

# Association Between Adherence to Generic Statin Therapy and Outcomes: Total Cost of Care and Medical Events Over Two Years

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## Background

- Prime's 2012 commercial book of business cholesterol drug cost trends identified the following:
  - Cholesterol medication was 6.9 percent of all pharmacy benefit expenditures;
  - Generic utilization rate was 72 percent, an increase from 58 percent in 2011;
  - Overall 2011 ingredient costs per claim were \$56.16 (brand \$146.98 and generic \$20.01);
- Member share for generic cholesterol lowering medication in 2012 was approximately 37 percent, or \$7.50.<sup>1</sup>
- A 2004 study found that patients exposed to statin copays between \$10 and \$20 or greater than \$20 had significantly lower rates of persistence (e.g., discontinued earlier) when compared to those exposed to a statin copy of less than \$10.<sup>2</sup>
- In 2011, CVS Caremark published a study utilizing 2005 to 2008 medical and pharmacy data examining the relationships of adherence on hospitalizations and medical costs of individuals with an average age of ≥65. The authors concluded that despite higher adherence to cholesterol medications resulting in higher pharmacy costs, the reductions in hospitalizations and emergency department use were associated with lower medical costs in the adherent population.<sup>3</sup>
- The cost analysis presented above are limited in their generalizability because data were representative of a retiree population and analyzed prior to the approval of many of the now available generic cholesterol lowering drugs.<sup>3</sup>
- Minimal data is available quantifying outcome and cost differences in members adherent and non-adherent to primarily generic statin medications among commercially insured individuals followed for more than one year.

## Objective & Purpose

Examine the association between medication adherence and all-cause hospitalization or emergency room (ER) events, and compare medical and pharmacy costs among individuals adherent and non-adherent to their generic statin medications.

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## Methods

- This retrospective concurrent cohort study utilized integrated administrative medical and pharmacy claims data from a commercial Blue Cross and Blue Shield (BCBS) Plan in the Central U.S. with Prime Therapeutics pharmacy benefit coverage covering approximately 1.2 million lives at any time during 2007 through 2010.
- Members were required to be continuously enrolled from January 1, 2007 through December 31, 2010.
- Members were required to have either two separate hypercholesterolemia office visits or a hypercholesterolemia related hospitalization in 2008.
- The members' first 2008 hypercholesterolemia medical encounter was defined as the index date.
- Members were required to have a statin supply on their index date or have been identified as having a high risk condition diagnosis at any time from January 1, 2007 through their medical index date in 2008. High risk conditions were defined as diabetes mellitus (DM), coronary artery disease (CAD), embolic stroke, or peripheral vascular disease (PVD).
- All members were followed for two years post their 2008 index date.
- Adherence was assessed using the proportion of days covered (PDC) method for the two-year follow-up period. All statin claims were used to calculate the PDC and members were considered adherent if their PDC was ≥80 percent.
- Only members with at least 80 percent of their statin claims as generic statin were included in the analyses.
- All medical and pharmacy claim total allowed amounts (plan and member) were summed to determine total cost of care.
- Members were excluded if the total medical costs were \$0 in the two-year follow-up, if there was evidence of any Medicare payments, or if demographic census data was missing.
- Members were also excluded from the analysis if they were not 18 years of age or older on the index date or if at any time in the three-year study period they had a medical claim indicating dementia, a pregnancy, or a nursing home stay.
- The following member characteristics were derived and used as a covariate: age, gender, Charlson Comorbidity Index score (Charlson risk score)<sup>4</sup>, enrollment at any time in a consumer directed health plan (CDHP), education and income based on ZIP code census data, presence of a primary or secondary diagnosis field coded medical claim for depression or bipolar disorder identified in the pre-period and high risk status.
- The Kaplan-Meier method with a log-rank statistical test was used for hospitalization or ER event rate calculation and association with adherence. To assess the association between hospitalization or ER event rate and adherence adjusting for covariates, a Cox proportional hazard regression model was created.
- Cost analyses were performed using a generalized linear model (GLM) with gamma log link and adjusted for the same covariates.

## Results

- Of the 144,564 members with hypercholesterolemia who were continuously enrolled January 1, 2007 to December 31, 2010, 21,910 met inclusion and exclusion criteria. (Figure 1)
- During the two-year follow-up there were 10,126 (46.2%) members adherent to their statin medication (PDC ≥80%) and 11,784 (53.8%) members non-adherent (PDC <80%).
- Significant baseline differences existed between the adherent and non-adherent groups. (Table 1)

### Hospitalization or ER Events Association with Statin Adherence

- The unadjusted two-year follow-up Kaplan-Meier curve shows that the adherent group had a lower hospitalization or ER event rate at 25 percent compared to the non-adherent group at 27.6 percent, p <0.001. (Figure 2)
- The Cox Proportional Hazards model, adjusting for baseline differences, found the adherent group had a 13 percent lower hospitalization or ER event rate (Hazard Ratio 0.87, 95% confidence interval, 0.83 to 0.92).

### Total Cost of Care Association with Statin Adherence (Figure 3)

- Overall average per-person two year total costs of care were \$161 lower in the adherent group (\$15,290 standard deviation [SD] \$9,346) compared to the non-adherent group (\$15,451, SD \$8,935), p <0.001. The adherent group had six percent relative lower cost (Relative Cost [RC] 0.94, 95% confidence interval [CI] 0.92 to 0.97).
- Medical costs were \$1,022 lower in the adherent group (\$11,353, SD \$6,814) compared to the non-adherent group (\$12,375, SD \$6,933), p <0.001. The adherent group had 13 percent relative lower cost (RC 0.87, 95% CI 0.84 to 0.90).
- Pharmacy costs were \$937 higher in the adherent group (\$4,016, SD \$3,912) compared to the non-adherent group (\$3,079, SD \$2,369), p <0.001. The adherent group had 26 percent relative higher costs (RC 1.26, 95% CI 1.22 to 1.30).

Table 1. Member characteristics

Member characteristics	Generic Statin PDC ≥80% n = 10,126	Generic Statin PDC <80% n = 11,784	p value*
Age, n (%)			<0.001
18-44	996 (9.8%)	1,900 (16.1%)	
45-54	3,599 (35.5%)	4,750 (40.3%)	
55-64	5,110 (50.5%)	4,819 (40.9%)	
65 and up	421 (4.2%)	315 (2.7%)	
Male, n (%)	5,746 (56.8%)	6,466 (54.9%)	0.005
Education, ZIP code prevalence of bachelor degree ≥20%, n (%)	5,822 (57.5%)	6,325 (53.7%)	<0.001
ZIP code median household income ≥\$50,000, n (%)	4,020 (39.7%)	4,348 (36.9%)	<0.001
Enrollment in consumer directed health plan, n (%)	723 (7.1%)	917 (7.8%)	0.072
High risk, n (%)	2,694 (26.6%)	2,650 (22.5%)	<0.001
Comorbidity (Charlson Index Score), mean (S.D.)	1.4 (0.9)	1.3 (0.9)	0.050
Depression/bipolar disorder, n (%)	599 (5.9%)	885 (7.5%)	<0.001

PDC= proportion of days covered; S.D.= standard deviation  
High risk defined as presence of DM, CAD, embolic stroke, PVD in pre-period  
\*Comparisons between groups were performed with the ANOVA test for continuous variables and the chi-square test for categorical variables.

Figure 1. Member flow diagram

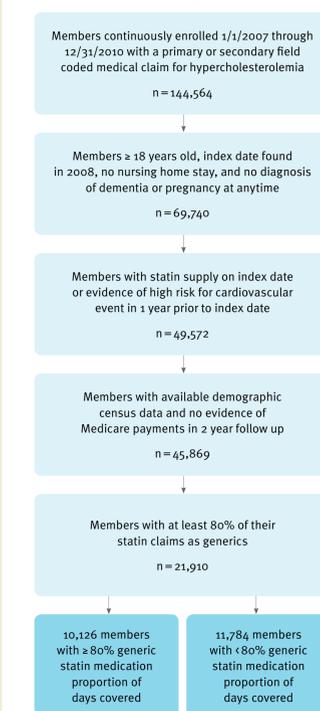


Figure 2. First hospitalization or emergency room visit event

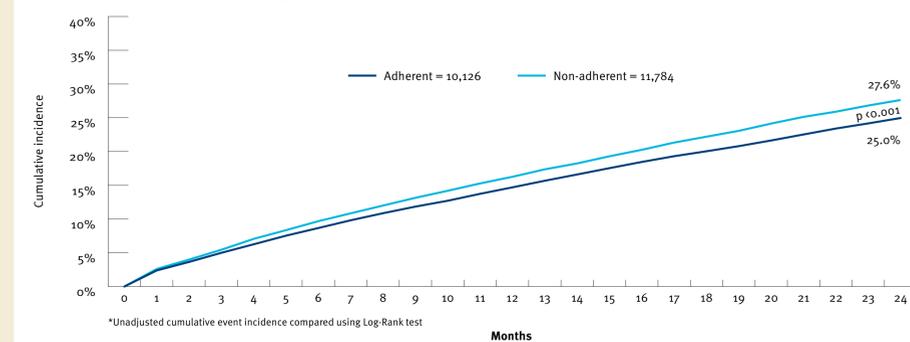
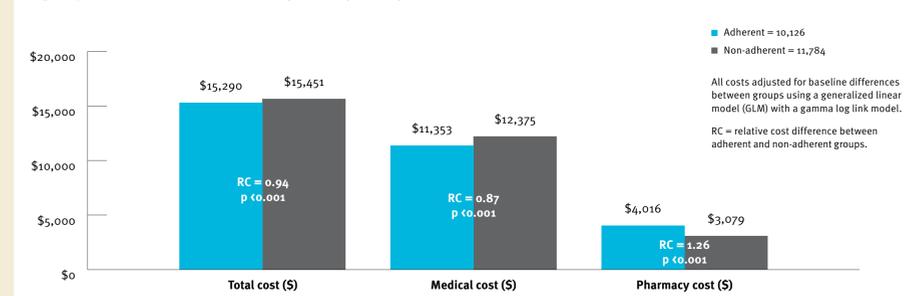


Figure 3. Total cost, medical cost, and pharmacy cost by statin adherence



## Limitations

- Administrative pharmacy and medical claims have the potential for miscoding and include assumptions of member actual medication use and diagnosis.
- Data are limited to a commercial population in the Central U.S.; therefore findings may not be generalized to Medicare or Medicaid populations or other geographic regions.
- Differences found in medical events and costs between the adherent and non-adherent populations may be influenced by healthier lifestyles. Lifestyle information is unavailable in administrative claims data and therefore could not be included as a covariate in this study.
- Prime defined adherence using the PDC ≥80 percent which is an arbitrary cut point, however this cut point has frequently been used in previous research.<sup>2,3</sup>
- Adherence was determined using only statin claims and did not include other cholesterol lowering medications.

## Conclusions

- In this two-year total cost of care analysis, individual's adherent to generic statin medication had an associated unadjusted 2.6 percentage point lower hospitalization or ER event rate, which remained a significant 13 percent lower in a multivariate analysis.
- In individuals with hypercholesterolemia, total annual cost of care was lower in the generic statin adherent group. The significant cost differences were the result of lower medical costs off-setting higher pharmacy costs. These findings differ from previous research, potentially due to population differences including younger age and primary use of generic statin medications.
- Future research is required to determine if interventions to improve adherence will result in lower total cost of care.

## References

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