Original Investigation

Different Time Trends of Caloric and Fat Intake Between Statin Users and Nonusers Among US Adults
Gluttony in the Time of Statins?

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IMPORTANCE Both dietary modification and use of statins can lower blood cholesterol. The increase in caloric intake among the general population is reported to have plateaued in the last decade, but no study has examined the relationship between the time trends of caloric intake and statin use.

OBJECTIVE To examine the difference in the temporal trends of caloric and fat intake between statin users and nonusers among US adults.

DESIGN, SETTING, AND PARTICIPANTS A repeated cross-sectional study in a nationally representative sample of 27 886 US adults, 20 years or older, from the National Health and Nutrition Examination Survey, 1999 through 2010.

EXPOSURES Statin use.

MAIN OUTCOMES AND MEASURES Caloric and fat intake measured through 24-hour dietary recall. Generalized linear models with interaction term between survey cycle and statin use were constructed to investigate the time trends of dietary intake for statin users and nonusers after adjustment for possible confounders. We calculated model-adjusted caloric and fat intake using these models and examined if the time trends differed by statin use. Body mass index (BMI) changes were also compared between statin users and nonusers.

RESULTS In the 1999-2000 period, the caloric intake was significantly less for statin users compared with nonusers (2000 vs 2179 kcal/d; $P = .007$). The difference between the groups became smaller as time went by, and there was no statistical difference after the 2005-2006 period. Among statin users, caloric intake in the 2009-2010 period was 9.6% higher (95% CI, 1.8-18.1; $P = .02$) than that in the 1999-2000 period. In contrast, no significant change was observed among nonusers during the same study period. Statin users also consumed significantly less fat in the 1999-2000 period (71.7 vs 81.2 g/d; $P = .003$). Fat intake increased 14.4% among statin users (95% CI, 3.8-26.1; $P = .007$) while not changing significantly among nonusers. Also, BMI increased more among statin users (+1.3) than among nonusers (+0.4) in the adjusted model ($P = .02$).

CONCLUSIONS AND RELEVANCE Caloric and fat intake have increased among statin users over time, which was not true for nonusers. The increase in BMI was faster for statin users than for nonusers. Efforts aimed at dietary control among statin users may be becoming less intensive. The importance of dietary composition may need to be reemphasized for statin users.

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The National Cholesterol Education Program Adult Treatment Panel guideline,[1-4] which was updated by 2013 American College of Cardiology/American Heart Association (ACC/AHA) guideline recently,[5] has consistently recommended dietary modification as a key component of antihyperlipidemic therapy. Since 2001, these guidelines also have stated that statins are more effective than other pharmacotherapies.[3] Statin use has grown rapidly in the United States over the past 25 years,[6,7] while caloric intake has increased overall in US adults from the 1970s through the 1990s[8] reaching a plateau starting in the 1999-2000 period.[9] The proportion of calories from fat ingested by US adults decreased from the 1970s to the 1990s,[8] followed by a stable trend since the 1999-2000 period.[9] To our knowledge, no studies have examined whether the temporal trend in food intake is related to statin use, although previous studies have investigated the cross-sectional and short-term relationship between statin use and food intake.[10-12] In this context, we examined whether the time trends of caloric and fat intake differed between statin users and nonusers.

Methods

Data Sources and Study Population

This is a repeated cross-sectional study using data from the National Health and Nutrition Examination Survey (NHANES), 1999 through 2010.[13] Written informed consent was obtained from all participants. The NCHS Research Ethics Review Board approved the NHANES protocols.[14]

NHANES is conducted by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention. It uses a stratified, multistage probability sampling design, which enables samples to represent the US civilian noninstitutionalized population.[13] Data are collected at their homes and mobile examination centers (MECs). Among adults in NHANES during the 1999-2010 period, the unweighted response rate for the household interview was 74.8%; that for the MEC examination was 70.8%.[15]

This study included data from individuals 20 years or older. Since pregnancy is a contraindication to statin use, we excluded pregnant women from our analyses (n = 1294), which resulted in a sample of 31 170. In the main analysis, we also excluded those with missing information on in-person dietary interview (n = 3210), statin use (n = 13), and potential confounders of our analyses (n = 61), which produced a final sample of 27 886.

Food Intake

During the MEC examination, trained interviewers conducted a 24-hour dietary recall interview and obtained dietary data on the last day before the interview. For the 1999-2001 survey period, dietary interviews were conducted using a computer-assisted automated data collection system with a multiple pass format.[16] Beginning in 2002, the NHANES dietary interview began to use the US Department of Agriculture (USDA) dietary data collection instrument, the Automated Multiple-Pass Method.[17] The individual foods and beverages reported in the dietary interview were assigned to USDA food codes (USDA Survey Nutrient Database for NHANES 1999-2000, USDA's Food and Nutrient Database For Dietary Studies for NHANES 2001-2010[18]), and their nutrient components were analyzed. For this study, we extracted data on total caloric intake and total fat intake as the primary outcome variables. We also extracted data on saturated fat intake and dietary cholesterol intake for additional analyses.

Cholesterol Levels and BMI

As secondary outcome variables, we extracted data on serum levels of total cholesterol and low-density lipoprotein cholesterol (LDL-C), and body mass index (BMI, calculated as weight in kilograms divided by height in meters squared). Blood specimens were collected during the MEC examination. Levels of LDL-C were calculated using the Friedewald equation[19] (total cholesterol − high-density lipoprotein cholesterol − triglycerides/5) for participants examined in the morning in their fasting states with triglyceride levels of 400 mg/dL or lower (to convert triglycerides to millimoles per liter, multiply by 0.0113). Sample size was reduced by 54% when we used fasting values, and sampling weight for fasting blood-sampling examinees prepared by NHANES was used to estimate the entire population parameters. Height and weight were measured during the MEC examination.

Hyperlipidemia and Statin Use

We defined *hyperlipidemia* as either self-reported diagnosis of hyperlipidemia (diagnosed and reported to the participant by a health care professional) or as documentation that the participant was taking medications for hyperlipidemia (statins and others). We did not use the measurements of cholesterol or fat for our definition of hyperlipidemia in this study. That is, we classified individuals with hyperlipidemia who were undiagnosed as not having hyperlipidemia. The rationale was that those who did not know their hyperlipidemia diagnosis would not modify their diets.

Statin use was defined on the basis of interviewer-confirmed medication containers matched to a comprehensive prescription drug database (*Lexicon Plus*).[13] We identified 7 types of statin ingredients prescribed for NHANES participants: lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin, cerivastatin, and rosuvastatin. *Statin use* was defined whether the statin ingredient came from a separate pill or a fixed-dose combination. We divided participants into statin users and nonusers. Statin nonusers included those without hyperlipidemia and those with hyperlipidemia but not receiving statins.

Potential Confounders

We extracted data on potential confounders including age, sex, race and ethnicity, educational attainment, and the diagnosis of diabetes. We categorized age into 3 groups: 20 to 39 years, 40 to 59 years, and 60 years or older. Race and ethnicity were classified into non-Hispanic white, non-Hispanic black, Mexican American, and others including other Hispanics and multiracial participants. We categorized educational attainment into greater than high school, high school graduation or Gen-

eral Education Development (GED) certificate, and less than high school. We defined *diabetes* as either self-reported diagnosis of diabetes or use of antidiabetic medications confirmed by interviewers.

Statistical Analysis

All statistical analyses were conducted using Stata (version 12.1; StataCorp LP), accounting for the complex survey design. Taylor series linearization was used for variance estimation.[20] We used an appropriate weight for each analysis selected based on the variables in the analysis. These weights accounted for unequal probabilities of selection and nonresponses to make unbiased national estimates. To conduct trend analyses, we combined 6 cycles of NHANES data (1999-2000 through 2009-2010).[21]

Proportion of statin use was calculated for each survey cycle. Descriptive statistics for patients' characteristics were calculated separately for statin users and nonusers. Linear trends over time were assessed based on χ^2 tests for categorical variables and linear regressions for continuous variables. We compared the characteristics between the groups using pooled samples across the study period. We also investigated whether time trends of cholesterol levels and BMI differed by group using models including interaction terms between survey cycle and statin use.

Next, we developed regression models to evaluate temporal time trends of caloric and fat intake separately for statin users and nonusers and to examine whether trends for caloric and fat intake differed by statin use. We used generalized linear models (GLMs) with log-link function to take into account the right-skewed distributions of the intake. The results of the Park test[22] indicated a γ-distribution as the most appropriate distribution for our data. We included interaction terms between survey cycle (categorical) and statin use (binary) to allow nonlinear time trends to be different by statin use. We also included age category, sex, race and ethnicity, educational attainment, and diabetes diagnosis for adjustment. We applied these models to calculate model-adjusted estimates of caloric and fat intake per day for each combination of statin use and survey cycle and tested the differences of caloric and fat intake by statin use within each survey cycle. We then calculated separately for statin users and nonusers the adjusted percentage changes of caloric and fat intake in each survey cycle, setting the 1999-2000 period as the reference cycle separately for statin users and nonusers. Linear time trend was used to approximate the change over the study period, and the significance tests of the interaction term between survey cycle (continuous) and statin use (binary) was performed to examine the difference in trends of intake between statin users and nonusers.

As additional analyses, we divided statin nonusers into those with and without a diagnosis of hyperlipidemia and compared the time trends of 3 groups. Moreover, we performed additional sensitivity analyses; we made trend graphs of caloric and fat intake estimates restricted to those who did not have diabetes diagnoses.

We also performed additional regression analyses to evaluate the temporal trends of saturated fat and dietary cholesterol intake separately for statin users and nonusers.

We also created GLMs for BMI, total cholesterol level, and LDL-C level. In the models, we controlled for age category, sex, race and ethnicity, and education attainment. The results of the Park test[22] indicated that a γ-distribution was the most appropriate for BMI, whereas a Poisson distribution was the most suitable for cholesterol levels. We included interaction terms between survey cycle (categorical) and statin use (binary), and we applied these models to calculate model-adjusted estimates of BMI, total cholesterol level, and LDL-C level for each combination of statin use and survey cycle. By creating additional models with a continuous survey cycle variable, we examined the differences in trends by statin use.

Results

The proportion of statin users from the NHANES 1999-2010 study population in our sample more than doubled from 7.5% to 16.5% over the decade of observation (**Table 1**) (eTable in the Supplement). We divided statin nonusers into those with and without hyperlipidemia and found that the proportion of the population who were nonusers without hyperlipidemia decreased from 74.6% to 67.8% ($P < .001$), whereas the proportion of the population who were nonusers with hyperlipidemia did not change significantly ($P = .14$) (eTable in the Supplement). We found time trends toward a smaller proportion of white race and a larger proportion of black race among statin users and a trend toward higher educational attainment among both groups. Diabetes diagnosis became more prevalent among statin users. Statin users were more likely to be older, male, white, less educated, have diagnosis of diabetes, and have higher BMI. Between the 1999-2000 and 2009-2010 periods, BMI increased by 1.3 among statin users compared with a 0.5 increase in nonusers ($P = .02$ for difference in trends), while the decrease of total cholesterol between statin users in the same period was greater than that among nonusers (from 201.9 to 178.1 mg/dL for statin users and from 203.6 to 199.6 mg/dL for nonusers) ($P < .001$ for difference in trends). Findings were similar for LDL-C levels. (To convert total cholesterol and LDL-C to millimoles per liter, multiply by 0.0259.)

Table 2 and **Figure 1** and **Figure 2** present model-adjusted caloric and fat intake estimates by survey cycle and the time trends. In the 1999-2000 period, caloric intake was 179 kcal/d lower (2000 vs 2179 kcal/d) ($P = .007$), and fat intake was 9.5 g/d lower (71.7 vs 81.2 g/d) ($P = .003$) among statin users than nonusers. For subsequent measurement periods, the gaps between the groups became smaller as cycles continued; we no longer found significant differences in caloric intake from the 2005-2006 period and in fat intake from the 2003-2004 period. By the 2009-2010 period, caloric and fat intake were both insignificantly higher among statin users than nonusers (54 kcal/d for caloric intake [$P = .31$] and 2.7 g/d for fat intake [$P = .32$]).

When we tested time trends of caloric intake separately for statin users and nonusers (**Table 3**), among statin users, we found an increase in caloric intake during the study period: the caloric intake among statin users in the 2009-2010 period was 9.6% greater (95% CI, 1.8-18.1; $P = .02$) than that among statin

Table 1. Characteristics of Study Samples by Survey Cycles and Statin Use, 1999-2010[a]

Characteristic	1999-2000	2001-2002	2003-2004	2005-2006	2007-2008	2009-2010	*P* Value for Trend[b]	Total	*P* Value for Between-Group Comparison[c]
Statin Users									
Unweighted sample, No.	374	537	652	717	1105	1158	NA	NA	NA
Weighted proportion of statin users	7.5	9.2	11.1	13.5	15.4	16.5	<.001	NA	NA
Age range, y[d]									
20-39	0.7	3.8	1.9	2.6	3.8	2.5	.31	2.7	<.001
40-59	39.8	39.5	39.6	34.8	31.9	36.8	.04	36.4	<.001
≥60	59.6	56.7	58.5	62.7	64.3	60.7	.10	60.9	<.001
Female sex	47.8	45.5	47.5	49.0	48.5	45.8	.89	47.4	<.001
Race/ethnicity[d]									
Non-Hispanic white	83.8	86.1	83.3	80.1	79.9	78.2	.03	81.1	<.001
Non-Hispanic black	4.9	6.1	7.4	10.0	8.7	9.2	.02	8.2	<.001
Mexican American	2.0	2.1	3.1	2.8	4.2	4.8	.12	3.5	<.001
Others[e]	9.3	5.7	6.2	7.1	7.3	7.8	.81	7.2	<.001
Educational attainment									
>High school	41.6	53.0	45.3	50.2	48.9	55.2	.03	49.9	<.001
High school or GED	31.5	27.1	33.6	30.7	29.9	24.2	.07	29.1	.002
<High school	26.9	19.9	21.1	19.1	21.2	20.6	.28	21.0	.04
Diabetes diagnosis, %	21.5	23.9	27.7	29.7	29.8	29.3	.009	27.9	<.001
Total cholesterol level, mean (SD), mg/dL	201.9 (32.1)	195.8 (35.7)	191.1 (37.6)	183.0 (35.1)	177.2 (36.5)	178.1 (33.7)	<.001	185.1 (36.3)	<.001
LDL-C level, mean (SD), mg/dL	119.3 (32.1)	112.4 (27.7)	100.6 (27.6)	96.7 (30.4)	96.4 (31.6)	99.8 (28.7)	<.001	101.8 (30.5)	<.001
BMI, mean (SD)	29.2 (4.6)	29.5 (5.3)	29.7 (5.2)	30.5 (5.4)	30.4 (6.3)	30.5 (6.0)	<.001	30.1 (5.7)	<.001
Statin Nonusers									
Unweighted sample, No.	4220	4552	4154	3926	4768	4991	NA	NA	NA
Age range, y									
20-39	43.5	40.7	42.4	42.1	43.1	43.0	.59	42.4	NA
40-59	35.5	40.8	39.0	40.6	40.4	39.1	.02	39.3	NA
≥60	21.0	18.5	18.6	17.3	16.5	17.9	.005	18.3	NA
Female, sex	51.3	52.0	51.8	51.2	51.9	52.3	.53	51.8	NA
Race/ethnicity[d]									
Non-Hispanic white	68.7	70.9	70.6	70.9	67.9	66.1	.39	69.2	NA
Non-Hispanic black	11.2	11.1	11.6	11.7	11.7	11.8	.69	11.5	NA
Mexican American	7.6	7.2	8.2	8.5	9.0	9.2	.33	8.3	NA
Others[e]	12.6	10.9	9.6	9.0	11.4	12.9	.88	11.1	NA
Educational attainment[d]									NA
>High school	49.4	55.3	55.7	58.4	54.9	58.7	.007	55.4	NA
High school or GED	25.5	25.3	26.3	24.2	24.6	22.7	.14	24.8	NA
<High school	25.1	19.5	18.0	17.4	20.5	18.7	.003	19.8	NA
Diabetes diagnosis	5.5	5.5	5.8	4.8	5.7	5.1	.56	5.4	NA
Diagnosed hyperlipidemia	19.3	18.5	22.0	21.6	21.7	18.8	.30	20.3	NA
Total cholesterol level, mean (SD), mg/dL	203.6 (32.3)	203.1 (35.0)	202.9 (33.5)	201.1 (31.3)	200.9 (34.2)	199.6 (36.1)	.002	201.8 (33.8)	NA
LDL-C level, mean (SD), mg/dL	126.2 (30.3)	121.7 (30.0)	118.9 (28.7)	118.0 (27.9)	119.5 (30.3)	119.8 (32.7)	<.001	120.6 (30.1)	NA
BMI, mean (SD)	27.9 (5.1)	27.9 (5.0)	28.0 (5.0)	28.2 (5.2)	28.2 (5.6)	28.4 (5.8)	.02	28.1 (5.3)	NA

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); GED, General Education Development certificate; LDL-C, low-density lipoprotein cholesterol; NA, not applicable.

[a] Unless otherwise indicated, data are reported as percentage of participants; sample sizes vary for certain characteristics; each analysis accounted for an appropriate sample weight and the complex study design.

[b] Trends over time were assessed using χ^2 tests for linear trends for categorical variables and linear regressions for continuous variables.

[c] Comparisons between statin users and nonusers were made using pooled samples across the study period.

[d] Percentages do not sum to 100% owing to rounding.

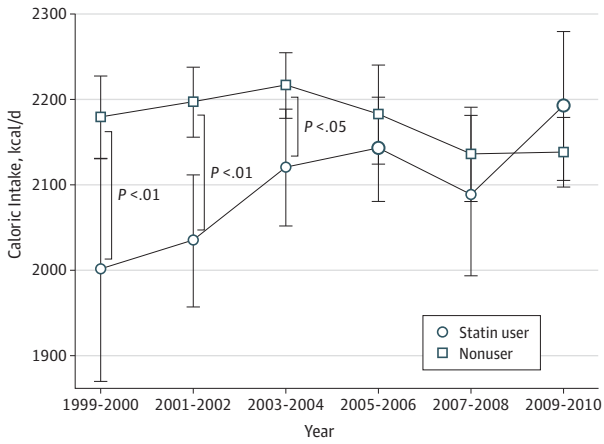
[e] The category includes other Hispanics and other races including multi-racial participants.

Table 2. Model-Adjusted[a] Caloric and Fat Intake Among US Adults by Statin Use Over Study Period, 1999-2010

Characteristic	Model-Adjusted Estimate of Nutrient Intake (95% CI)		*P* Value for Group Comparison Within a Survey Cycle
	Statin User	Statin Nonuser	
Caloric Intake, kcal/d			
1999-2000	2000 (1870-2131)	2179 (2132-2227)	.007
2001-2002	2034 (1956-2112)	2197 (2156-2237)	<.001
2003-2004	2120 (2051-2189)	2217 (2178-2255)	.03
2005-2006	2142 (2080-2203)	2183 (2124-2241)	.29
2007-2008	2088 (1994-2181)	2136 (2083-2191)	.28
2009-2010	2192 (2105-2280)	2138 (2098-2179)	.31
Fat Intake, g/d			
1999-2000	71.7 (65.7-77.7)	81.2 (79.4-83.0)	.003
2001-2002	73.7 (69.8-77.7)	82.6 (80.7-84.6)	.001
2003-2004	79.5 (74.5-84.5)	84.3 (82.3-86.2)	.09
2005-2006	81.9 (78.3-85.5)	83.2 (80.1-86.3)	.52
2007-2008	80.4 (76.2-84.5)	81.0 (78.4-83.7)	.73
2009-2010	82.0 (77.8-86.3)	79.3 (77.1-81.5)	.32

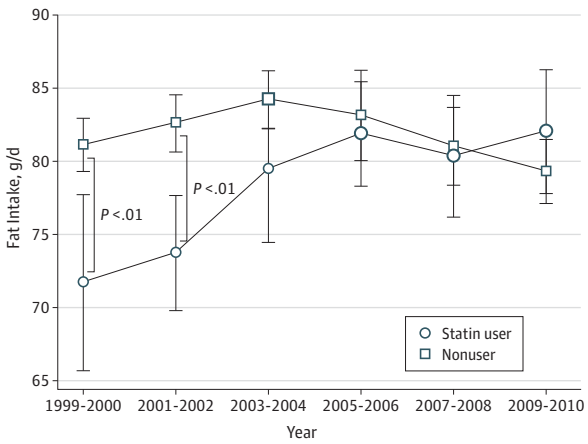
[a] Adjusted for age category, sex, race and ethnicity, educational attainment, and diabetes diagnosis.

Figure 1. Trends of Estimates for Caloric Intake Among US Adult Statin Users and Nonusers, 1999-2010



Adjusted for age category, sex, race and ethnicity, educational attainment, and diabetes diagnosis. Error bars represent 95% CIs. Larger points represent significant changes from 1999-2000.

Figure 2. Trends of Estimates for Fat Intake Among US Adult Statin Users and Nonusers, 1999-2010



Adjusted for age category, sex, race and ethnicity, educational attainment, and diabetes diagnosis. Error bars represent 95% CIs. Larger points represent significant changes from 1999-2000.

users in the 1999-2000 period. Among nonusers, we did not observe a significant time trend. With regard to fat intake, we found similar patterns: for statin users, fat intake in the 2009-2010 period was 14.4% (95% CI, 3.8-26.1; *P* = .007) greater than in the 1999-2000 period. For nonusers, fat intake increased 3.8% (95% CI, 0.5-7.2; *P* = .02) in the 2003-2004 period compared with the 1999-2000 period, followed by a gradual decline to an insignificant 2.3% decrease (95% CI, −5.6 to 1.1; *P* = .19) in the 2009-2010 period compared with the 1999-2000 period. The interactions between survey cycle and statin use were significant in the models with a continuous survey cycle variable (*P* = .001 for caloric intake and *P* < .001 for fat intake), which indicates that time trends for caloric and fat intake in the 2 groups were significantly different.

eFigures 1 and 2 in the Supplement present the results of the additional analyses stratifying statin nonusers into those with and without hyperlipidemia, comparing 3 groups in total. As a result, both nonuser groups (those with and without hyperlipidemia) had similar time trends of caloric intake (upward in the earlier survey cycles and downward in the later survey cycles), whereas the trend among statin users was consistently upward. The difference of the trends for caloric and fat intake between statin users and nonusers with hyperlipidemia was significant (*P* = .02 for caloric intake and *P* = .01 for fat intake). To determine if the findings were driven by increased prevalence of diabetes, we examined time trends in caloric and fat intake in those without diabetes; time trends were similar to those for the entire sample (eFigures 3 and 4 in the Supplement).

In the additional time trend analyses, we found similar patterns for saturated fat and dietary cholesterol intake (eFigures 5 and 6 in the Supplement). The interaction term was

Table 3. Model-Adjusted[a] Relative Changes in Caloric and Fat Intake Among US Adults by Statin Use, 1999-2010

Characteristic	Change From 1999-2000 to 2009-2010, % (95% CI)		*P* Value for Difference in Trends[b]
	Statin User	Statin Nonuser	
Caloric Intake			
1999-2000	0 [Reference]	0 [Reference]	.001
2001-2002	1.7 (−5.6 to 9.5)	0.8 (−2.0 to 3.6)	
2003-2004	6.0 (−1.2 to 13.7)	1.7 (−1.0 to 4.5)	
2005-2006	7.1 (0.2 to 14.8)	0.1 (−3.2 to 3.6)	
2007-2008	4.4 (−3.4 to 12.8)	−2.0 (−5.2 to 1.3)	
2009-2010	9.6 (1.8 to 18.1)	−1.9 (−4.6 to 0.9)	
Fat Intake			
1999-2000	0 [Reference]	0 [Reference]	<.001
2001-2002	2.8 (−6.9 to 13.6)	1.8 (−1.4 to 5.1)	
2003-2004	10.9 (−0.1 to 23.0)	3.8 (0.5 to 7.2)	
2005-2006	14.2 (3.9 to 25.4)	2.5 (−1.8 to 6.9)	
2007-2008	12.1 (1.6 to 23.6)	−0.2 (−4.0 to 3.8)	
2009-2010	14.4 (3.8 to 26.1)	−2.3 (−5.6 to 1.1)	

[a] Adjusted for age category, sex, race and ethnicity, educational attainment, and diabetes diagnosis.

[b] Significance of interaction terms between survey cycle (continuous) and statin use (binary).

significant for saturated fat intake ($P < .001$) but not for dietary cholesterol intake ($P = .09$).

The trends of model-estimated BMI revealed a 1.3 (95% CI, 0.5-2.1; $P = .001$) increase among statin users and a 0.4 (95% CI, −0.1 to 1.0; $P = .10$) increase among nonusers during the study period (eFigure 7 in the Supplement). The test for interaction effects revealed a faster increase of BMI for statin users ($P = .03$), although the increasing trends were significant for both statin users ($P < .001$) and nonusers ($P = .02$). The trends of model-estimated cholesterol levels among statin users and nonusers showed a decrease among statin users from 193.4 mg/dL in the 1999-2000 period to 171.4 mg/dL in the 2009-2010 period and showed a decrease among nonusers from 205.1 mg/dL to 200.8 mg/dL (eFigure 8 in the Supplement). The LDL-C level among statin users decreased from 113.3 mg/dL in the 1999-2000 period to 95.8 mg/dL in the 2009-2010 period; the level among nonusers decreased from 127.3 mg/dL to 120.7 mg/dL (eFigure 9 in the Supplement). The time trends of total cholesterol and LDL-C levels significantly differed by statin use ($P < .001$ for both).

Discussion

In the 1999-2000 period, statin users consumed fewer calories and less fat than nonusers, as we would expect in persons attempting to control their cholesterol level and weight. During the ensuing decade, statin use expanded rapidly, and statin users consumed more calories and fat than earlier cohorts, which was not true for nonusers. As a result, differences in intake between statin users and nonusers disappeared by the 2005-2006 period for caloric intake and by the 2003-2004 period for fat intake. This difference in the time trends for caloric and fat intake between statin users and nonusers was not explained by presence or absence of diagnoses of hyperlipidemia in nonusers or higher prevalence of diabetes among statin users.

To the best of our knowledge, this is the first study showing that time trends for caloric and fat intake differ by statin use in the United States. A cross-sectional study in early 2000s in Rhode Island found that statin use was associated with an insignificant decrease in caloric intake among older adults.[10] Another cross-sectional study in 2004 in Sweden found that statin-using adults were more likely to avoid food with high fat content than nonusers.[11] These results were consistent with our findings from earlier survey cycles that statin users had less caloric and fat intake than nonusers. A cohort study in Veterans Affairs primary care clinics observed newly prescribed statin users for 6 months in 2005 and found no increase in caloric and fat intake.[12] Although that longitudinal study design allowed stronger causal inference, 6 months may be too short to conclude that statin use is not associated with dietary laxity. We used cross-sectional data collected over 12 years that allowed us to see the trends of caloric and fat intake during the time when statin prescription rapidly increased.

What are the implications of the observed change in caloric intake among statin users in terms of effect size and relationship with dietary recommendations in the guideline? Given that 7000 kcal extra caloric imbalance is estimated to induce 1 kg weight gain in an adult,[23] the estimated 192 kcal/d increase among statin users could have contributed to the observed 1.3 increase in BMI (equivalent to a 3- to 5-kg weight gain) over a decade. Since the guideline recommends that patients should prevent weight gain,[3] the observed increase in caloric intake and more rapid increase in BMI among statin users are of concern. According to the guidelines, people who receive statin therapy also should take steps to reduce fat intake,[3,5] but we did not observe a pattern of combining statin use with dietary control. The observed 14.4% increase in fat intake was greater than overall increase in caloric intake (9.6%). While the proportion of calories from fat did not exceed the upper limit of the recommended range (25%-35%),[3] the proportion increased from 32.3% in the 1999-2000 period to 33.7% in the 2009-2010 period. The proportion of calories from saturated

fat in the 2009-2010 period was 11.0%, whereas dietary cholesterol intake in the same period was 277.8 mg/d; both were well above 7% and 200 mg/d that are upper limits of recommended amounts in the guideline.[3]

Owing to the self-reported nature of the information on diet in the present study, and the repeated cross-sectional design, the observed increase in caloric and fat intake should be interpreted carefully. First, because the information on nutrients was collected through dietary recall interview, the result was subject to social desirability bias (tendency to provide answers that convey a favorable image of the interviewee[24]); in the extreme, if statin users became less likely to hesitate to reveal their true intake, our observations might not reflect true change in diet. However, the magnitude of our findings may be too large to be explained only by changes attributable to social desirability bias.

Second, our data are a serial cross-section in which participants change from one panel to the other rather than cohort data in which same individuals are examined repeatedly. Therefore, we cannot infer that a particular individual who took statins throughout the study period consumed more calories and fat in recent years than a decade ago. However, given that the sampling weights of the NHANES allow us to make national estimates, we reasonably can conclude that an average American treated with statin in the 2009-2010 period consumed more calories and fat compared than an average American taking statin in the 1999-2000 period. We can only speculate on the mechanisms behind the observed trends: one possibility is that statin use may have undermined the perceived need to follow dietary recommendations. Patients who recognized that their LDL-C levels were lowered drastically by statins may have lost the incentive to pursue dietary modifications. Physicians might have contributed to this process by shifting the focus of consultations from diet to statin regimen adherence once statin treatment had begun. This hypothesis is compatible with the lower cholesterol levels seen among statin users than among nonusers in later survey cycles (Table 1).

Another possible mechanism is that expanded statin use occurred in people who were likely to eat more. Some patients may have agreed to initiate statin therapy because they did not want to restrict their diet, whereas others who did not want to take medication may have declined the proposed pharmacotherapy in favor of following dietary recommendations. We adjusted for differences in characteristics among statin users across survey cycles in the models but did not adjust for cholesterol levels and BMI because they could have been consequences of food intake.

As to physical activity, NHANES measured it, but we did not include it in the main analyses owing to inconsistent measurement: it changed between the 2005-2006 and 2007-2008 periods. As a sensitivity analysis, we included a physical activity variable in spite of the inconsistency, which did not change the results.

However, other unmeasured factors may have affected the findings. For example, it is possible that those participants taking statins in the early survey cycles exhibited more severe hyperlipidemia, while those with less severe hyperlipidemia initiated statin treatment in later cycles as their use increased. The greater decrease of cholesterol levels among statin users over time may be partially explained by expanded therapeutic use.

Our study design precluded evaluation of the extent to which these scenarios explain the findings. A cohort study with sufficiently long follow-up could address these questions.

Conclusions

Whatever the mechanism, our results indicate that caloric and fat intake among statin users in the 2009-2010 period was significantly greater than they were in the 1999-2000 period. We may need to reemphasize the importance of dietary modification for statin users.

At the same time, it may be appropriate to reevaluate and discuss dietary recommendations in the time of statins. The recently published ACC/AHA guideline emphasized extensive statin use for patients who are likely to experience a net benefit[5]; statin use is predicted to expand further if practitioners follow the guideline.[25] Although the guideline articulates that lifestyle modification remains the foundation for cardiovascular disease risk reduction,[5] further expansion of statin use may result in more statin users not following dietary recommendations (extrapolating from our study results). From the perspective of effectiveness, although the additional effects of low-fat diet on lowering LDL-C level among statin users have been shown,[26,27] the incremental benefit of low-fat diet on cardiovascular disease prevention among those taking statins has not been fully investigated. Moreover, cost-effectiveness and ethical considerations should be taken into account. Particularly in a time when obesity and diabetes have become epidemics and US health care costs have been soaring, we need to consider if it is an acceptable public health strategy to encourage statin use without also taking measures to decrease the likelihood that its use will be associated with increased caloric and fat intake as well as weight gain. We believe that the goal of statin treatment, as with any pharmacotherapy, should be to allow patients to decrease risks that cannot be decreased without medication, not to empower them to put butter on their steaks.

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