SE)	26.7 (−0.1)	23.4 (−3.5)	24.4 (−8.0)	24.7 (−12.5)	24.8 (−17.0)
Difference from counterfactual	−1.8 (−0.1)	−0.1 (−3.5)	0.1 (−8.0)	0.2 (−12.5)	−0.4 (−17.0)

a Represents the difference in average predicted values between coupon users and their counterfactual noncoupon using counterparts within each group (initial, subsequent, nonstatin). Source: IMS Health LifeLink LRx Data, 2007–2013.

Table A2. Differences in Expenditures Stratified by Type of Statin

	Time				
	1 mo	1 Yr	2 Yrs	3 Yrs	4 Yrs
Time following incident statin fill					
Average atorvastatin copayment, $					
No coupons					
Predicted level (SE)	18.1 (−0.1)	14.8 (−0.1)	16.4 (−0.1)	15.3 (−0.2)	13.8 (−0.2)
Other coupon					
Predicted level (SE)	15.3 (−0.2)	12.7 (−4.2)	13.3 (−9.5)	12.4 (−13.6)	11.5 (−17.2)
Difference from counterfactual[a]	−2.7 (−0.2)	−2.1 (−4.2)	−3.0 (−9.5)	−2.8 (−13.6)	−2.3 (−17.2)
Initial statin coupon					
Predicted level (SE)	19.8 (−2.6)	8.1 (−11.8)	7.3 (−23.2)	7.1 (−35.2)	3.4 (−23.2)
Difference from counterfactual	2.8 (−2.6)	−5.0 (−11.8)	−8.0 (−23.2)	−8.2 (−35.2)	−11.3 (−23.2)
Subsequent statin coupon					
Predicted level (SE)	13.4 (−0.3)	16.6 (−14.7)	18.9 (−36.5)	18.4 (−54.8)	14.6 (−59.0)
Difference from counterfactual	−6.4 (−0.3)	1.4 (−14.7)	2.2 (−36.5)	2.8 (−54.8)	0.5 (−59.0)
Average atorvastatin monthly cost, $					
No coupons					
Predicted level (SE)	128.3 (−0.2)	103.0 (−0.2)	110.4 (−0.3)	113.4 (−0.3)	118.0 (−0.5)
Other coupon					
Predicted level (SE)	127.9 (−0.5)	104.7 (−8.7)	113.3 (−20.6)	116.4 (−32.7)	118.3 (−45.0)
Difference from counterfactual	−1.4 (−0.4)	1.3 (−8.7)	2.5 (−20.6)	2.5 (−32.7)	−0.1 (−45.0)
Initial statin coupon					
Predicted level (SE)	160.7 (−1.8)	122.4 (−19.3)	120.6 (−41.0)	123.4 (−64.6)	119.2 (−84.8)
Difference from counterfactual	19.5 (−1.7)	6.1 (−19.4)	−2.3 (−41.0)	1.2 (−64.6)	−4.7 (−84.8)
Subsequent statin coupon					
Predicted level (SE)	118.8 (−0.5)	110.8 (−12.5)	115.3 (−28.3)	120.5 (−45.6)	124.8 (−63.8)
Difference from counterfactual	−11.0 (−0.4)	5.3 (−12.5)	2.1 (−28.3)	5.2 (−45.6)	4.9 (−63.8)
Average rosuvastatin copayment, $					
No coupons					
Predicted level (SE)	21.4 (−0.1)	17.3 (−0.1)	17.7 (−0.2)	17.3 (−0.2)	17.5 (−0.3)
Other coupon					
Predicted level (SE)	16.9 (−0.2)	13.3 (−4.3)	13.3 (−9.2)	12.9 (−13.7)	12.9 (−18.7)
Difference from counterfactual	−4.3 (−0.2)	−3.9 (−4.3)	−4.2 (−9.2)	−4.3 (−13.7)	−4.3 (−18.7)
Initial statin coupon					
Predicted level (SE)	15.3 (−2.3)	11.8 (−17.6)	12.6 (−41.1)	14.9 (−74.9)	15.5 (−105.7)
Difference from counterfactual	−6.8 (−2.3)	−5.8 (−17.6)	−5.4 (−41.1)	−2.6 (−74.9)	−2.2 (−105.7)
Subsequent statin coupon					
Predicted level (SE)	12.0 (−0.5)	12.8 (−17.1)	11.4 (−33.3)	9.9 (−44.8)	9.2 (−55.9)
Difference from counterfactual	−9.8 (−0.5)	−4.8 (−17.1)	−6.4 (−33.3)	−7.5 (−44.8)	−8.4 (−55.9)
Average rosuvastatin monthly cost, $					
No coupons					
Predicted level (SE)	128.6 (−0.2)	106.9 (−0.2)	114.7 (−0.3)	119.5 (−0.3)	126.8 (−0.6)
Other coupon					
Predicted level (SE)	126.6 (−0.5)	109.0 (−8.5)	116.5 (−20.0)	120.7 (−31.9)	126.4 (−45.3)
Difference from counterfactual	−3.4 (−0.4)	1.1 (−8.5)	0.9 (−20.0)	1.0 (−31.9)	−0.3 (−45.3)
Initial statin coupon					
Predicted level (SE)	106.6 (−1.4)	101.9 (−21.6)	113.9 (−52.4)	121.9 (−86.4)	124.9 (−120.1)
Difference from counterfactual	−17.0 (−1.4)	−2.7 (−21.6)	−2.1 (−52.4)	0.0 (−86.4)	−4.1 (−120.1)
Subsequent statin coupon					
Predicted level (SE)	117.0 (−0.6)	107.3 (−17.2)	116.1 (−40.7)	122.5 (−66.3)	125.8 (−92.2)
Difference from counterfactual	−8.2 (−0.6)	0.6 (−17.2)	0.7 (−40.7)	1.2 (−66.3)	−1.6 (−92.2)

a Represents the difference in average predicted values between coupon users and their counterfactual noncoupon using counterparts within each group (initial, subsequent, nonstatin). Source: IMS Health LifeLink LRx Data, 2007–2013.

Table A3. Average Monthly Statin Utilization in Alternative Cohorts

	Time				
	1 mo	1 Yrs	2 Yrs	3 Yrs	4 Yrs
Time following incident statin fill					
Open cohort (average pill-days dispensed)					
No coupons					
Predicted level (SE)	29.2 (0.0)	23.5 (0.0)	24.5 (0.0)	24.7 (0.0)	25.6 (0.0)
Other coupon					
Predicted level (SE)	28.6 (0.0)	23.6 (−0.8)	24.9 (−1.7)	25.5 (−2.8)	26.5 (−3.9)
Difference from counterfactuala	−0.5 (0.0)	0.1 (−0.8)	0.4 (−1.7)	0.8 (−2.8)	0.9 (−3.9)
Initial statin coupon					
Predicted level					
Standard error					
Difference from counterfactual	28.2 (−0.2)	24.1 (−2.0)	24.0 (−4.3)	24.5 (−6.8)	25.4 (−9.6)
Standard error	−1.2 (−0.2)	0.2 (−2.0)	−0.6 (−4.3)	−0.2 (−6.8)	−0.1 (−9.6)
Subsequent statin coupon					
Predicted level (SE)	27.2 (−0.1)	24.1 (−1.4)	24.9 (−3.1)	25.5 (−4.9)	26.4 (−6.9)
Difference from counterfactual	−1.8 (−0.1)	0.5 (−1.4)	0.3 (−3.1)	0.7 (−4.9)	0.7 (−6.9)
No mail-order cohort (average pill-days dispensed)					
No coupons					
Predicted level (SE)	28.9 (0.0)	23.4 (0.0)	24.3 (0.0)	24.5 (0.0)	25.3 (0.0)
Other coupon					
Predicted level (SE)	28.0 (−0.1)	23.3 (−0.9)	24.4 (−2.1)	24.8 (−3.2)	25.3 (−4.5)
Difference from counterfactual	−0.8 (0.0)	0.0 (−0.9)	0.1 (−2.1)	0.3 (−3.2)	0.1 (−4.5)
Initial statin coupon					
Predicted level	27.6 (−0.2)	23.8 (−2.3)	23.6 (−5.0)	23.9 (−7.9)	24.6 (−11.0)
Difference from counterfactual	−1.6 (−0.2)	0.1 (−2.3)	−0.8 (−5.0)	−0.6 (−7.9)	−0.7 (−11.0)
Subsequent statin coupon					
Predicted level (SE)	26.7 (−0.1)	23.9 (−1.6)	24.6 (−3.5)	25.1 (−5.6)	25.6 (−7.7)
Difference from counterfactual	−2.2 (−0.1)	0.4 (−1.6)	0.1 (−3.5)	0.4 (−5.6)	0.2 (−7.7)
Limited opioid use cohort (average pill-days dispensed)					
No coupons					
Predicted level (SE)	29.9 (0.0)	24.1 (0.0)	24.3 (−0.1)	24.3 (−0.1)	25.6 (−0.1)
Other coupon					
Predicted level (SE)	29.0 (−0.1)	23.6 (−1.9)	24.0 (−4.1)	24.5 (−6.5)	25.8 (−9.2)
Difference from counterfactuala	−1.1 (−0.1)	−0.5 (−1.9)	−0.2 (−4.1)	0.2 (−6.4)	0.2 (−9.2)
Initial statin coupon					
Predicted level (SE)	28.5 (−0.3)	24.4 (−3.7)	24.6 (−8.1)	24.9 (−12.6)	25.8 (−17.7)
Difference from counterfactual	−1.9 (−0.3)	−0.2 (−3.7)	0.1 (−8.1)	0.7 (−12.6)	0.3 (−17.7)
Subsequent statin coupon					
Predicted level (SE)	26.6 (−0.1)	24.6 (−3.1)	24.7 (−6.8)	25.0 (−10.6)	25.4 (−14.6)
Difference from counterfactual	−3.5 (−0.1)	0.3 (−3.1)	0.2 (−6.8)	0.6 (−10.6)	−0.3 (−14.6)

[a] Represents the difference in average predicted values between coupon users and their counterfactual noncoupon using counterparts within each group (initial, subsequent, nonstatin). Source: IMS Health LifeLink LRx Data, 2007–2013.

References

Aiken M. Use and shifting costs of healthcare: a review of the use of medicines in the U.S. in 2013. IMS Health. Available from http://www.imshealth.com/en/thought-leadership/ims-institute/reports/use-of-medicines-in-the-us-2013. Accessed April 3, 2015.

Starner CI, Alexander GC, Bowen K, Qiu Y, Wickersham PJ, Gleason PP. Specialty drug coupons lower out-of-pocket costs and may improve adherence at the risk of increasing premiums. Health Aff 2014; 33: 1761–9.

Grande D. The cost of drug coupons. JAMA 2012; 307: 2375–6.

Visante. How copay coupons could raise prescription drug costs by $32 billion over the next decade [white paper]. Pharmaceut Care Manage Assoc. November 2011.

Schultz D. Drug coupons: a good deal for the patient, but not the insurer. Kaiser Health News. http://kaiserhealthnews.org/news/drug-coupons/. Accessed April 3, 2015.

Kornfield R, Donohue J, Berndt ER, Alexander GC. Promotion of prescription drugs to consumers and providers, 2001–2010. PLoS ONE 2013; 8: e55504.

Bhutada NS, Cook CL, Perri M 3rd. Consumers responses to coupons in direct-to-consumer advertising of prescription drugs. Health Mark Q 2009; 26: 333–46.

Alexander GC, Zhang J, Basu A. Characteristics of patients receiving pharmaceutical samples and association between sample receipt and out-of-pocket prescription costs. Med Care 2008; 46: 394–402.

Daugherty JB, Maciejewski ML, Farley JF. The impact of manufacturer coupon use in the statin market. J Manag Care Pharm 2013; 19: 765–72.

Ross JS, Kesselheim AS. Prescription-drug coupons—no such thing as a free lunch. N Engl J Med 2013; 369: 1188–9.

Coupons for Patients, But Higher Bills for Insurers. New York Times. January 1, 2011.

IMS Health. Longitudinal LRX Insights. Available from http://www.imsbrogancapabilities.com/en/market-insights/lrx.html. Accessed April 3, 2015.

Hess LM, Raebel MA, Conner DA, Malone DC. Measurement of adherence in pharmacy administrative databases: a proposal for standard definitions and preferred measures. Ann Pharmacother 2006; 40: 1280–8.

Clark DO, Von Korff M, Saunders K, Baluch WM, Simon GE. A chronic disease score with empirically derived weights. Med Care 1995; 33: 783–95.

Korn EL, Graubard BI. Analysis of Health Surveys. New York, NY: Wiley, 1999: 126–40.

Li Z, Mahendra G. Using “Recycled Predictions” for Computing Marginal Effects. Available from http://www.lexjansen.com/wuss/2009/hor/HOR-Li.pdf. Accessed July 28, 2015.

Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. Biometrika 1986; 73: 13–22.

Graubard B, Edward L, Korn E. Predictive margins with survey data. Biometrics 1999; 55: 652–9.

Drug companies fend off competition from generics by offering discount coupons. Available from http://www.washingtonpost.com/national/health-science/drug-companies-fend-off-competition-from-generics-by-offering-discount-coupons/2012/10/01/c7a393be-f05f-11e1-ba17-c7bb037a1d5b_story.html. Accessed June 10, 2015.

Levinson DR (Inspector General). Manufacturer Safeguards May Not Prevent Copayment Coupon Use for Part D Drugs. Department of Health and Human Services, Office of the Inspector General. September, 2014 (OEI-05-12-00540).