

# Primary Nonadherence to Statin Medications in a Managed Care Organization

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## ABSTRACT

**BACKGROUND:** Primary nonadherence to a medication occurs when a drug is prescribed but the patient fails to pick the prescription up from the pharmacy. Managed care organizations that provide integrated care using electronic medical records (EMR) are an ideal setting to study primary nonadherence.

**OBJECTIVE:** To identify patient and provider characteristics that are significantly associated with primary nonadherence to statin medications compared with a population of patients who picked up their first statin order.

**METHODS:** This was a retrospective cohort study of patients with a new statin prescription. Patients with a new order for a statin prescription between December 1, 2009, and February 28, 2010, were eligible. A statin order was considered new if the patient had no statin prescriptions in the previous 12 months. Study participants were 24 years and older with 12 months of continuous membership prior to the statin order. Patients were defined as primary nonadherent if they did not pick up their new prescription within 90 days. Descriptive and multivariate (conditional logistic regression) analyses of patients who did and did not pick up their new statin prescriptions were performed using demographic and socioeconomic information, health care utilization, health conditions, medical benefits, and prescriber characteristics.

**RESULTS:** A total of 19,826 patients with a new statin order that met all of the inclusion and exclusion criteria was identified. Of these, 3,049 patients (15.4%) did not pick up their statin prescriptions within 90 days of the order date. Primary nonadherent patients tended to be younger (55 vs. 57 years,  $P < 0.001$ ) and healthier, with fewer comorbid conditions (Charlson Comorbidity Index  $\geq 1$ , 42.2% vs. 52.3%,  $P < 0.001$ ), lower rates of hospitalizations (7.2% vs. 12.0%,  $P < 0.001$ ), fewer concurrent prescriptions (3 vs. 4,  $P < 0.001$ ) and fewer clinic (4 vs. 5,  $P < 0.001$ ) and emergency department visits (18.2% vs. 24.6%,  $P < 0.001$ ) in the prior year than adherent patients. Although the multivariate model agreed well with the observed data, the characteristics included had a poor ability to predict primary nonadherence (c-statistic = 0.603).

**CONCLUSION:** Primary nonadherence has been recognized as a significant problem for many years, and electronic health records are allowing researchers to investigate the extent of the problem. In this study, almost 1 in 6 patients (15.4%) failed to pick up their new statin order within 90 days. However, clinical and demographic information available in electronic health care data may not be useful in predicting primary nonadherence. New methods and interventions need to be developed to improve primary adherence.

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## What is already known about this subject

- Primary nonadherence occurs when a prescription is written but the patient never takes the prescription to the pharmacy, or, if the prescription is taken to the pharmacy, the patient never comes back to pick up the medication (abandonment).
- Historically, in a paper-based system, it has been difficult to quantify the extent of primary nonadherence because there was no easy way to track when the prescription was written and when, if ever, it was filled.
- A study by Fischer et al. (2010) captured e-prescribing data and then linked this back to pharmacy claims to determine rates of primary medication nonadherence. They found that medication class was a significant predictor of primary nonadherence and that some chronic conditions such as diabetes (31.4%), hypertension (28.4%), and hyperlipidemia (28.2%) had high rates of nonadherence to a new prescription.
- Two other recent studies, Liberman et al. (2010) and Raebel et al. (2012), reported primary nonadherence rates of 34.1% and 13%, respectively, for antihyperlipidemic drugs. Liberman et al. used a methodology similar to Fischer, connecting e-prescribing data with administrative pharmacy claims, while Raebel et al. studied patients in a managed care setting.

## What this study adds

- This study is the largest to focus exclusively on primary nonadherence to statin medications with close to 20,000 new orders identified over a 3-month period of time.
- Within an integrated health care delivery system, a high rate (15.4%) of primary nonadherence to statin medications was identified in a population of patients with a drug benefit.
- Primary nonadherent patients tended to be younger with fewer comorbid conditions, fewer concomitant medications, and lower utilization of health care services than those who were adherent to their new statin prescriptions.
- Health care data provide useful information regarding primary nonadherent patients; however, models built using health care data may not be predictive of nonadherent behavior.

Until recently, most medication adherence research focused on identifying factors and outcomes associated with secondary nonadherence (i.e., whether or not patients refill their prescriptions after the initial fill.<sup>1</sup>) Current technology, including electronic prescribing and the development of electronic medical records, now allows for more rigorous population-based studies of primary medication nonadherence.<sup>1,2</sup> Primary nonadherence occurs when a provider prescribes (or orders) a new medication for a patient and the order is never filled or dispensed. In this scenario, the patient either never takes the prescription to the pharmacy, or does take the prescription to the pharmacy but never comes back to pick up the drug. The extent and clinical outcomes of primary medication nonadherence are relatively unknown.<sup>1</sup>

Patients who are nonadherent to their initial prescriptions represent an important opportunity for clinicians to intervene and improve health outcomes and care delivery. This is especially true for medications to treat chronic conditions such as hyperlipidemia. A few studies have recently looked at primary nonadherence to lipid-lowering therapies by leveraging these new technologies.<sup>3-5</sup> Fischer et al. (2010)<sup>3</sup> examined e-prescriptions written in community-based practices in Massachusetts and found 28.2% of new prescriptions for hyperlipidemia medications were not filled prior to the end of the study. Liberman et al. (2010),<sup>4</sup> using e-prescribing and pharmacy claims data from a large insurer in New Jersey, estimated that 34.1% of new prescriptions for antihyperlipidemic drugs were unfilled within 60 days of the date the prescription was written, while Raebel et al. (2012)<sup>5</sup> reported a primary nonadherence rate of 13% for antihyperlipidemics within 30 days of the order date in a Colorado managed care organization.

These differences are not necessarily surprising, since primary nonadherence rates are known to vary depending on the research methodology, the patient population, and the health care setting.<sup>6</sup> Data from closed-network integrated health care delivery systems with electronic medical records may provide the best estimates of primary nonadherence, since patients have a financial incentive to fill prescriptions within the network, which allows more comprehensive capture of prescription fills and more accurate calculations of primary nonadherence rates.<sup>6,7</sup>

This study examines primary nonadherence to statins in a large integrated health care delivery system. The objectives of the study were to compare individuals who did and did not pick up their newly prescribed statin medications within 90 days of the order being written and to identify significant factors associated with primary nonadherence.

## Methods

### Setting

Kaiser Permanente Southern California (KPSC) is a nonprofit, group-model managed care organization (MCO) providing

integrated health care services to approximately 3.4 million members in Southern California. KPSC membership closely mirrors the Southern California population, is racially diverse, and includes a wide socioeconomic spectrum.<sup>8</sup> Approximately 10% of the members are Medicare age, and a small percentage (<5%) are Medicaid eligible. Care is provided by the Southern California Permanente Medical Group (SCPMG), a multispecialty practice group, which contracts exclusively with the health plan and provides a full range of services to the membership. SCPMG includes close to 5,000 partner and associate physicians practicing at 14 medical centers and 197 outpatient clinics in Southern California.

### Patients

KPSC has a large population of members who are taking statin medications; in 2010, KPSC outpatient pharmacies dispensed 1.49 million statin prescriptions to approximately 500,000 members. For this analysis, all prescription orders for a statin medication written between December 1, 2009, and February 28, 2010, were eligible for inclusion. This includes all drugs in the statin class plus combination statin products. To be eligible, a patient needed to have 12 months of continuous membership with drug benefit prior and 3 months continuous membership after the order date. In addition, patients needed to be at least 24 years of age at the time the order was written. We restricted the analysis to new statin orders, which we defined as being written for those individuals who had not received a statin prescription or refill in the 365 days prior to the new order date (index date).

Patients were followed for a period of 90 days after the index date. Patients who did not pick up their new statin prescriptions within this 90-day window were considered primary nonadherent. Because orders can change, new orders can be rewritten, and the drug product or strength can be changed to address new clinical circumstances, patients were considered adherent if they picked up any statin or statin combination within the 90-day time window.

### Statistical Analysis

A patient-level analysis was undertaken where the endpoint of interest was primary nonadherence, defined as the patient not picking up a new statin prescription within 90 days of the index date. Primary nonadherent patients were compared with those who were adherent to their new statin prescriptions. Patient baseline information was captured during the 365 days prior to the order date. Baseline information included patient demographic characteristics and socioeconomic factors; health care utilization; health conditions; medical benefits; and prescriber characteristics.

Patient demographic characteristics and socioeconomic factors included age, gender, and race information, plus geocoded median household income. Information on health care

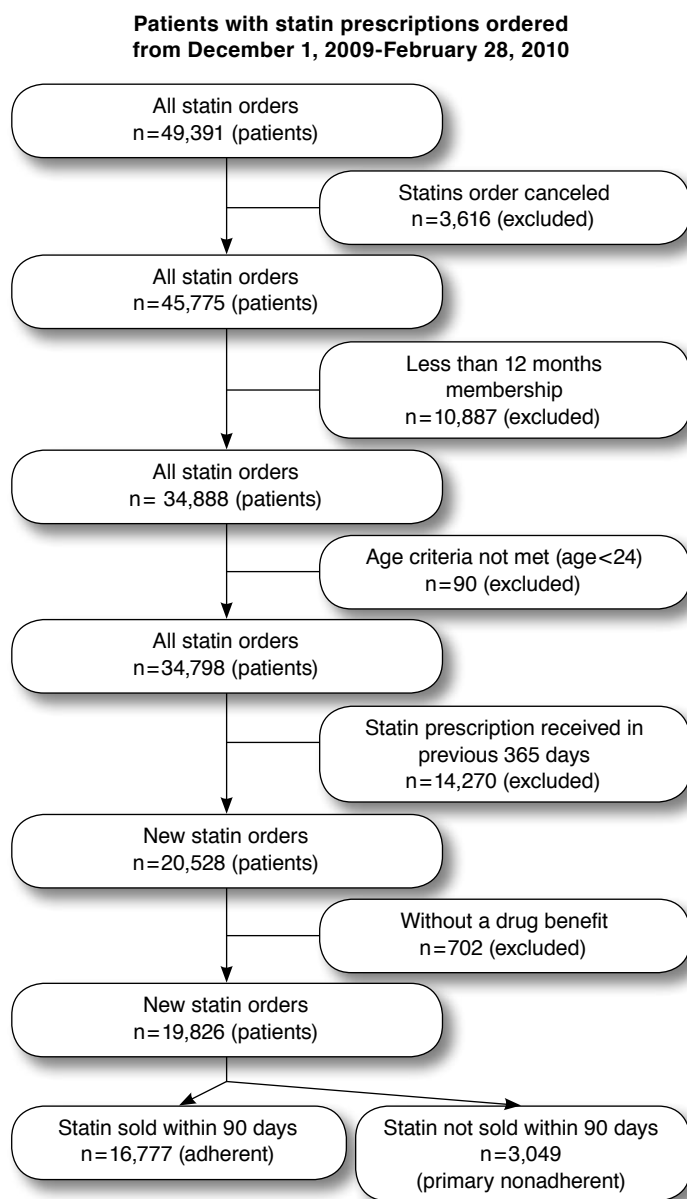
utilization in the 12 months prior to the order date included the number of distinct medications (based on the generic product identifier [GPI] subclass), the number of medical office visits, the number of emergency department (ED) visits, and hospital admissions. The indication for statin treatment (primary vs. secondary prevention) was also captured for patients at baseline. A Charlson Comorbidity Index (CCI), using *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-DM) codes from inpatient and outpatient encounters rolled into 17 predefined disease categories, was determined for all eligible patients to control for severe chronic conditions and mortality risk (see Appendix A, available online).<sup>9-11</sup> The CCI was broken down into a dichotomous variable with patients categorized into a CCI score of 1 or greater versus those with a CCI score equal to 0. Baseline low-density lipoprotein (LDL) cholesterol test results, done in the 12 months prior and closest to the index date, were grouped into 4 categories: LDL < 100 milligrams per deciliter (mg/dL), LDL between 100-160 mg/dL, LDL > 160 mg/dL, and nonmeasurement (no tests in the prior 12 months). Patient medical benefit information included an indicator for dual insurance coverage at the time of the index date when the patient had medical coverage under a personal plan and also coverage under a spouse's or other health plan.

Lastly, we captured prescriber information to determine if specific demographic characteristics were associated with increased rates of primary nonadherence to the new statin prescription. Prescriber demographic information included age, gender, race, and specialty. For each provider, we also determined the number of new statin orders written during the 90-day study window. A high-prescriber indicator was generated based on whether the provider wrote for more than or less than the median number of new statin orders.

Descriptive analyses are reported for individual risk factors at baseline. Continuous variables were expressed as median values, and values across groups were compared using the Kruskal-Wallis test. Categorical variables were expressed as proportions and compared using chi-square tests. Univariate logistic regression analyses were performed to identify important covariates that were at least moderately associated with primary nonadherence prior to including them in the multivariate analysis. Variables with a  $P < 0.25$ , along with the variables of known clinical interest, were selected for the final model. A multiple logistic regression model using the selected variables was fitted, and interaction terms were tested using the likelihood ratio test after the primary main effect model was fitted. Odds ratio and 95% confidence intervals for predictors of primary nonadherence were estimated from the final multivariate logistic model. Discriminative ability of the final model was tested using the c-statistic.

All analyses were conducted using SAS 9.1 software (SAS Institute, Cary, NC). A two-sided  $P < 0.05$  was considered statistically significant. The study was approved by the Institutional Review Board at KPSC.

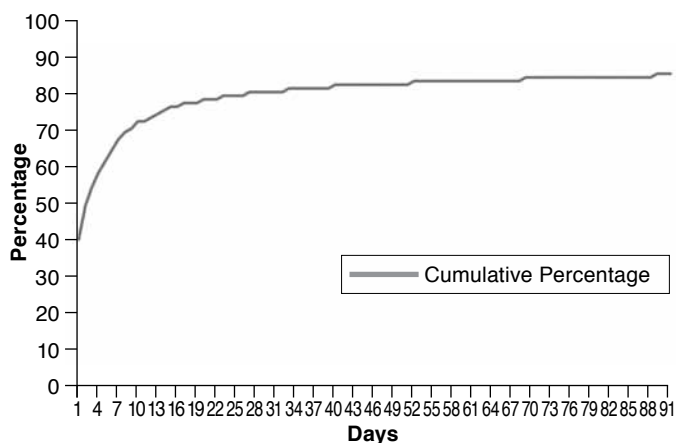
**FIGURE 1** Patient Disposition



**Results**

During the 90-day study window, 49,391 patients received a new order for a statin medication. Most individuals were excluded from the final cohort because they either did not have 12 months of continuous membership prior to the new statin order, the order was cancelled, or they had received a statin prescription in the previous 12 months (Figure 1). Of the 19,826 individuals with a qualified new statin order, 3,049 (15.4%) did not pick up their statin prescriptions (primary nonadherent) within 90 days. Approximately 40% of patients

**FIGURE 2** Sold Statin Prescriptions As a Percentage of Total Prescription Orders<sup>a</sup>



<sup>a</sup>90 days following order date.

(7,890) picked up their statin prescriptions on the day it was ordered, and 78% (15,521) did so within the first 21 days (Figure 2). The 78% of patients who picked up their prescriptions within 21 days represents 93% of all patients who filled their prescriptions in the 90-day study window.

Table 1 lists the unadjusted baseline characteristics for the eligible population of adherent and primary nonadherent patients. On univariate analysis, differences were found between patients who picked up their new prescriptions versus those who were primary nonadherent. The mean age of primary nonadherent patients was slightly lower; fewer primary nonadherent patients had comorbid conditions (based on the CCI), and they were taking fewer medications. Primary nonadherent patients were less likely to have had an ED visit or hospitalization in the prior 12 months, and racial differences were also evident, with a higher rate of primary nonadherence among blacks. The absolute difference in baseline characteristics between adherent and primary nonadherent patients was generally small. Having any prescription filled in the previous year was associated with a higher rate of picking up the new statin prescription. Lastly, there was no difference in the median household income between the adherent and primary nonadherent groups.

Prescriber information is listed in Table 2. Overall, there were few provider differences between prescriptions given to patients who were primary nonadherent compared with those who were adherent. The median number of new statin orders written during the study window per provider was 7. Interestingly, providers who wrote more than 7 new statin orders (high prescribers) had a higher proportion of primary nonadherent patients than providers who wrote fewer than 7 new statin orders.

**TABLE 1** Unadjusted Baseline Characteristics of Adherent and Primary Nonadherent Patients

Characteristics <sup>a</sup>	Nonadherent n = 3,049	Adherent n = 16,777
Median age, years (range) <sup>b</sup>	55 (24-103)	57 (24-101)
Male (n, %)	1,577 (51.7)	8,707 (51.9)
<b>Race/ethnicity (n, %)</b>		
White	1,331 (43.7)	7,635 (45.5)
Black	384 (12.6)	1,753 (10.4)
Hispanic	1,023 (33.6)	5,684 (33.9)
Asian	274 (9.0)	1,532 (9.1)
Other/multi/unknown	37 (1.2)	173 (1.0)
<b>Median household income (n, %)</b>		
≤ \$45,000	729 (23.9)	4,108 (24.5)
\$45,001-\$65,000	929 (30.5)	4,966 (29.6)
\$65,000-\$85,000	704 (23.1)	3,817 (22.8)
> \$85,000	680 (22.3)	3,856 (23.0)
Unknown	7 (0.2)	30 (0.2)
<b>Most recent LDL (n, %)</b>		
< 100 mg/dL	179 (5.9)	1,095 (6.5)
100-160 mg/dL	1,536 (50.4)	8,235 (49.1)
> 160 mg/dL	1,019 (33.4)	5,677 (33.8)
Unknown	315 (10.3)	1,770 (10.6)
<b>Primary prevention (n, %)<sup>b</sup></b>	2,839 (93.1)	15,225 (90.8)
<b>Number of medications (median)<sup>b</sup></b>	3	4
<b>Number of clinic visits (median)<sup>b</sup></b>	4	5
<b>Prior 12-month ED visits (n, %)<sup>b</sup></b>	556 (18.2)	4,135 (24.6)
<b>Prior 12-month hospitalizations (n, %)<sup>b</sup></b>	220 (7.2)	2,020 (12.0)
<b>Dual insurance (n, %)</b>	105 (3.4)	675 (4.0)
<b>Any Rx in prior year (n, %)<sup>b</sup></b>	2,609 (85.6)	15,306 (91.2)
<b>Charlson Comorbidity Index (n, %)<sup>b</sup></b>		
Score = 0	1,761 (57.8)	8,010 (47.7)
Score ≥ 1	1,288 (42.2)	8,767 (52.3)

<sup>a</sup>Wilcoxon rank sum test for median number of medications and median number of clinic visits; all others are from chi-square test.

<sup>b</sup>Adjusted P < 0.001 using Bonferroni correction method (2 sample t-tests for median age).

ED = emergency department; LDL = low-density lipoprotein; mg/dL = milligram per deciliter; Rx = prescription.

In the multivariate logistic regression model (Table 3), black race was associated with a 30% higher odds of primary nonadherence, while having a high baseline LDL (> 160 mg/dL) was associated with 25% lower odds of primary nonadherence. All of the utilization characteristics (prior ED visits, hospitalizations, clinic visits, and prior prescription utilization) were associated with lower odds of primary nonadherence, as was a higher CCI. Male providers had lower odds of primary nonadherent patients, and higher prescribers had increased odds of primary nonadherent patients.

### Discussion

Although primary nonadherence has been investigated for many years, these studies have often been small in size,

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**TABLE 2** Prescriber Characteristics for Adherent and Nonadherent Patients

Characteristics	Nonadherent n = 3,532	Adherent n = 16,996
Male (n, %)	1,820 (59.7)	10,290 (61.3)
Prescriber age (median) <sup>a</sup>	43	42
<b>Provider specialty</b>		
Family medicine	2,304 (65.2)	10,944 (64.4)
Internal medicine	1,161 (32.9)	5,769 (33.9)
Other	67 (1.9)	283 (1.7)
<b>Prescriber race (n, %)</b>		
White	1,106 (36.3)	6,080 (36.2)
Black	195 (6.4)	877 (5.2)
Hispanic	407 (13.3)	2,382 (14.2)
Asian	1,314 (43.1)	7,267 (43.3)
Other/unknown	27 (0.9)	171 (1.0)
<b>High prescriber<sup>b</sup></b>	2,700 (88.6)	13,769 (82.1)

<sup>a</sup>Adjusted  $P < 0.001$  using Bonferroni correction method.

<sup>b</sup>Greater than 7 new statin prescriptions in the study window.

frequently involving a single pharmacy, utilizing surveys or patient self-reporting to capture adherence, or in care settings such as EDs or hospitals with electronic methods of capturing data.<sup>6</sup> These methodological issues have made it difficult to extrapolate findings to other populations or different care settings. Only recently have large population-based studies been undertaken for patients taking chronic medications, such as antihyperlipidemic drugs.<sup>3-5</sup> In large part, this is because technology, in the form of electronic prescribing and electronic medical records, has allowed researchers to capture and track the life cycle of a prescription from the time it is ordered to the time it is purchased by the patient at the pharmacy.<sup>1,2</sup>

In a relatively large and racially diverse population receiving care within an MCO, the rate of primary nonadherence to statin medications was 15.4% within 90 days after the order date. Others have reported primary nonadherence rates to statin medications ranging from 13% to 34.1%, so our results are consistent with previous studies.<sup>3-5</sup> The findings from this study, however, are more in line with the 13% rate of primary nonadherence to antihyperlipidemic drugs reported in a managed care population.<sup>5</sup> The higher rates reported by Fischer et al. and Liberman et al. reflect differences in the definition of primary nonadherence and differences in study populations, as these studies evaluated insured populations that were not part of a closed managed care system such as KPSC.<sup>3,4</sup> Patients who pay cash for their prescriptions, order through the Internet, or import their drugs from another country (Canada or Mexico) do not generate claims, which could also explain the higher rates of primary nonadherence reported by Fischer et al. and Liberman et al.<sup>3,4</sup> Lastly, population care management efforts focused on improving cholesterol treatment within KPSC may have reduced the numbers of primary nonadherent patients.

**TABLE 3** Multivariate Logistic Regression:<sup>a</sup> Characteristics Associated with Primary Nonadherence

Variable	Odds Ratio	95% CI	
<b>Patient demographics</b>			
Age	0.991	0.988	0.995
Male	0.942	0.867	1.023
<b>Race/ethnicity</b>			
Non-Hispanic white	1.00		
Asian	0.935	0.810	1.080
Black	1.299	1.144	1.476
Hispanic	0.956	0.872	1.049
Unknown	1.040	0.722	1.497
<b>Low-density lipoprotein</b>			
< 100	1.00		
100-160	0.907	0.764	1.078
> 160	0.753	0.628	0.902
unknown	0.760	0.619	0.934
<b>Utilization</b>			
ED visits in past year	0.853	0.764	0.952
Hospitalizations in past year	0.787	0.668	0.927
Clinic visits in past year	0.674	0.513	0.885
Any Rx in past year	0.616	0.546	0.695
<b>Charlson Comorbidity Index</b>	0.733	0.673	0.798
<b>Dual insurance</b>	0.829	0.671	1.024
<b>Provider characteristics</b>			
Male	0.872	0.802	0.949
Age <sup>b</sup>	1.012	1.008	1.017
High prescriber <sup>c</sup>	1.584	1.403	1.789

<sup>a</sup>C-statistic = 0.603.

<sup>b</sup>Patient and provider age in 10-year intervals.

<sup>c</sup>High prescriber = greater than 7 new statin prescriptions in the study window.

CI = confidence interval; ED = emergency department; LDL = low-density lipoprotein; Rx = prescription.

These reported rates mean that anywhere from 1 in 3 to 1 in 6 patients do not pick up their new cholesterol medication.

Results from the univariate and multivariate analyses suggest that primary nonadherent patients are younger and healthier, with fewer comorbid conditions, fewer concurrent prescriptions, and lower rates of hospitalizations, clinic, and ED visits in the year prior than adherent patients. While the baseline differences between adherent and primary nonadherent patients were statistically significant, the absolute differences were often small. This suggests that the clinical and demographic characteristics derived from electronic sources may not allow clinicians to predict who will be adherent to a new statin order and who will be nonadherent. Additional evidence for this exists because—although the multivariate model agreed well with the observed data—the characteristics included had a poor ability to explain or predict primary nonadherence (c-statistic = 0.603). At that level, the c-statistic is below the threshold for acceptable discrimination, and, hence,

the variables included in the model have poor ability to explain or predict primary nonadherence.<sup>12</sup> Caution therefore needs to be exercised in the interpretation of these findings. Others have also suggested that patient characteristics collected from electronic sources may not be predictive of adherence to medications.<sup>5,13</sup>

The drivers of primary nonadherence appear to be more complex than the clinical and demographic characteristics that can be extracted from electronic data. In a recent study, McHorney and Spain (2011) reported results of a national Internet-based survey identifying reasons for primary nonadherence and nonpersistence across 6 chronic conditions (asthma, diabetes, hyperlipidemia, hypertension, osteoporosis, and cardiovascular disease).<sup>14</sup> The top reasons for primary nonadherence in this study were financial hardship, fear of side effects, general concerns about medications, lack of perceived need, change in health benefits, and the belief that their condition was not life threatening.<sup>14</sup> In another study focused specifically on nonadherence to statin therapy, Fung et al. (2010) grouped the reasons patients gave into major categories, the top 3 of which were: (1) concerns or experiences with adverse effects; (2) uncertainty about the benefits or importance of statins; and (3) lack of convenience.<sup>15</sup> Patients often provide multiple reasons for not initiating therapy with a new antihyperlipidemic medication, so this type of behavior often has complex origins.<sup>14,15</sup> More research into the reasons for primary nonadherence is needed and should include investigations into the possible behavioral economic drivers and other barriers (access, complexity, support) associated with this type of nonadherence.

While we may not be able to electronically predict a patient's likelihood of being nonadherent to a new statin order, it does appear that our ability to identify primary nonadherence will improve as the nation moves increasingly toward electronic prescribing and electronic medical records. More than 90% of patients who eventually start a statin drug do so within the first 3 weeks. Therefore, focusing on early detection (after 2 to 3 weeks) and early interventions for primary nonadherence could result in significant reductions in the number of individuals who do not pick up their new prescriptions. Derose et al. (2013) found that a simple intervention using automated telephone calls and letters resulted in a significant reduction in the number of primary nonadherent patients.<sup>16</sup> Interventions could also be tailored to first identify the concerns and barriers that patients express as leading to their decision not to initiate therapy. Asking open-ended questions and probing for detail is likely to provide the best results because the reasons for not initiating therapy may be multifaceted and subtle. Adopting a strategy where the focus is on patient barriers and concerns may be another effective way to reduce primary nonadherence.

### Limitations

The limitations associated with retrospective analyses also exist when conducting observational studies of medication adher-

ence; specifically, in this study we did not interview patients to determine reasons for nonadherent behavior. In an effort to identify new statin orders, we restricted our population to those who did not receive a statin prescription in the past 12 months; however, some patients may have received a statin prescription more than 12 months before the index date, which could have confounded our results. We also restricted our analysis to those patients with a prescription drug benefit; therefore, the results may not be applicable to individuals without a drug benefit. The majority of patients (~95%) within our health system have a prescription drug benefit. Another factor to consider is that 98% of the prescriptions sold to our adherent population were for a generic statin. The generic copayment was  $\leq$  \$25 for 81.8% of these prescriptions. Requiring a drug benefit for inclusion may make these results less generalizable to populations without a drug benefit, and the low copayment rates could explain why we saw no difference in primary nonadherence between the various strata of median household incomes.

One of the strengths of our study was the ability to capture a relatively large and racially diverse population of patients with a new statin order; KPSC members generally reside within 7 of the most populous counties in Southern California. In addition, we were able to capture a comprehensive set of clinical and demographic characteristics for patients and providers, allowing us to study a number of factors potentially associated with primary nonadherence.

The study also benefits from our ability to capture all prescription transactions between the electronic medical record and dispensing pharmacy and to report on all sold prescriptions. In the process, we were able to exclude prescriptions that were printed and provided to the patient, as these are often taken to outside pharmacies along with handwritten prescriptions from providers outside the medical group and the electronic ordering process, as we had no valid way to date/time stamp when the order was written.

### Conclusion

Statins are the primary treatment used in lowering elevated cholesterol in at-risk patients and play an important role in the treatment of chronic diseases such as cardiovascular disease, cerebrovascular disease, diabetes, and familial hypercholesterolemia. More and more, primary nonadherence is becoming recognized as a significant problem. The full extent of the problem is being revealed through studies with access to electronic prescribing and electronic medical records.

High levels of statin adherence are associated with reductions in clinical outcomes such as all-cause mortality, coronary heart disease events, and hospitalizations,<sup>17</sup> and lead to reduced overall health care costs for patients with hypercholesterolemia even though there are increased costs for drugs.<sup>18,19</sup> In addition, it is estimated that the total direct health care cost associated with nonadherence to medications used to treat

diabetes, hypertension, and dyslipidemia in the United States is \$105.8 billion.<sup>20</sup> These findings and estimates do not take into account the issue of primary nonadherence.

Our data and those from others indicate that primary nonadherence is a significant problem in a variety of care settings. Moving forward, efforts need to be made to better understand the reasons for, and the effectiveness of interventions aimed at reducing, primary nonadherence. Taking a quote from former U.S. Surgeon General C. Everett Koop, “Drugs don’t work in patients who don’t take them.”<sup>21</sup>

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### DISCLOSURES

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## Primary Nonadherence to Statin Medications in a Managed Care Organization

### APPENDIX A Charlson Comorbidity Index and Related ICD-9-CM Codes

Comorbidities	Enhanced ICD-9-CM
Myocardial infarction	410.x, 412.x
Congestive heart failure	398.91, 402.01, 402.11, 02.91, 404.01, 404.03, 404.11, 04.13, 404.91, 404.93, 425.4-425.9, 428.x
Peripheral vascular disease	093.0, 437.3, 440.x, 441.x, 443.1-443.9, 47.1, 557.1, 557.9, V43.4
Cerebrovascular disease	362.34, 430.x-438.x
Dementia	290.x, 294.1, 331.2
Chronic pulmonary disease	416.8, 416.9, 490.x-505.x, 506.4, 508.1, 508.8
Rheumatic disease	446.5, 710.0-710.4, 714.0-714.2, 714.8, 725.x
Peptic ulcer disease	531.x-534.x
Mild liver disease	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9, 570.x, 571.x, 573.3, 573.4, 573.8, 573.9, V42.7
Diabetes without chronic complication	250.0-250.3, 250.8, 250.9
Diabetes with chronic complication	250.4-250.7
Hemiplegia or paraplegia	334.1, 342.x, 343.x, 344.0-344.6, 344.9
Renal disease	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582.x, 583.0-583.7, 585.x, 586.x, 588.0, V42.0, V45.1, V56.x
Any malignancy, including lymphoma and leukemia, except malignant neoplasm of skin	140.x-172.x, 174.x-195.8, 200.x-208.x, 238.6
Moderate or severe liver disease	456.0-456.2, 572.2-572.8
Metastatic solid tumor	196.x-199.x
AIDS/HIV	042.x-044.x

AIDS = acquired immune deficiency syndrome; HIV = human immunodeficiency virus; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.