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Insurance, self-reported medication adherence and LDL cholesterol: The REasons for Geographic and Racial Differences in Stroke study

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Abstract

Background—Lack of health insurance may adversely impact medication adherence and the control of cardiovascular risk factors. We examined if the association between insurance and LDL-C is due to self-reported low medication adherence.

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Methods—This cross-sectional study included 8,685 black and white men and women aged 45 and older who participated in the REasons for Geographic And Racial Differences in Stroke (REGARDS) cohort and used statins. Medication adherence was assessed using the 4-item Morisky Medication Adherence Scale (MMAS-4). Mean differences in LDL-C between participants with and without insurance were calculated using generalized linear models before and after adjustment for MMAS-4. Subgroups stratified by age, annual household income, diabetes, and CHD were compared. Separately, individual MMAS-4 questions were examined for mediation effects.

Results—After multivariable adjustment but without MMAS-4, LDL-C was 2.5 mg/dL (95% CI –0.6, 5.6) higher among uninsured versus insured participants. After further adjustment for MMAS-4, LDL-C was 2.6 mg/dL (95% CI –0.5, 5.6) higher. Stratified analyses produced similar results. No mediating effect was observed when each MMAS-4 question was examined separately.

Conclusion—High medication adherence does not mediate the association between having health insurance and lower LDL-C.

Keywords

Low density lipoprotein cholesterol; medication adherence; insurance

Background

Despite efforts to increase health insurance coverage in the US, in 2015 29 million American adults were uninsured[1]. A majority of these individuals are under 64 years old, racial minorities or have lower socioeconomic status[1]. Lack of health insurance is associated with greater barriers to preventive services [2] and treatment of both acute and chronic illnesses [3] resulting in worse reported health status. [4] Being uninsured also adversely impacts medication adherence [5] and the control of cardiovascular risk factors [6]. For example, elevated low density lipoprotein cholesterol (LDL-C) is an important risk factor for future cardiovascular (CV) events [7], and having no insurance is associated with higher LDL-C in primary and secondary prevention populations [6, 8].

The Morisky Medication Adherence Scale (MMAS-4) is a validated self-reported scale [9]. Worse adherence, defined using the MMAS-4, has been associated with higher prevalence of uncontrolled LDL-C [10]. However, there is limited research assessing the mediating effect of MMAS-4 on the association between insurance and LDL-C. A mediation effect by MMAS-4 would suggest that taking medications as prescribed is a mechanism by which having health insurance is associated with having low LDL-C. We examined this association in a cross-sectional analysis of the REasons for Geographic and Racial Differences in Stroke (REGARDS) study.

Methods

The REGARDS study is a population-based observational cohort study of 30,183 black and white adults aged 45 from the continental United States enrolled between January 2003 and October 2007 [11]. Institutional review boards (IRB) at participating centers approved this study, and participants provided written informed consent. The University of Alabama at

Birmingham IRB approved this project which conforms to the ethical guidelines of the 1975 Declaration of Helsinki. We excluded participants who were not taking statins (n=20,716), or had missing LDL-C values, insurance status, or did not complete the MMAS-4 (n=802). Characteristics of included and excluded participants are presented in Supplemental Table 1. After these exclusions were applied, all analyses included 8,685 participants.

LDL-C was calculated using the Friedewald equation for participants with serum triglycerides < 400 mg/dL. Participants with self-reported private or public insurance were considered insured. Medication adherence was assessed using MMAS-4. The four questions in the MMAS-4 are: “Do you ever forget to take your medication?”, “Are you careless at times about taking your medicine?”, “Sometimes if you feel worse when you take medicine, do you stop taking it?”, and “When you feel better do you sometimes stop taking your medication?” Affirmative responses were assigned 1 point to create an overall score ranging from 0–4. Consistent with previous studies, adherence was dichotomized as “high” (score 0) or “not high” (scores 1–4) [12].

Covariates were selected based on a behavioral model of healthcare utilization proposed by Andersen and Aday, and consist of predisposing, enabling, and need-based health factors [13]. Predisposing factors were age, sex, race, and body mass index (BMI). Enabling factors were geographic region (stroke belt/buckle, non-belt/buckle), annual household income (< \$35,000, \$35,000), education (less than high school, completed high school), and health professional shortage area (HPSA) (full, partial, non-HPSA). Need factors were self-reported history of coronary heart disease (CHD), stroke, diabetes, hypertension, current smoking, depressive symptoms (>4 on Centers for Epidemiologic Study Depressive Scale), cognitive impairment (Six-item screener), and number of medications being taken.

Participant characteristics were calculated overall and by insurance status with the statistical significance of the difference calculated using chi-square tests for proportions and t-tests for means. The univariate associations between participant characteristics and LDL-C were examined using a generalized linear model. Covariates with missing data were imputed using fully conditional specification [14]. Using a generalized linear model we determined the association of insurance status with LDL-C. Using the Judd and Kenny approach [15], mediation was examined by comparing mean differences in the association of insurance with LDL-C in regression models with and without MMAS-4. Confidence intervals (95% CI) for the mean and percent differences were calculated using bootstrapping.[16] Subgroup analysis examined the extent to which adherence mediated the association of insurance status on LDL-C by age (<65, 65 years), annual household income (<\$35,000, \$35,000), diabetes, and CHD. Finally, we examined the mediation effect of individual MMAS-4 questions. Analyses were conducted using SAS 9.4 (Cary, NC).

Results

Participant characteristics are listed in Table 1, overall and for those with and without health insurance. Uninsured compared to insured participants were younger (60.7 vs 66.9 years), more likely to be female (65.8% vs 48.3%), black (62.5% vs 37.1%), and have less education (75.4% with high school education vs 87.1%). They also reported lower income

(68.2% making less than \$35,000 annually vs 41.3%), were more likely to live in the stroke belt/buckle of the US (65.8% vs 55.0%), and had higher proportions of smoking (22.2% vs 12.1%), diabetes (44.4% vs 33.1%), hypertension (82.6% vs 71.0%), and depressive symptoms (17.1% vs 7.4%) but a lower percentage reported a history of CHD (27.6% vs 32.3%). High medication adherence was not statistically different between groups (67.6% of uninsured participants vs 68.1% of insured participants).

Mean LDL-C was higher among uninsured versus insured participants (103.5 mg/dL vs 95.8 mg/dL) despite all participants taking a statin. LDL-C was higher among uninsured versus insured participants before and after adjustment for MMAS-4 (Table 2). In a multivariable adjusted model that did not include MMAS-4, LDL-C was 2.5 mg/dL (95% CI–0.6, 5.6) higher among uninsured versus insured participants. After further adjustment for MMAS-4, LDL-C was 2.6 mg/dL (95% CI–0.5, 5.6) higher among uninsured versus insured participants. LDL-C remained higher among uninsured versus insured participants after adjustment for each MMAS-4 item individually, and no mediation effect was observed; stratified analyses produced similar results.

Discussion

In the current study, mean LDL-C was higher among uninsured versus insured statin users. This effect remained before and after we accounted for mediation by MMAS-4. A negligible portion of the association between insurance and LDL-C was explained by self-reported medication adherence. These data suggest poor medication adherence, as perceived by participants, is not a mediator of the association between health insurance and LDL-C.

The current analysis should be interpreted within the context of several known and potential limitations. First, we used self-report to ascertain insurance status and comorbidities. Additionally, the small proportion of uninsured participants (3.8%) in our sample may contribute to the observed wide confidence intervals. The MMAS-4 is a self-reported measure subject to reporting bias, however previous studies examining LDL-C among statin users [10] and blood pressure among antihypertensive medication users [17] provides evidence of construct validity for this measure. There were some differences between statin users included in these analyses and those that were excluded for missing insurance, LDL-C, or MMAS-4 measures which may affect the generalizability of our results from this select population. The current study also has several strengths. The REGARDS study enrolled a large, diverse population of middle-aged and older black and white individuals in the US. Progressive adjustment accounted for health behavior and utilization covariates; however, residual confounding may still be a concern.

Conclusions

Although high self-reported medication adherence is associated with lower LDL-C, it does not mediate the association between having health insurance and lower LDL-C. Based on the results of the current study, we infer that adherence may not be the mechanism by which insurance is associated with lower LDL-C. However, some aspects of insurance plans such

as medication coverage, which would impact access to medications, may have an important impact on LDL-C.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Uninsured compared to insured participants had higher mean LDL-C.
- After multivariable adjustment but without MMAS-4, LDL-C was 2.5 mg/dL higher among uninsured versus insured participants.
- After adjustment for MMAS-4, LDL-C was 2.6 mg/dL higher comparing uninsured versus insured participants.
- Examining subgroups stratified by age, annual household income, diabetes, and CHD did not change this association.
- Medication adherence does not mediate the association between having health insurance and lower LDL-C.

Table 1

REGARDS Participant Characteristics, Overall and by Insurance Status

	Overall (n=8685)	Insured (n=8352)	Uninsured (n=333)	p-value*
Age, mean (SD)	66.7 (8.7)	66.9 (8.6)	60.7 (7.5)	<0.001
Female, n (%)	4253 (49.0)	4034 (48.3)	219 (65.8)	<0.001
Race, n (%)				
White	5382 (62.0)	5257 (62.9)	125 (37.5)	ref
Black	3303 (38.0)	3095 (37.1)	208 (62.5)	<0.001
BMI**, kg/m ² , mean (SD)	29.9 (5.9)	29.8 (5.6)	32.3 (7.2)	<0.001
High School Education**, n (%)	7525 (86.6)	7274 (87.1)	251 (75.4)	<0.001
Income, n (%)				
\$35,000	3946 (45.4)	3889 (46.6)	57 (17.1)	ref
<\$35,000	3679 (42.4)	3452 (41.3)	227 (68.2)	<0.001
Declined to Report	1060 (12.2)	1011 (12.1)	49 (14.7)	—
Geographic Region, n (%)				
Stroke Belt/Buckle	4816 (55.4)	4597 (55.0)	219 (65.8)	0.001
Non-Stroke Belt	3869 (44.6)	3755 (45.0)	114 (34.2)	ref
HPSA**, n (%)				
Non	4957 (57.1)	4773 (57.1)	184 (55.3)	ref
Partial	3064 (35.3)	2955 (35.4)	109 (32.7)	—
Full	660 (7.6)	620 (7.4)	40 (12.0)	0.008
Current smoking**, n (%)	1082 (12.5)	1008 (12.1)	74 (22.2)	<0.001
Depressive Symptoms (CESD-4), n (%)	672 (7.7)	615 (7.4)	57 (17.1)	<0.001
Cognitive Impairment**, n (%)	598 (6.9)	576 (6.9)	22 (6.6)	0.67
Chronic Conditions, n (%)				
CHD**	2792 (32.2)	2700 (32.3)	92 (27.6)	0.08
Stroke**	833 (9.6)	802 (9.6)	31 (9.3)	0.87
Diabetes**	2909 (33.5)	2761 (33.1)	148 (44.4)	<0.001
Hypertension**	6203 (71.4)	5928 (71.0)	275 (82.6)	<0.001
Total number of medications, mean (SD)	7.8 (3.9)	7.8 (3.9)	7.1 (3.5)	0.001
LDL-C, mg/dL, mean (SD)	96.1 (28.8)	95.8 (28.7)	103.5 (32.2)	<0.001
High medication Adherence				
Yes	5912 (68.1)	5687 (68.1)	225 (67.6)	ref
No	2773 (31.9)	2665 (31.9)	108 (32.4)	0.84

Abbreviations: BMI, body mass index; CESD, Center for Epidemiologic Studies Depression Scale; CHD, coronary heart disease; HPSA, health professional shortage area; LDL-C, low density lipoprotein cholesterol; SD, standard deviation

* alpha=0.05 used for statistical significance;

** contains missing values for some participants

Table 2

Difference in low density lipoprotein cholesterol between participants without insurance compared to participants with insurance and mediating effect of self-reported medication adherence

	Difference in LDL-C without self-reported adherence, β (SE)	Difference in LDL-C with self-reported adherence, β (SE)	Absolute mediation effect of self-reported adherence, β (95% CI ^{**})	Percent change mediation effect of self-reported adherence, % (95% CI ^{**})
Unadjusted	7.7 (1.6)	7.6 (1.6)	—	—
Multivariable adjusted [*]	2.5 (1.6)	2.6 (1.6)	0.1 (−0.14, 0.29)	2.6 (−33.3, 50.3)
Subgroup Analysis, Multivariable adjusted [*]				
Age				
<65 years	2.0 (1.9)	2.2 (1.9)	0.2 (−0.17, 0.56)	5.3 (−80.8, 139.2)
65 years	4.5 (3.6)	4.5 (3.6)	0.0 (−0.30, 0.35)	0.6 (−31.7, 27.3)
Income				
<\$35,000	1.2 (2.0)	1.2 (2.0)	0.0 (−0.38, 0.32)	−0.4 (−85.0, 76.3)
\$35,000	9.1 (3.5)	9.1 (3.5)	0.0 (−0.49, 0.37)	−0.2 (−9.3, 10.5)
Diabetes				
Yes	0.6 (2.5)	0.6 (2.5)	0.0 (−0.29, 0.21)	−0.3 (−51.2, 57.9)
No	4.0 (2.1)	4.2 (2.1)	0.2 (−0.12, 0.52)	4.4 (−21.7, 50.1)
CHD				
Yes	1.3 (1.9)	1.4 (1.9)	0.1 (−0.14, 0.35)	1.0 (−7.2, 22.0)
No	5.7 (2.9)	5.8 (2.9)	0.1 (−0.26, 0.39)	1.2 (−63.4, 64.0)
Exploratory Analysis, Multivariable adjusted [*]				
Mediation by MMAS-4	2.5 (1.6)	2.5 (1.6)	0.0 (−0.17, 0.22)	1.4 (−23.3, 38.7)
Question 1 [†]				
Mediation by MMAS-4	2.5 (1.6)	2.4 (1.6)	−0.1 (−0.26, 0.12)	−1.7 (−27.1, 26.9)
Question 2				
Mediation by MMAS-4	2.5 (1.6)	2.6 (1.6)	0.1 (−0.05, 0.25)	2.6 (−24.8, 33.5)
Question 3				
Mediation by MMAS-4	2.5 (1.6)	2.4 (1.6)	−0.1 (−0.52, 0.25)	−3.7 (−64.3, 58.5)
Question 4				

Abbreviations: CI, confidence interval; CHD, coronary heart disease; LDL-C, low density lipoprotein cholesterol; MMAS-4, Morisky medication adherence scale; SE, standard error

^{*} Multivariable adjusted for predisposing (age, sex, race, body mass index), need (geographic region, income, education, health professional shortage area), and enabling (history of coronary heart disease, diabetes, stroke, hypertension, smoking, depressive symptoms, cognitive impairment, # medications taken) factors

^{**} 95% CI generated with bootstrap analysis of 1000 simulations

[†] MMAS-4 Question 1: “Do you ever forget to take your medication?”

MMAS-4 Question 2: “Are you careless at times about taking your medicine?”

MMAS-4 Question 3: “Sometimes if you feel worse when you take the medicine, do you stop taking it?”

MMAS-4 Question 4: “When you feel better do you sometimes stop taking your medication?”