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Predictors of statin adherence, switching, and discontinuation in the USAGE survey: Understanding the use of statins in America and gaps in patient education

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BACKGROUND: Although statins have been shown to reduce cardiovascular disease mortality, less than half of U.S. adults achieve their low-density lipoprotein cholesterol goal. In many patients initiated on a statin, adherence rates decrease over time.

OBJECTIVE: To characterize current and former statin users, identify reasons for the discontinuation or switching of statins, and identify factors associated with adherence.

METHODS: The USAGE survey is a cross-sectional, self-administered Internet-based survey of 10,138 U.S. adults fielded September to October 2011. The following statin users were identified and compared: adherent nonswitchers, adherent switchers, non-adherent switchers, and discontinuers. Univariate and multivariate models using a priori covariates for adherence and discontinuation were examined.

RESULTS: Most participants were current statin users who adhered with their prescribed statin (82.5%, n = 8371). Former statin users or discontinuers (12%, n = 1220) cited muscle pain, a side effect, as the primary reason for discontinuation (60%), followed by cost (16%), and then perceived lack of efficacy (13%). Discontinuers were less satisfied with their physicians' explanation of cholesterol treatment, more likely to use the Internet to research statins, and less likely to undergo frequent cholesterol monitoring. Among adherent statin users, the primary reasons for switching were muscle side effects (33%) and cost (32%). Individuals at risk for non-adherence included those with low household income, those who experienced muscle pain as a side effect while on statin therapy, and those taking medication for cardiovascular disease.

CONCLUSION: Statin-related muscle side effects are common and contribute significantly to rates of discontinuation, switching, and non-adherence. Improved physician patient communication about side effects and benefits of statins are necessary to improve both adherence and outcomes.

After therapeutic lifestyle modification, statins are the first-line treatment for elevated low-density lipoprotein cholesterol (LDL-C) levels (Expert Panel 2002).[1] Randomized clinical trials and epidemiologic studies have shown that

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statins reduce the rates of myocardial infarction, stroke, and revascularization procedures. Statins also reduce the rate of cardiovascular and all-cause mortality in high-risk patients.[2]

Despite strong evidence for the cardiovascular benefits of statins, the efficacy demonstrated in clinical trials does not necessarily translate to similar effectiveness in the general population. Clinical trials may select healthier individuals who are more likely to adhere with statin therapy, a bias known as volunteer or self-selection bias.[3,4] Even in clinical trials, adherence rates are suboptimal, with 5-year discontinuation rates of 33% and 18% in primary and secondary prevention trials, respectively.[5,6] In most observational studies, long-term adherence with statins has been low, with approximately 50% adherence at 6 months and 25% adherence at 1 year.[7] In the National Cholesterol Education Program (NCEP) Evaluation ProjecT Utilizing Novel E-Technology (NEPTUNE) II, 67% of participants achieved their LDL-C treatment goal.[8] Thus, a large percentage of the U.S. population still remains at levels greater than recommended LDL-C target levels.[9]

Barriers to adherence with statins are complex and multilevel occurring at the physician, health care system, and individual levels. Whether patients meet national lipid goals may in part depend on whether physicians are following national guidelines. In previous studies authors reported greater adherence among patients whose statins were prescribed by their primary care provider (PCP). Having a cardiologist, regardless of PCP status, was also associated with greater adherence.[10] Health care system factors associated with increased adherence include lower out-of-pocket costs and good insurance status.[11] Previous studies authors reported mixed patient characteristics of patients with low adherence, including age (younger and older adults), nonwhite race, comorbidities, and side effects.[12,13]

The Understanding Statin Use in America and Gaps in Patient Education (USAGE) Survey was conducted to characterize current and former statin users, identify reasons for the discontinuation or switching of statins, and identify factors associated with adherence.

Methods

Sources of data

The USAGE Survey is a cross-sectional, self-administered Internet-based survey of U.S. adults fielded between September 21, 2011 and October 17, 2011. All participants in the study must have been at least 18 years of age, reported being diagnosed with high cholesterol by a physician, currently or previously on a statin, able to read and write English, and have provided informed consent to participate in the study. Participants were recruited through opt-in e-mail, co-registration with MySurvey.com partners, electronic newsletter campaigns, banner placements, and both internal and external affiliate networks. Details have been reported previously.[14]

Survey

The USAGE survey aimed to better understand statin adherence and the reasons for switching or discontinuing statin therapy, such as side-effects and cost. Example questions included, "Why did you stop the most recent statin medication you were taking?" and "In the past, did you ever stop taking a statin due to muscle-related side effects (such as worsened muscle aches, muscle pain, muscle cramps, or muscle weakness)?" The development and administration of the survey were published previously,[14] and additional information about the USAGE survey can be found at http://www.statinusage.com.

Comparisons of interest

Current statin users were defined as patients currently taking a statin, either alone or in combination with a cholesterol-absorption inhibitor, niacin, or calcium channel blocker. Former statin users, or discontinuers, were patients who were previously on a statin, either alone or in combination with another medication, but who were currently not taking any statin.

Patients were then further divided by their level of adherence and whether they had previously switched statins. Adherent participants were defined as taking at least 80% of their current prescribed statin dose in the past month.[15] In the survey we asked two separate questions about adherence: In the past month, "How many times did you miss a dose?" or "take less than the amount prescribed?" adherence was calculated by adding these two variables together. All other current statin users taking less than 80% of their prescribed statin dose were designated as non-adherent. Adherent nonswitchers were those who continued their original statin without having switched statins in the past. Adherent switchers were individuals who changed statins in the past but were then adherent with their new statin. Non-adherent nonswitchers were individuals who never switched statins but were non-adherent on their original statin. Discontinuers (or former statin users) stopped taking their statin altogether.

Statistical analysis

Baseline characteristics were obtained through the survey and computed by the use of univariate analyses. Student t-tests and χ^2 tests were used to assess for differences in the means and proportions of characteristics between comparison groups. Two-sided $P < .05$ were considered statistically significant.

A multinomial model was then used for prediction in four groups of patients that were determined a priori: discontinuers vs adherent nonswitchers, non-adherent switchers vs adherent nonswitchers, adherent switchers vs adherent nonswitchers, and non-adherent nonswitchers vs

adherent nonswitchers. A priori predictors for adherence or discontinuation were selected for examination in the multivariate model. The final predictors included in the model were age, sex, education, income, race/ethnicity, region, health insurance type, body mass index, satisfaction with how well one's doctor explained cholesterol treatments, influence of out-of-pocket costs, use of prescriptions for cardiovascular disease, diabetes, hypertension or psychiatric disorders, current or past history of stroke, heart attack, coronary heart disease or peripheral vascular disease, satisfaction with current/most recent medication, muscle-related symptoms while taking a statin, frequency of cholesterol monitoring, use of the Internet to learn about statin treatments, and use of an Internet medical resource such as WebMD as the most used information source.

Results

A total of 10,138 adults participated in the internet-based USAGE survey between September 21, 2011 and October 17, 2011. Of 27,946 individuals who were contacted due to self-reporting a high cholesterol on the Ailment Panel of Lightspeed Online Research, 54.9% (n = 15,346) responded. The overall cohort was predominantly white (92%), middle-aged (mean age 61 years), female (61%), highly educated (38% with college degree vs 28% in the U.S. population), well insured (93% vs 84% in the general U.S. population),[16] with a median household income of $44,504, and who spent an average of $88/month for out-of-pocket costs for prescription medications (Table 1). The majority of participants was overweight or obese (35% and 46%, respectively) and had at least one comorbidity that required pharmaceutical intervention, such as hypertension (66%), arthritis (31%), diabetes mellitus (28%), depression (20%), and coronary heart disease (11%). Most patients were diagnosed with high cholesterol, initially prescribed medication for and currently managed by a family practitioner, general practitioner, or internist for their high cholesterol.

Table 1 Baseline characteristics by current and former statin adherence in the USAGE survey, 2011

Characteristic	Comparison groups		
	Total respondents	Current statin users	Former statin users
No. participants	10,138	8,918	1,220
Age, y	61.0	61.2*	59.4
Age at diagnosis of high cholesterol, y	50.2	50.4*	48.8
Sex, %			
Male	39	40*	32
Female	61	60	68*
Race/ethnicity, %			
White	92	92	92
Black/African American	4	4	4
Hispanic	1	1	2
Asian or Pacific Islander	1	1	1
Current BMI, mean kg/m^2	30.6	30.7	29.9
Household income, median $	44,504	45,270*	39,452
Insurance, %	93	94*	87
Commercial	68	67	69
Medicare or Medicaid	46	47*	43
Comorbidities, %			
Coronary heart disease, heart attack, bypass surgery and/or stent	20	21*	16
Diabetes	28	29*	22
Hypertension	66	67*	55
Depression	20	19	22
Arthritis	31	31	35
Taking medications for comorbidities, %			
Diabetes medication	25	26	17
Hypertension medication	63	65	48
Depression medication	16	16	15
Arthritis medication	24	24	26
General practitioner cholesterol management, %			
Diagnosis of high cholesterol	87	87	87
Initial prescription	76	86	85
Current management	82	85*	63

LDL, low-density lipoprotein; N/A, not applicable.
*Significant at $P < .05$ between current statin and former statin user groups.

Demographic characteristics comparing current and former statin users are highlighted in Table 1. Compared with former statin users, current statin users were slightly older (61.2 years vs 59.4 years) and diagnosed with high cholesterol at a later age (age 50.4 vs 48.8 years). Women comprised a significantly greater proportion of former statin (68%) users than current statin users (60%). Current statin users had a significantly greater annual income and were more likely to have insurance than former statin users. However, current statin users also had a significantly greater burden of comorbidities, and in most cases required concurrent prescriptions for these chronic conditions. There was a significantly greater prevalence of individuals with LDL-C goals less than 70 for current (20%) compared with former (12%) statin users.

Of the total respondents (n = 10,138), 168 (1.7%) participants were excluded from the analysis because they were not taking a daily statin dose, whereas 1220 (12%)

Table 2 Baseline characteristics according to adherence groups in the USAGE survey, 2011

Characteristic	Former statin users	Current statin users			
	Discontinuers	Non-adherent switchers	Adherent switchers	Adherent nonswitchers	*P* value
No. of participants	1,220	161	3,743	4,628	
Age, mean, y	59.4	59.0	62.4	60.4	<.0001
<55, %	29.8	29.8	40.7	40.5	<.0001
>55, %	70.2	70.2	59.3	59.5	<.0001
Sex, %					
Male	32.5	34.2	40.7	40.5	<.0001
Female	67.5	65.8	59.3	59.5	<.0001
Race/ethnicity, %					
White	92.0	88.2	93.5	91.9	.0006
Black/African American	3.7	4.4	2.9	3.7	.024
Hispanic	1.5	2.5	0.8	1.0	.12
Other	2.7	5.0	2.4	2.9	.34
Highest level of education, %					
High school graduate or less	23.9	27.3	21.8	24.1	.07
Some college or associates degree	39.8	37.3	38.8	37.3	.22
College graduate	36.2	35.4	39.3	38.4	.08
Household income, %					
<$50,000	48.6	59.0	41.5	42.4	<.0001
>$50,000	40.6	36.1	48.5	48.6	<.0001
Insurance, %					
Private	51.7	44.7	54.1	55.1	.005
Federal	40.6	42.9	50.6	45.0	<1.0001
Other	10.4	8.7	12.2	10.4	.09
Uninsured	13.2	12.4	5.7	6.4	<.0001
History of stroke, coronary heart disease, heart attack, or peripheral vascular disease, %	15.3	17.4	21.6	15.2	<.0001
Taking medications for comorbidities, %					
Cardiovascular disease	27.8	44.1	31.0	25.2	<.0001
Diabetes medication	16.3	29.8	26.6	24.9	<.0001
Hypertension medication	46.3	58.4	66.7	64.2	<.0001
Psychiatric medication	15.4	24.2	16.5	16.9	.11
Satisfaction with current or most recent statin, %	27.2	59.0	83.7	87.1	<.0001
Muscular side effects while taking statin, %	60.3	51.6	32.9	16.5	<.0001
Out-of-pocket costs have a large influence on taking current statin, %	27.8	44.1	31.0	25.2	<.0001
Satisfied with physicians' explanation of treatments, %	65.3	65.2	85.2	83.0	<.0001
Besides one's physician, use the internet to learn about statins, %	41.3	34.8	31.5	25.9	<.0001
Internet medical resource as the most used information source, %	48.4	48.5	39.3	36.6	<.0001

LDL, low-density lipoprotein; N/A, not applicable.

were designated as former statin users who permanently discontinued their statin in the past. Current statin users (8918) were further divided into categories based on their switching of statins (Table 2). Among adherence comparison groups, 8371 (82.5%) were adherent current statin users, and 379 (3.8%) were non-adherent current statin users defined as taking less than 80% of their medicines in the last month. Of the adherent statin users, 45.6% (n = 4628) had not switched statins in the past, whereas 36.9% (n = 3743) had switched statins in the past but were currently adherent.

Table 2 shows the baseline characteristics of the four groups. Among current statin users, adherent switchers and nonswitchers were significantly more likely to be older (mean ages 62.4 yrs and 60.4 years, respectively) than non-adherent switchers (59 years). Compared with adherent switchers and nonswitchers, non-adherent switchers had a significantly lower household income, were more likely to be uninsured, reported greater muscular side effects while taking a statin, were less satisfied with their statin, and less satisfied with their physicians' explanation of cholesterol treatment.

Adherence vs non-adherence with statins

Almost all current statin users (98%) reported being prescribed a statin for daily use. Current statin users also reported high adherence with dosing instructions: 86% follow dosing instructions all the time, 13% follow dosing instructions most of the time, and 1% do not follow dosing instructions. Missed doses (one to more than six in the past month) were reported by 31% of current statin users (Fig. 1).

In the multivariate model adjusted for potential confounders, there was a significant increased likelihood of statin adherence (compared with either missing or taking less than prescribed) among individuals with federal insurance (Medicare/Medicaid; odds ratio [OR] 1.20, $P = .002$), satisfaction with current medication (OR 1.43, $P < .001$), satisfaction with their doctors' explanation of high cholesterol treatments (OR 1.42, $P < .001$), and concomitant use of medications for diabetes (OR 1.14, $P = .024$) and hypertension (OR 1.35, $P < .001$), Table 3. There was no difference in prediction of statin adherence by body mass index (BMI), education level, income, and out-of-pocket costs.

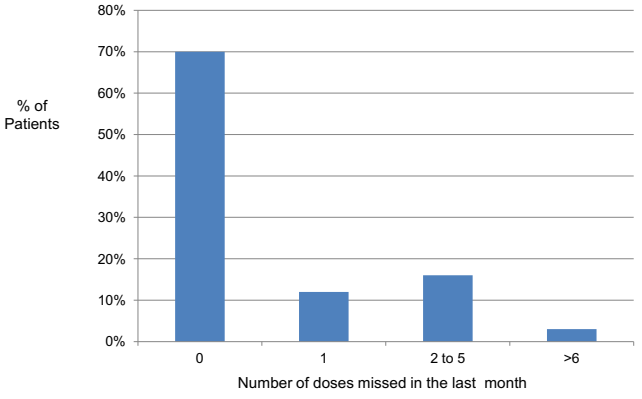

Figure 1 Number of doses missed in the last month among current statin users.

In multivariate-adjusted analysis, there was a significant increased risk of statin non-adherence among those of black ethnicity (OR 2.0, $P < .001$), those who experienced muscular side effects on statin therapy (OR 2.53, $P < .001$), those who used the internet for health information (OR 1.18, $P = .001$), and those who reported implementing an action to help remind themselves to take statin medication (OR 1.14, $P = .007$).

Switching of statins

Major reasons for switching statins were similar for former and current users (Fig. 2). Among former statin users, the most common reason cited for switching was side effects (65%), followed by cost (16%), and perceived efficacy (13%). Among current statin users, the reasons cited most often for switching was cost (36%), followed by side effects (28%), and concerns about efficacy (22%). Among current statin users, cost concerns were significantly greater among non-adherent switchers (44%), followed by adherent switchers (31%), and lastly adherent nonswitchers (25%; $P < .0001$), Table 2. The prevalence of muscle side effects was also greatest among non-adherent switchers (51.6%) followed by adherent switchers (32.9%) and then adherent nonswitchers (16.5%), $P < .0001$ between groups.

Adherent switchers were significantly more likely to have had a history of cardiovascular disease and to be taking medications for cardiovascular disease, diabetes, and hypertension compared with adherent nonswitchers. Adherent switchers were more likely to have muscular side effects and large out-of-pocket costs compared with adherent nonswitchers. Adherent switchers and adherent nonswitchers were otherwise similar in age, sex, race/ethnicity, BMI, education, household income, and insurance status.

Compared with stable treatment respondents (defined as adherent nonswitchers), dissatisfaction with their most recent/current medication and experiencing muscle pain when taking a statin were positive predictors for suboptimal statin use.

In the multivariate analysis, significant predictors of participants who were adherent switchers vs adherent nonswitchers included federal insurance (OR 1.18, $P = .001$), being impacted by out-of-pocket costs (OR 1.44, $P < .001$), taking concomitant medication for cardiovascular disease (OR 1.52, $P < .001$), experiencing muscular side effects (OR 2.34, $P < .0001$), and using the internet to research statin treatment (OR 1.17, $P = .004$), Table 3.

Participants had a significantly increased likelihood of being an adherent switcher vs adherent nonswitcher if they were younger (<55 years of age, OR 1.35, $P < .001$), black (OR = 1.32, $P = .036$), and completed at most a high school education (vs college graduate, OR = 1.23, $P = .001$).

Table 3 Multivariate* adjusted odds ratios (95% confidence intervals) comparing the participant characteristics of the different treatment groups (discontinuers, non-adherent switchers, and adherent switchers) with those on stable statin therapy (defined as adherent non-switchers) in the USAGE survey, 2011

	Former statin users		Current statin users			
	Discontinuers, n = 1220		Non-adherent switchers, n = 161		Adherent switchers, n = 3743	
Covariate	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age						
<55 years	1.32 (1.10, 1.58)	.002	1.12 (0.77, 1.62)	.550	0.74 (0.66, 0.83)	<.001
≥55 years (ref)						
Sex						
Male	0.97 (0.82, 1.15)	.705	0.94 (0.65, 1.34)	.716	0.96 (0.87, 1.06)	.396
Female (ref)						
Ethnicity						
Black	0.92 (0.62, 1.36)	.676	1.06 (0.48, 2.36)	.885	0.76 (0.59, 0.98)	.037
Hispanic	1.32 (0.67, 2.61)	.422	1.92 (0.66, 5.63)	.234	0.77 (0.48, 1.24)	.278
Other	0.65 (0.41, 1.03)	.068	1.37 (0.64, 2.95)	.414	0.83 (0.63, 1.10)	.199
White (ref)						
Body mass index						
Underweight	2.38 (0.94, 6.01)	.663	1.99 (0.25, 16.13)	.518	0.87 (0.41, 1.86)	.724
Normal (ref)						
Overweight	0.96 (0.27, 1.19)	.715	1.28 (0.78, 2.09)	.329	1.07 (0.94, 1.22)	.320
Obese	0.81 (0.65, 1.01)	.056	0.96 (0.58, 1.58)	.873	1.05 (0.92, 1.20)	.443
Education						
High school graduate or less	0.89 (0.72, 1.09)	.259	0.88 (0.57, 1.36)	.569	0.81 (0.72, 0.92)	.001
Some college or associates degree	0.87 (0.73, 1.04)	.133	0.77 (0.52, 1.13)	.191	0.93 (0.83, 1.03)	.142
College graduate (ref)						
Annual household income						
<$50,000 (ref)						
≥$50,000	0.81 (0.68, 0.96)	.018	0.65 (0.44, 0.95)	.028	1.11 (1.00, 1.23)	.049
Insurance						
Uninsured	2.33 (1.77, 3.07)	<.001	1.47 (0.84, 2.57)	.174	1.11 (0.91, 1.36)	.282
Federal	1.06 (0.89, 1.26)	.511	0.96 (0.66, 1.39)	.827	1.18 (1.07, 1.30)	.001
Private (ref)						
Current or previous cardiovascular disease (stroke, heart attack, coronary heart disease, or peripheral vascular disease)						
Yes	1.04 (0.82, 1.30)	.766	0.83 (0.50, 1.39)	.485	1.24 (1.08, 1.41)	.002
No (ref)						
Cost						
Large influence	1.04 (0.87, 1.23)	.692	2.01 (1.44, 2.81)	<.001	1.44 (1.30, 1.59)	<.001
No/mild/moderate influence (ref)						
Concurrent medication for cardiovascular disease						
Yes	0.99 (0.64, 1.53)	.952	2.71 (1.33, 5.49)	.006	1.52 (1.21, 1.90)	<.001
No (ref)						
Concurrent medication for diabetes						

(*continued on next page*)

Table 3 (*continued*)

	Former statin users		Current statin users			
	Discontinuers, n = 1220		Non-adherent switchers, n = 161		Adherent switchers, n = 3743	
Covariate	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Yes	0.74 (0.61, 0.91)	.004	1.29 (0.88, 1.88)	.187	1.04 (0.94, 1.16)	.461
No (ref)						
Concurrent medication for hypertension						
Yes	0.55 (0.46, 0.64)	<.001	0.75 (0.53, 1.06)	.108	1.02 (0.92, 1.12)	.771
No (ref)						
Concurrent medication for psychiatric condition						
Yes	0.80 (0.65, 0.99)	.040	1.24 (0.84, 1.83)	.283	0.96 (0.85, 1.08)	.504
No (ref)						
Satisfaction with physician explanation of treatment						
Satisfied or Extremely Satisfied	1.32 (1.10, 1.58)	.003	0.75 (0.52, 1.10)	.138	1.30 (1.14, 1.48)	<.001
Dissatisfied, extremely dissatisfied, neutral (ref)						
Cholesterol monitoring frequency						
At most annually	1.71 (1.46, 1.20)	<.001	1.22 (0.87, 1.70)	.246	0.89 (0.81, 0.98)	.013
Monthly to every 6 months (ref)						
Satisfaction with current statin						
Satisfied or Extremely satisfied	0.07 (0.06, 0.09)	<.001	0.32 (0.23, 0.47)	<.001	0.84 (0.73, 0.96)	.010
Dissatisfied or Extremely Dissatisfied (ref)						
New or worsened muscle aches, cramps, or pain while taking statin						
Yes	4.64 (3.95, 5.45)	<.001	4.13 (2.95, 5.79)	<.001	2.34 (2.10, 2.60)	<.001
No (ref)						
Internet use to research statin						
Yes	1.50 (0.23, 0.58)	<.001	1.15 (-0.24, 0.51)	.476	1.17 (0.05, 0.26)	.005
No (ref)						
Internet medical resource as most used information source						
Yes	1.11 (0.94, 1.31)	.220	1.29 (0.91, 1.83)	.156	1.03 (0.93, 1.14)	.558
No (ref)						

BMI, body mass index; CI, confidence interval; OR, odds ratio; ref, reference group.

*Multivariate model adjusted for age, sex, education, income, race/ethnicity, region, health insurance type, BMI, satisfaction with how well one's doctor explained cholesterol treatments, influence of out-of-pocket costs, use of prescriptions for cardiovascular disease, diabetes, hypertension or psychiatric disorders, current or past history of stroke, heart attack, coronary heart disease or peripheral vascular disease, satisfaction with current/most recent medication, muscle-related symptoms while taking a statin, frequency of cholesterol monitoring, use of the Internet to learn about statin treatments, and use of an Internet medical resource such as WebMD as the most used information source. The variable used for stratification was excluded from the model.

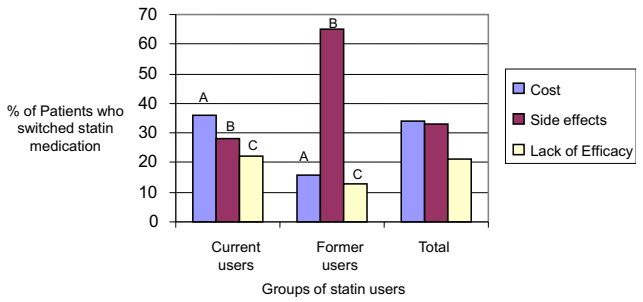

Figure 2 Reasons for switching statin therapy among current and former statin users. Paired groups A (current vs former), B (current vs former), and C (current vs former) for cost, side effects, and lack of efficacy, respectively, differ significantly at $P < .05$.

Discontinuation of statins

Baseline characteristics of former statin users have been published previously[14] and are briefly highlighted in Table 1. In univariate analyses, a significantly greater proportion of former statin users experienced muscular side effects compared with current statin users. Former statin users also were more concerned about potential interactions with their other medications and were less satisfied with their statin.

In multivariate analyses, participants had a significantly increased risk of being a discontinuer compared with a adherent nonswitcher statin user if they were younger than 55 years of age (OR 1.32, $P = .002$), uninsured (OR 2.33, $P < .001$), experienced symptoms of muscle aches, pain, cramps, or weakness while taking a statin (OR 4.64, $P < .001$), had annual cholesterol monitoring (OR 1.71, $P < .001$), used the internet to learn about statin treatment (OR 1.50, $P < .001$), and were not satisfied with their doctor's explanation of high cholesterol treatments (OR 1.31, $P < .003$), Table 3. There was no significant difference by sex, ethnicity, BMI, education, or region of the United States.

Participants had a significantly decreased likelihood of being a discontinuer compared with a adherent statin user if their annual household income exceeded $50,000 (OR 0.81, $P = .018$), they were satisfied with their medication (OR 0.07, $P < .001$), and they took a concomitant medication for diabetes (OR 0.74, $P = .003$), hypertension (OR 0.54, $P < .0001$), or a psychiatric condition (OR 0.80, $P = .393$). There was a significant increased risk of discontinuing statins because of side effects, especially among those who reported experiencing muscular side effects while taking a statin (OR 4.64, $P < .001$).

Discussion

Prevalence of adherence

In the USAGE Survey 82.5% of individuals were current adherent statins users. This finding is greater than previous studies that report annual statin adherence between 25% and 40% among elderly patients regardless of coronary artery disease status[7,17] and similarly low adherence of 36.4% among privately insured patients.[11] In a cohort of 19,232 participants ages 18-102, adherence with statins using the proportion of days covered classified as low (proportion of days covered 21%-40%), intermediate-low (41%-60%), intermediate-high (61%-90%), and high (>80%) was 23%, 16.2%, 19.7%, and 41.1%, respectively.[18] Statin adherence has been shown to further decline over time.

The differences in adherence among USAGE survey participants compared with other populations probably reflects the bias inherent in self-reporting of adherence, a healthier more highly educated population, and those with resources for both internet access and health insurance. Also, another explanation is that the USAGE survey captured a large population of statin switchers. Among participants, 38.5% reported switching statins at least once, and among those who switched, 84% continued to use statins after they had switched. Individuals who switched statins were further characterized by adherence vs nonadherence after switching. There are multiple reasons for statin discontinuation and switching, and these can be broadly characterized into individual, physician and health care system issues.

Individual factors

Demographic factors were analyzed as possible predictors of statin adherence and reasons for switching statins. After adjusting for potential confounders, age was not associated with increased statin adherence. Participants younger than 55 years of age were significantly more likely to be discontinuers but also adherent switchers. The authors of previous studies report a "U-shaped" association between age and adherence, where the greatest adherence was observed among individuals 50 to 65 years of age and lower rates were found among those either younger or older.[12] Adherence has also been reported to be lower among elderly individuals, although this may vary depending on the time of initial prescription.[17]

Patients of black ethnicity were less likely to be adherent with statins, and this has been reported previously for statins and other cardiovascular medications.[13] Black patients were also less likely to be adherent after switching statins.

Socioeconomic factors, including education and income, differed between groups of current and former users and among switchers but were not significant predictors of adherence or switching of statins. However, participants with an annual household income that exceeded $50,000 had a significantly decreased risk of being a discontinuer. The Internet was used as a medical resource by more than a quarter of respondents. Former statin users were more likely to use the Internet to research statins compared with current users, and use of the internet to learn about statin treatment was associated with a significant increased risk of being a discontinuer. Adherent switchers were also more likely to use the Internet to research statins compared with adherent nonswitchers, suggesting the Internet may serve as

a useful reservoir on statins and potentially help guide decisions for switchers.

However, Internet access may not be clearly beneficial or detrimental because the resource can be used in support of an individual's preconceived biases. Because Internet use was the greatest among former compared with current statin users (in all categories of adherence), the Internet may also be a proxy for a number of factors such as patient concerns about side effects, doubts about the efficacy of statins, patients seeking nonprescription medication alternatives, lack of a regular provider, or lack of trust between the provider and patient. For reasons that may only be speculated, greater access to information might have undermined patient beliefs in the efficacy of the medication, heightened concerns about side effects, or encouraged nonpharmaceutical or alternative therapies. The multivariate model was adjusted for potential confounders, so the internet was not simply a proxy for individuals already experiencing problems with their statin who then researched the internet. Further qualitative data would be necessary to understand the role of the internet in statin adherence and perhaps ways to utilize the internet to help increase adherence.

The presence of comorbidities with concomitant use of medications for diabetes, hypertension, or a psychiatric condition was associated with a significant decreased risk of statin discontinuation. Previous studies on the role of comorbidities have been mixed. In general, individuals with more cardiovascular risk factors tend to have better adherence.[19] The authors of a previous study also reported increased non-adherence with statin use among participants with concomitant medications (hypoglycemic agents, antihypertensives, and platelet aggregation inhibitors. In the USAGE survey, self-reported adherence seemed to track with self-reported adherence to other medications.

Comorbidities may also impact the switching of statins, such as for tighter LDL control. Adherent switchers were more likely to have cardiovascular disease and to be taking medications for cardiovascular disease and diabetes compared with adherent nonswitchers. It is possible that patients were switched to more potent statins by their physicians.

The strongest predictor of statin discontinuation in the USAGE survey was current muscular side effects. This study reports the side effect of muscular pain in 30% of participants, which is significantly greater than previously reported even on high dose statins.[20] Individuals who reported side effects during current statin use had an increased likelihood of statin non-adherence, increased risk of non-adherence after switching, and a significant 10-fold greater risk of discontinuing their statin. Side effects may also contribute to reasons for switching statins among current statin users, as side effects were higher among switchers compared with nonswitchers. On the other side of the spectrum, patients who were satisfied with their recent statin and presumably without significant muscle side effects had a decreased risk of discontinuing their statin.

The high prevalence of reported statin-induced muscle side effects and their association with statin discontinuation will be an important target in the future for improving adherence. The reporting of a greater rate of muscle side effects than generally appreciated represents an opportunity for better patient physician communication and an opportunity for physicians to learn about methods to reduce statin-related muscle side effects.[21]

In some individuals, the type of statin influences the presence and degree of statin-induced myalgia. Greater rates of discontinuation have been reported for statins that are metabolized through the cytochrome P450 3A4 (CYP 3A4) system such as simvastatin, lovastatin, and atorvastatin compared with statins that are non-CYP 3A4 metabolized.[22] The CYP 3A4 system metabolizes a large majority of drugs in common use and form the basis for several statin relative contraindications or suggestions for reduced doses.[23] Differences in the tolerance to types of statins may also be attributed to the use of greater statin doses, the presence of significant comorbidities such as diabetes mellitus, chronic kidney disease, and hypothyroidism, and advanced age or frailty.

The Prediction of Muscular Risk in Observational Conditions (PRIMO) study, the largest study of muscle side effects in patients on high dose statins, reported a prevalence of muscle symptoms of 10%-15%[20], which is significantly greater than the rates of 1%-2% reported in large scale clinical trials. In addition, the PRIMO study reported that some high doses of statins such as fluvastatin had a significantly lower frequency of muscle side effects than simvastatin or atorvastatin. Recently several genetic polymorphisms (eg, SLCO1B1) have been identified that have been shown to increase the risk of statin myopathy.[24] Concomitant medications that inhibit these and other efflux and influx transporters may increase the risk of statin-induced muscle related side effects and impact patient adherence. This will be examined further in subsequent analysis from the USAGE survey.

Finally, individual habits and perceived self-efficacy play a role in long-term adherence. Adherence self-efficacy, the belief that one's ability to organize and perform behaviors necessary to attain one's health goals, is associated with greater adherence to therapy.[25] Paradoxically, individuals in the USAGE survey who implemented an action to help remind themselves to take statin medication had a significant decreased likelihood of statin adherence. This may be a proxy for individuals prone to forgetting medications and those with complex medication regimens.

A validated "Adherence Estimator" developed by McHorney[26,27] identified three items to predict adherence with prescription medications for chronic medical conditions. On the basis of multivariate analyses, side effects, perceived need for medications and perceived medication affordability were most predictive of self-reported adherence. Similarly in USAGE, side effects, cost and concerns about efficacy were the top three reasons cited for discontinuing and switching statins.

Physician factors

Physicians and allied health providers provide a vital source of information about cholesterol-lowering treatment for their patients. Half the participants cited physicians as their only source of information about statins. Patient satisfaction with their physician's explanations of cholesterol treatments was 81%, which was significantly greater among current compared with former statin users (83% and 65%, respectively). Physicians may also contribute to increased adherence, as adherent statin users (both switchers and nonswitchers) had significantly greater satisfaction with their physicians' explanation of cholesterol treatments compared with non-adherent switchers. After multivariate adjustment, there was a significant increased likelihood of adherence among individuals satisfied with their doctors' explanation of high cholesterol treatments.

Physicians may also impact the switching of statins, particularly for individuals with comorbid cardiovascular disease and diabetes who require stricter LDL-C control. In this survey, individuals who switched statins were significantly more likely to have cardiovascular disease and to be taking medications for cardiovascular disease and diabetes. Almost 10% of current statin users cited that they switched statins due to insufficient LDL lowering on their prior statin. However, this study cannot infer whether switching to more potent statins to achieve stricter LDL-C goals affected subsequent adherence.

A long term patient–physician relationship may also improve adherence. Prior studies report that patients with PCP who had written the index statin prescription were more likely to have full adherence with statins than patients whose PCPs did not write the index prescription. Regardless of PCP status, having a cardiologist write the index prescription was also associated with increased likelihood of adherence.[11]

Although health care providers may have a crucial impact on patient adherence to medications, whether patients attain their target lipid level also depends on physician monitoring and knowledge of national guidelines. Adherence with national guidelines for lipid management improved from 45.9% to 66.2% of physicians from 2003 to 2007.[28] Patients with less frequent cholesterol monitoring were significantly more likely to be a discontinuer than adherent statin users. This may reflect a population of individuals with either suboptimal lipid levels or frequent changes in statin medication.

Health care system factors

In addition to patient and physician factors, cost in the form of medication costs as well as copayments for office visits and laboratory draws also impacts patient adherence. Perceived impact of medication cost depends on insurance status, type of insurance, and out-of-pocket expenditures. Individuals who were uninsured had a 2.3 times increased risk of discontinuing their statin. In the fully adjusted model, out-of-pocket costs did not significantly predict adherence. However, among individuals who had switched statins, both federal insurance and being impacted by out-of-pocket costs were significant predictors of adherent switchers. Among participants who switched statins, those impacted by out-of-pocket costs had a 2-fold greater likelihood of non-adherence. In a retrospective cohort of managed care patients, those who paid at least $20 in out-of-pocket costs were more than four times likely to discontinue their statin compared with patients who paid less than $10.[29] In another study, a greater average daily copayment for a statin was significantly associated with decreased adherence, with nearly one-half the likelihood of adherence related to the daily copay and this also remained significant in the fully adjusted multivariate model.[11] In addition to medication costs are the time investment and copayments for cholesterol lab draws and follow-up office visits. These were not directly measured in this study.

Strengths and limitations

USAGE is one of the largest, comprehensive surveys of self-reported statin use in the United States. Compared with previous studies, this survey specifically aimed to better characterize statin users and understand predictors of statin adherence as well as reasons for discontinuation and switching of statins.

A limitation of this survey is that the data were based on a self-reported questionnaire, which may be subject to overreporting, underreporting, and recall bias. This may explain the greater rates of adherence in our population compared with data from the National Health and Nutrition Examination Survey.[9] With the cross-sectional Survey design, individuals were surveyed at one point in time, which may not reflect current use for those who recently began or switched statins. This survey also reflects a population of individuals with computer and internet access and interest in health through web-based medical resources that may not be representative of the general population. Also, the USAGE respondents were predominantly white (92%), more educated, and more likely insured than individuals in the general U.S. population. Further, the Survey did not include information on specific statins (aside from differentiating brand name versus generic statin) used by the participants.

Future studies should be expanded to include participants representing other racial/ethnic minorities. Questionnaire data may also be expanded to include more qualitative data to better understand reasons for non-adherence. In addition, a study design that follows patients prospectively may give further insight on patterns of switching and discontinuation behavior, as well as effects on cardiovascular outcomes and health care costs.

Conclusion

Statins have been shown to reduce LDL-C and decrease the risk of cardiovascular events and all-cause mortality. Individuals with high long-term adherence have demonstrated greater cardiovascular disease risk reduction compared with individuals with poor adherence. Despite this evidence, there remains a high prevalence of statin nonadherence and statin discontinuation. In the USAGE survey, among the most important reasons reported for non-adherence and discontinuation were muscle side effects, cost, and concerns about efficacy. The high reporting of muscle side effects among former compared with current statin users, as well as among adherent switchers compared with adherent nonswitchers, invites an opportunity for improved patient-physician communication, new methods to reduce statin muscle side effects, and further studies to identify the etiology and possible predisposing factors of statin- induced myalgia. In addition, physicians may target individuals at-risk for non-adherence including those with multiple medical conditions and low annual household income. Although individuals in this population had access to the Internet, physicians remained an important source of information about cholesterol treatment and statins. Patients who were the most satisfied with their physician's explanations of cholesterol treatments were also more likely to remain current statin users, to have greater adherence and to switch statins less often. Physicians should continue to use the opportunity at each visit to improve counseling about statin benefits, side effects, and the importance of adherence.

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