Blood pressure-lowering effects of statins: who benefits?

Leonelo E. Bautista

Objectives **To evaluate if the effect of statins on blood pressure is similar in patients grouped by use of antihypertensive medication, level of blood pressure, and high-density lipoprotein cholesterol (HDL-C).**

Methods **Blood pressure was compared in statins users ($n = 995$) and nonusers ($n = 9536$) from the National Health and Nutrition Examination Surveys. The overall effect of statins and their interactions with antihypertensive medication, blood pressure, and HDL-C were estimated using multiple linear and quantile regression.**

Results **Adjusted systolic blood pressure was on average 1.8 mmHg lower in statins users than in nonusers ($P = 0.05$). Although statins had no significant effect among nonusers, it decreased systolic blood pressure by 3.3 mmHg among users of antihypertensive medication (interaction $P = 0.02$). The effect of statins on systolic blood pressure was similar in individuals with HDL-C levels above and below the median (49 mg/dl). Statins also lowered diastolic blood pressure by an average of 1.9 mmHg ($P < 0.01$), regardless of antihypertensive medication use. Among individuals with high HDL-C statins did not lower diastolic blood pressure, whereas in those with low HDL-C diastolic blood pressure was reduced by 3.4 mmHg. The effect of statins on systolic and diastolic blood pressure increased with higher blood pressure and changed little with adjustment for total cholesterol.**

Conclusion **Statins lower blood pressure by cholesterol-independent mechanisms, and the reduction is larger in individuals with higher blood pressure and those with low HDL-C. Statins may be beneficial in preventing hypertension and may contribute to better blood pressure control in hypertensive patients.** *J Hypertens* **27:1478–1484 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Keywords: antihypertensive agents, blood pressure, hydroxymethylglutaryl-CoA reductase inhibitors, hypertension, National Health and Nutrition Examination Surveys

Abbreviations: BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; NHANES, National Health and Nutrition Examination Surveys

Department of Population Health Sciences, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA

Correspondence to Leonelo E. Bautista, MD, MPH, DrPH, University of Wisconsin School of Medicine and Public Health, Population Health Sciences, 610 Walnut Street, 703 WARF, Madison, WI 53726-2397, USA
Tel: +1 608 265 6176; fax: +1 608 263 2820; e-mail: lebautista@wisc.edu

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Introduction

Large randomized clinical trials have shown that inhibitors of 3hydroxy3methylglutaryl-coenzyme A reductase (statins) significantly reduce the incidence of coronary and cerebrovascular events in high-risk individuals with increased plasma cholesterol levels with or without established cardiovascular disease [1–6]. The beneficial effects of statins are mostly attributed to lower levels of blood cholesterol resulting from a decreased hepatic synthesis and an increased clearance of low-density lipoproteins from the bloodstream. However, there is considerable evidence that statins have multiple biological effects that may contribute to their efficacy in preventing cardiovascular events [7,8]. In particular, statins may exert a favorable effect on blood pressure (BP) by improving endothelial-mediated vasodilation [9,10], reducing oxidative stress [11,12], decreasing inflammation [13,14], and downregulating the angiotensin II type I receptor [15].

The effects of statins on BP have been studied in several clinical trials [16–19]. In a recent meta-analysis of these trials, Strazzullo *et al.* [20] found that systolic but not diastolic BP was significantly lower in patients using statins. However, the majority of the trials included in Strazzullo's meta-analysis had not been specifically designed to test the effect of statins on BP and had small sample sizes. Moreover, there was significant heterogeneity in study design, in the target populations, and in the BP effects of statins. Although current evidence suggests that statins have a modest BP-lowering effect, it is still unclear if the effect depends on concomitant antihypertensive treatment, baseline level of BP, or high-density lipoprotein cholesterol (HDL-C) level, as suggested by a recent trial [21]. Data from the National Health and Nutrition Examination Surveys (NHANES) have been used in this study to assess: whether statins produce a clinically significant reduction in BP; if the reduction in BP is similar in individuals receiving and not receiving antihypertensive drugs; if the statins effect is larger in individuals with higher BP; if the effect of statins depends on HDL-C levels; and if the effect of statins on BP is independent of their cholesterol-lowering effect.

Methods

This analysis is based on data from NHANES 1999–2000, NHANES 2001–2002, and NHANES 2003–2004 ($n = 31\,126$) [22]. The sample for NHANES is selected

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through a complex multistage design based on primary sampling units (counties), household segments within the counties, and finally, sampled persons from selected households. This design is aimed to obtain a representative sample of the civilian noninstitutionalized population of the United States. African–American, Mexican–American, people 12–19 and more than 60 years old, low-income Whites and pregnant women are over sampled to obtain precise estimates in these groups. NHANES participants provide informed consent and the data collection procedures are approved by the Centers for Disease Control and Prevention Institutional Review Board as ensuring confidentiality. Details on survey design, medical examination, and laboratory procedures are available at http://www.cdc.gov/nchs/nhanes.htm.

A total of 10 531 NHANES participants were included in this study. Out of the 31 126 participants in the original surveys, 14 were excluded because they had no data on medication use during the 30 days before the survey date; 1529 because they had no BP data; 968 because they were pregnant; and 148 because they were users of cholesterol-lowering drugs other than statins. People less than 30 years old were also excluded ($n = 17\,933$) because there was only one user of statins in this age group. Trained NHANES interviewers verified the medications being used during the 30 days prior to the survey date by direct inspection of medication containers. BP was measured three to four times at home or in a mobile examination unit, following the recommendations of the American Heart Association [23]. When more than one BP reading was available, the mean of all measurements, excluding the first one, was used for the analysis. The analysis was aimed at testing whether participants who were taking statins (atorvastatin calcium, simvastatin, pravastatin sodium, lovastatin, or fluvastatin sodium) had lower levels of systolic and diastolic BP than those who were not, and if the effect of statins depended on the level of BP, the use of antihypertensive medication, and the level of HDL-C.

All analyses were statistically weighted to maintain the representativeness of the sample for the United States population, to avoid selection bias and to correctly estimate the precision of regression coefficients [22]. Multivariate imputation by chained equations was used to fill out missing values and to generate 10 imputed data sets [24]. Each completed data set was analyzed independently and the parameters of interest were averaged across the 10 copies, using Rubin's formula [25], to obtain a single estimate.

Univariate (crude) differences between users and nonusers of statins were estimated using simple linear regression with sampling weights. The statistical significance of these differences was evaluated using the Wald test. Multiple linear regressions with sampling weights was used to estimate the mean difference in BP between users and nonusers of statins, while adjusting for other factors related to BP (e.g. gender, age, etc). Separate analyses were conducted for systolic and diastolic BP. Multiplicative interaction terms were added to the final regression models to test if the effect of statins was significantly different in users and nonusers of antihypertensive medication and in individuals with high and low high-density lipoprotein cholesterol (HDL-C). Low HDL-C was defined by an HDL-C of 49 mg/dl or less (the observed median). Quantile regression models were used to explore how a specified quantile of the distribution of BP values changed with the use of statins. Quantile regression provided a more complete picture of the effect of statins over the distribution of BP values than linear regression and allowed testing if statins had a similar effect at higher and lower levels of BP [26,27]. Quantile regression was conducted in the imputed datasets without accounting for sampling weights. However, failure to account for sampling weighting does not change the consistency of the quantile regression estimates because probability weighting does not affect either the shape or location of the conditional distributions [28]. Standard errors for the quantile regression estimates were obtained by bootstrapping 100 random samples selected with replacement within each stratum defined in NHANES [29,30]. All analyses were conducted using Stata 10 (StataCorp, 2005).

Results

This analysis includes 10 531 individuals who were at least 30 years old; 3398 from NHANES 1999–2000; 3709 from NHANES 2001–2002; and 3424 from NHANES 2003–2004. A total of 995 were statins users, for a national weighted average of 6.7%. Out of them 416 used simvastatin (50.0%); 349 used atorvastatin calcium (28.6%); and 230 used lovastatin, pravastatin sodium, or fluvastatin sodium (21.4%). Use of statins was much more frequent among users (19.2%) than in nonusers of antihypertensive medications (3.2%). Slightly more than a fifth (22.1%) of the participants were users of antihypertensive medications. Among users of antihypertensive medications 61% were using only one drug, 31% were using two drugs and the rest were using three or more drugs. The most frequently used antihypertensive drugs were diuretics (43.5%), ACE inhibitors (30.1%), β-blockers (26.0%), and calcium channel blockers (17.3%).

Statins users were in average about 13 years older than nonusers (Table 1). They were also more likely to be men and of White race/ethnicity, had higher BMI, and higher prevalence of diabetes and cardiovascular disease. On the contrary, statins nonusers were more likely to be smokers and had higher alcohol intake. Regarding BP levels, statins users had significantly higher systolic and significantly lower diastolic BP than statins nonusers (Table 2).

Table 1 Sociodemografic and health characteriscts by use of statins

Risk factor	Statins nonuser ($n=9536$)	Statin-user ($n=995$)	All ($n=10531$)
Age (mean)	50.3 (49.8, 50.8)[a]	63.5 (62.5 64.6)	51.2 (50.8, 51.7)
Male gender (%)	47.6 (46.4, 48.8)	57.4 (52.7, 62.1)	48.2 (47.2, 49.3)
Race (%)			
White	74.2 (69.8, 78.7)	83.3 (80.0, 86.7)	74.9 (70.5, 79.2)
Hispanic	10.8 (7.7, 14.0)	5.2 (3.2, 7.2)	10.5 (7.5, 13.5)
Black	10.5 (8.0, 12.9)	8.1 (6.0, 10.3)	10.3 (7.9, 12.7)
Other	4.4 (3.4, 5.4)	3.4 (1.6, 5.0)	4.4 (3.4, 5.3)
BMI (kg/m^2)	28.3 (28.0, 28.5)	29.3 (28.8, 29.7)	28.3 (28.1, 28.6)
Waist circumference (cm)	97.5 (96.8, 98.1)	102.8 (101.7, 103.9)	97.8 (97.2, 98.4)
Total cholesterol (mg/dl)	207.7 (206.3, 209.1)	197.0 (193.3, 200.6)	207.0 (205.6, 208.3)
HDL cholesterol (mg/dl)	53.5 (52.9, 54.1)	49.6 (48.3, 50.8)	53.2 (52.7, 53.8)
Diabetes (%)	7.3 (6.4, 8.2)	23.4 (19.8, 26.9)	8.4 (7.4, 9.3)
Cardiovascular disease (%)	7.6 (6.4, 8.8)	36.3 (32.7, 40.0)	9.5 (8.3, 10.7)
Use of NSAID[b]	8.6 (7.6, 9.7)	14.8 (11.6, 18.1)	9.0 (8.0, 10.1)
Current smoker (%)	24.0 (22.3, 25.7)	14.8 (11.6, 18.1)	23.5 (21.7, 25.0)
Alcoholic drinks/week			
None	64.4 (61.8, 67.1)	71.0 (65.8, 76.2)	64.9 (62.3, 67.5)
1–7	22.3 (20.3, 24.3)	19.3 (15.2, 23.5)	22.1 (20.1, 24.1)
≥8	13.3 (11.7, 14.8)	9.7 (6.8, 12.6)	13.0 (111.5, 14.5)

[a] Figures in parenthesis are 95% confidence intervals. [b] Nonsteroidal antinflammatory drugs.

Correspondingly, the crude prevalence of a systolic BP at least 140 mmHg was higher but the crude prevalence of diastolic BP at least 90 mmHg was lower in statins users as compare to nonusers.

After adjustment for significant confounders and predictors (age, gender, race, alcohol intake, C-reactive protein, and obesity) systolic BP was on average 1.8 mmHg lower in statins users than in nonusers ($P=0.05$; Table 3). Further adjustment for total cholesterol decreased the effect of statins to −1.4 mmHg. However, different patterns of the effect of statins were evident in separate analyses among users and nonusers of antihypertensive medications. Although statins had no significant effect among nonusers, it decreased systolic BP by 3.3 mmHg among users of antihypertensive medication ($P<0.01$). This interaction between statins and use of antihypertensive medication was statistically significant ($P=0.02$). This pattern did not changed significantly after further adjustment for total cholesterol. The results from the quantile regression analysis, with adjustment for the earlier-mentioned variables, showed that the effect of statins among nonusers of antihypertensive medication was around zero for all quantiles of systolic BP, but with a tendency to greater reduction in individuals with higher BP values (Fig. 1). Indeed, statins had no effect on systolic BP among nonusers of antihypertensive medications with systolic BP less than 140 mmHg, but reduced systolic BP by 4.6 mmHg among those with a systolic BP at least 140 mmHg ($P<0.01$; Table 3). In contrast, among users of antihypertensive medications, statins users had an average systolic BP 4 mmHg lower than nonusers across all levels of the distribution of systolic BP values (Fig. 1).

After adjustment for age, gender, race, alcohol intake, smoking, and obesity diastolic BP was in average 1.9 mmHg lower among users as compared with nonusers of statins ($P<0.01$; Table 4). This difference changed very little after further adjustment for total cholesterol. Contrary to systolic BP, the effect of statins on diastolic BP were similar in participants who were and those who were not using antihypertensive medication ($P=0.27$ for interaction test; Table 4). Also, among nonusers of antihypertensive medications, statins did not have a significant effect on diastolic BP neither in those with diastolic BP below nor above 90 mmHg ($P=0.32$ for interaction test). However, the quantile regression analysis showed that statins significantly lower diastolic BP and that the higher the diastolic BP the larger the degree of

Table 2 Unadjusted blood pressure levels by use of statins

Risk factor	No statins ($n=9536$)	Statins ($n=995$)	All ($n=10531$)
Systolic BP	124.7 (123.9, 125.5)[a]	131.8 (129.9, 133.8)	125.2 (124.3, 126.0)
Diastolic BP	73.2 (72.6, 73.7)	70.2 (69.4, 71.0)	73.0 (72.4, 73.5)
Systolic BP ≥140 mmHg	18.0 (16.6, 19.4)	30.2 (25.4, 34.9)	18.8 (17.3, 20.3)
Diastolic BP ≥90 mmHg	7.6 (6.4, 8.8)	5.4 (3.3, 7.4)	7.6 (6.4, 8.8)
Hypertension[b]	21.4 (19.7, 23.1)	32.2 (27.4, 37.1)	22.1 (20.4, 23.8)

[a] Figures in parenthesis are 95% confidence intervals. [b] Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg. All $P<0.001$ with the exception of diastolic BP ($P=0.052$).

Table 3 Crude and adjusted difference in average systolic blood pressure (SBP) in users as compared to nonusers of statins

	Difference in SBP (mmHg)					
	Crude	*P*	Adjusted[a]	*P*	+ Cholesterol[b]	*P*
All	7.2 (5.4, 8.9)[c]	<0.01	−1.8 (−3.7, −0.0)	0.05	−1.4 (−3.2, 0.30)	0.10
User of antihypertensive drugs[‡]						
No	7.9 (5.4, 10.4)	<0.01	0.2 (−2.3, 2.7)	0.85	0.5 (−1.9, 2.9)	0.66
Yes	−1.4 (−3.8, 1.0)	0.25	−3.3 (−5.4, −1.2)	<0.01	−2.8 (−4.9, −0.8)	<0.01
Nonusers of antihyper-tensive drugs[§]						
SBP < 140	4.2 (2.7, 5.8)	<0.01	0.0 (−1.6, 1.6)	0.98	0.2 (−1.5, 1.8)	0.83
SBP ≥ 140	−2.9 (−6.2, 0.4)	0.08	−4.6 (−7.9, −1.4)	<0.01	−4.5 (−7.8, −1.3)	<0.01

[a] Difference in blood pressure adjusted for age, race, gender, alcohol intake, C-reactive protein, and obesity. [b] Furtherly adjusted for total cholesterol levels. [c] Figures in parenthesis are 95% confidence intervals. [‡] *P*-value for interaction: 0.024. [§] *P*-value for interaction: 0.012.

BP-reduction (Fig. 2). For example, statins reduced diastolic BP by 1.4 mmHg (95% confidence interval – 95% CI: −2.6, −0.2) in people around the 30th quantile of diastolic BP (67 mmHg) and by 2.4 mmHg (95% CI: −3.6, −1.1) in people around the 80th quantile (82 mmHg).

The effect of statins on systolic BP was similar in individuals with high and low HDL-C levels (*P*-value for interaction: 0.80). In contrast, the effect of statins on diastolic BP depended on HDL-C level (*P*-value for interaction: 0.002). Among individuals with an HDL-C more than 49 mg/dl, statins lowered diastolic BP by a small nonsignificant amount (−0.14 mmHg; 95% CI: −1.33, 1.04), whereas in those with HDL-C 49 mg/dl or less diastolic BP was reduced by 3.44 mmHg (95% CI: −4.97, −1.90).

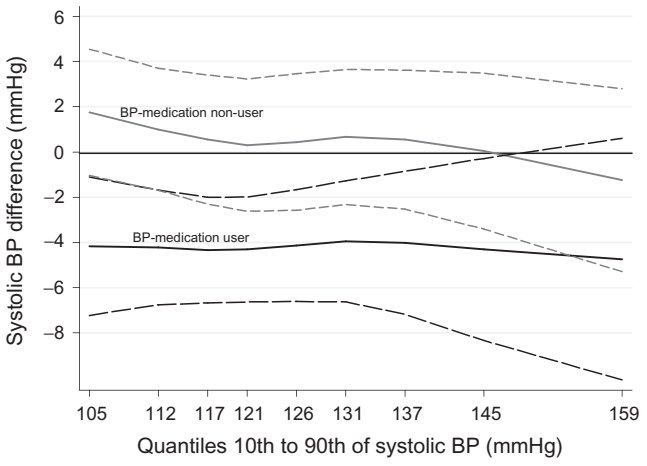
Discussion

This study confirms in a large random sample of community individuals that statins significantly lowers systolic and diastolic BP. A significant decrease in systolic BP was observed in individuals using antihypertensive medication, at all levels of systolic BP. Statins also lowered systolic BP among nonusers of antihypertensive medications, but only in those with a systolic BP at least 140 mmHg. In contrast, statins lowered diastolic BP by a similar amount in users and nonusers of antihypertensive medication. Moreover, among nonusers of antihypertensive medications the BP-lowering effect of statins increased with higher levels of diastolic BP. These results are consistent with and complement those from a recent meta-analysis of randomized controlled trials [20] and from a recent large trial [21].

Although the statins-associated reduction in systolic BP was significant only in individuals using antihypertensive medication, this does not necessarily imply a synergistic effect between these two types of drugs. In fact, among nonusers of antihypertensive drugs statins lowered both systolic and diastolic BP at all levels of BP, and the effect increased with higher BP. Therefore, the interaction between statins and antihypertensive drugs could be explained by a larger BP-lowering effect among persons with higher systolic BP, who are also more likely to use antihypertensive medication.

Although the statins' effect on systolic BP was similar in individual with high and low HDL-C, the effect of diastolic BP seemed to be limited to persons with low HDL-C (≤40 mg/dl). This is in contrast with the results of a recent randomized trial, which suggested that systolic BP was preferentially reduced in individuals with high HDL-C [21]. However, a statins-by-HDL-C interaction was not formally tested in that trial. Low HDL-C is known to be associated with endothelial dysfunction, as measured by flow-mediated vasodilation, and with increased oxidative stress [31]. Since the effects of statins on BP seem to be mediated mostly by endothelial effects, an improved endothelial function could explain the stronger effect of statins in diastolic BP in individuals with low HDL-C. In contrast, systolic BP elevation is partly due to large artery wall thickening [32], a process that may be altered by statins, but is not entirely reversible.

Fig. 1



Average adjusted difference in systolic blood pressure between statins users and nonusers and 95% confidence limits (dashed-lines) by blood pressure quantile.

Table 4 Crude and adjusted difference in average diastolic blood pressure (DBP) in users as compared with nonusers of statins

	Difference in DBP (mmHg)					
	Crude effect	*P*	Adjusted effect[a]	*P*	+ Cholesterol[b]	*P*
All	−2.9 (−3.9, −2.0)[c]	<0.01	−1.9 (−2.9, −0.9)	<0.01	−1.5 (−2.5, −0.6)	<0.01
User of antihypertensive drugs[‡]						
No	−1.5 (−3.2, 0.1)	0.07	−1.0 (−2.9, 0.9)	0.29	−0.7 (−2.4, 1.1)	0.44
Yes	−2.9 (−4.6, −1.3)	<0.01	−2.6 (−4.1, −1.0)	<0.01	−2.1 (−3.6, −0.6)	<0.01
Nonusers of antihyper-tensive drugs[§]						
DBP < 90	−0.5 (−2.1, 1.1)	0.52	−0.4 (−2.2, 1.3)	0.61	−0.2 (−1.9, 1.5)	0.82
DBP ≥ 90	0.3 (−3.1, 3.7)	0.86	0.9 (−1.3, 3.0)	0.44	0.7 (−1.4, 2.8)	0.50

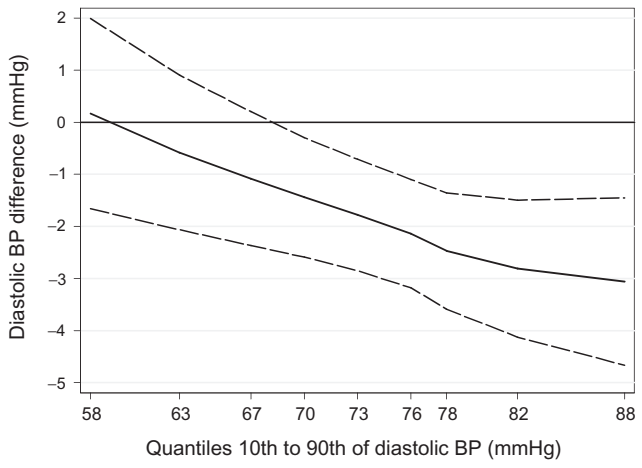
[a] Difference in blood pressure adjusted for age, gender, race, alcohol intake, smoking, and obesity. [b] Furtherly adjusted for total cholesterol level. [c] Figures in parenthesis are 95% confidence intervals. [‡] *P*-value for interaction: 0.27. [§] *P*-value for interaction: 0.32.

This may explain why statins reduce systolic BP by a similar degree in individuals with high and low HDL-C.

Adjustment for total cholesterol level decreased the BP-reducing effect of statins by a small amount. This suggests that the BP lowering effects of statins are mediated mostly by mechanisms other than cholesterol lowering. The mechanisms by which statins could lower BP have been amply described [8,33–35] and include reduction of large artery stiffness [19,36], downregulation of the angiotensin II-type I receptor [15], and improvement of endothelial function. Statins improve endothelial function, particularly endothelium-mediated vasodilation, by increasing endothelial nitric oxide synthesis [9,37], reducing oxidative stress [11,38], and by decreasing circulating levels of inflammatory markers [11,13,39].

The magnitude of the average BP-lowering effect of statins in this study was similar to that from previous studies [21,40]. Moreover, this study unambiguously showed that the BP-lowering effect of statins was stronger the higher the BP, particularly in people who are not using antihypertensive drugs. However, such a trend was not as marked for systolic as for diastolic BP, particularly among individuals receiving antihypertensive drugs (Fig. 2). The effect of statins on systolic BP may depend less on the level of BP because in addition to endothelial function systolic BP depends on arterial stiffness, a process that can only be partially reversed by statins. Also, among users of antihypertensive medications, the effect of antihypertensive drugs may mask a trend in the effect of statins, particularly if systolic BP is used as a therapeutic target, as currently recommended [41].

Fig. 2



Average adjusted difference in diastolic blood pressures between statins users and nonusers and 95% confidence intervals (dashed-lines) by quantiles of blood pressure.

A potential limitation of this study is the cross-sectional nature of the data. A bias in the estimate of the effect of statins on BP could occur if survival in statins users differs from that in nonusers. It is reasonable to expect that most of the statins users in this study were hypercholesterolemic, whereas nonstatins users were a mixed of normocholesterolemic and nondiagnosed hypercholesterolemic individuals. If these two groups developed hypertension at the same rate, one should expect higher mortality in nonusers of statins, because the proportion of individuals with both hypercholesterolemia and hypertension would be higher in this group. In that case, higher instead of lower levels of BP should be observed in a cross-sectional sample of statins users as compared with nonusers. This is in contrast to what was actually observed in this study. In consequence, the lower BP observed in statins user cannot be explained by the use of cross-sectional data.

Another potential source of bias in this study is the selective prescription of statins (confounding by indication). Indeed, among persons with BP within the 'normal' range, statins are more likely to be prescribed to hypercholesterolemic individuals who have higher than to those who have lower BP. In consequence, confounding by indication cannot explain the BP-lowering effect of statins observed in this study, as it should result in higher instead of lower BP among statins users. It is also possible that healthier individuals are more likely to use statins and to have behaviors or characteristics that lower BP. However, in this study the effects of statins were adjusted

for characteristics and behaviors that are known to influence BP, with the exception of salt intake, which is an unlikely confounder as it should not be independently associated with the use of statins. The possible roles of statins dose and treatment duration on BP were not evaluated in this study, as these data are not collected in NHANES. Also, sample size limitations made it impossible to explore if the effect of different statins was different or whether the effect of statins varied with the type of antihypertensive medication.

This is the largest study on the BP effects of statins. The large sample size allowed for the evaluation of interactions that have been suggested but not tested in previous studies. Also, the generalizability of the results of this study is warranted by the use of a representative sample of the United States population. Finally, this study used quantile regression to explore how the effect of statins changed across increasing levels of BP. Whether the effect of statins is more marked at the upper end of the distribution of BP values is of clinical importance, as antihypertensive treatment is usually reserved and more beneficial in patients with higher BP.

The BP-lowering effect of statins in this study was similar to that observed in actively controlled trials (0.1–3.2 mmHg) [42] and is of public health and clinical importance. Even modest decreases in the average BP, like the ones observed in this study, could delay the onset of hypertension and substantially reduce hypertension-related morbidity and mortality. For instance, using data from observational studies and randomized trials, Cook *et al.* [43] showed that a reduction of 2 mmHg in the average diastolic BP in the United States population would result in a 17% lower prevalence of hypertension, a 6% lower risk of CHD, and a 15% lower risk of stroke. Moreover, in a meta-analysis of nine randomized clinical trials including more than 62 thousand patients, Staessen *et al.* [44] found that in older patients with isolated systolic hypertension a reduction of 10 mmHg in systolic BP and 4 mmHg in diastolic BP reduced the risk of stroke and myocardial infarction by 30 and 23%, respectively. More important, a substantial part of the beneficial effects was achieved by a reduction of only 5 mmHg in systolic BP.

In conclusion, the results of this study suggest that statins could be used for the prevention of hypertension, particularly in individuals with prehypertension and with low HDL-C levels. In addition, statins may contribute to better BP control in patients with hypertension, particularly those in the upper tail of the BP distribution. Randomized clinical trials to test the extent of the benefits of statins in these type of patients are warranted.

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