

Novel relationship of serum cholesterol with asthma and wheeze in the United States

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Background: Cholesterol exerts complex effects on inflammation. There has been little investigation of whether serum cholesterol is associated with asthma, an inflammatory airways disease with great public health impact.

Objective: To determine relationships between levels of 3 serum cholesterol measures (total cholesterol [TC], high-density lipoprotein cholesterol [HDL-C], and non-HDL-C) and asthma/wheeze in a sample representative of the US population.

Methods: Cross-sectional study of 7005 participants age ≥ 6 years from the 2005 to 2006 National Health and Nutrition Examination Survey.

Results: Serum TC and non-HDL-C were lower in patients with current asthma than in subjects without current asthma in the overall population (TC, 188.5 vs 192.2 mg/dL; non-HDL-C, 133.9 vs 137.7 mg/dL; $P < .05$ for both), whereas HDL-C was not different. Adjusted odds ratios (ORs) from multivariate logistic regression per 1-SD increase of TC and non-HDL-C for current asthma were 0.92 (95% CI, 0.86-0.98) and 0.91 (95% CI, 0.85-0.98), respectively. On racial/ethnic stratification, these relationships reflect marked reductions unique to Mexican Americans (MAs; TC, 171.4 vs 189.3 mg/dL; $P < .001$; OR, 0.62; 95% CI, 0.48-0.80; non-HDL-C, 119.8 vs 137.9 mg/dL; $P < .001$; OR, 0.62; 95% CI, 0.48-0.79). Among MAs, the adjusted OR for wheeze requiring medical attention was 0.57 (95% CI, 0.43-0.75) for TC and 0.53 (95% CI, 0.33-0.85) for non-HDL-C. Relationships between cholesterol and asthma/wheeze were independent of body mass index and serum C-reactive protein, and similar between atopic and nonatopic participants.

Conclusion: Serum TC and non-HDL-C are inversely related to asthma in the US population, chiefly reflecting a relationship among MAs. (J Allergy Clin Immunol ■■■■;■■■:■■■-■■■.)

Key words: Lung, asthma, wheeze, cholesterol, atopy, Hispanic

Complex interactions have been reported between cholesterol and inflammation. Both cholesterol loading and cholesterol depletion of leukocytes, including macrophages, neutrophils, and mast cells, may trigger proinflammatory cellular responses.¹⁻³ Dyslipidemia (ie, elevated non-high-density lipoprotein cholesterol [HDL-C], reduced HDL-C) causes vascular inflammation through activation of innate immunity,⁴ although it may also attenuate innate immunity and skew adaptive immunity toward a T_H2 response in other settings,⁵ with differential effects depending on the genetic background of the host.⁶ Conversely, serum cholesterol declines during inflammation.⁷ Collectively, these reports suggest that bidirectional interactions between cholesterol and inflammation may affect disease differentially among human populations, and that cholesterol may influence inflammatory diseases other than atherosclerosis.

To date, relationships between cholesterol and inflammatory lung disease have been little studied, although emerging research indicates that cholesterol metabolism and inflammation are linked in the lung.⁸⁻¹⁰ Given the high prevalences in the United States of dyslipidemia and asthma, relationships between these disease entities may carry tremendous clinical implications. The few studies to date examining relationships between serum cholesterol and asthma have been limited in statistical power and demographic sampling. One group reported elevated serum total cholesterol (TC) to be associated with asthma,¹¹ whereas 2 others found no association.^{12,13} Significant interracial/ethnic differences exist not only in asthma prevalence¹⁴⁻¹⁷ but also in the prevalence and molecular features of dyslipidemia, and in the relationship between dyslipidemia and disease, such as atherosclerotic cardiovascular disease (CVD).¹⁸⁻²⁰ Mexican Americans (MAs), an understudied group, are distinguished by having an unexplained low prevalence of asthma,¹⁴⁻¹⁷ as well as a relatively low prevalence of CVD despite increased rates of dyslipidemia and inflammation.¹⁸⁻²⁰ As with cholesterol and CVD, the relationship between cholesterol and asthma may be anticipated to differ among racial/ethnic backgrounds.

The National Health and Nutrition Examination Survey (NHANES) 2005 to 2006 measured serum cholesterol and characterized asthma and wheeze in a sample of subjects representative of the US population. We hypothesized that serum TC and non-HDL-C would be directly associated with current asthma and wheeze requiring medical attention in the NHANES,

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Abbreviations used

BMI:	Body mass index
CRP:	C-reactive protein
CVD:	Cardiovascular disease
HDL-C:	High-density lipoprotein cholesterol
LDL-C:	Low-density lipoprotein cholesterol
MA:	Mexican American
NHANES:	National Health and Nutrition Examination Survey
NHB:	Non-Hispanic black
NHW:	Non-Hispanic white
OR:	Odds ratio
TC:	Total cholesterol

and that these relationships would differ among racial/ethnic groups. Thus, stratification by race/ethnicity was prespecified. Our primary goal was to test for an independent relationship between serum cholesterol concentrations and asthma prevalence. Our secondary goal was to test for an independent relationship between serum cholesterol and wheeze requiring medical attention, a surrogate indicator of poorly controlled asthma and other obstructive lung disease. Given that cholesterol might have different relationships with allergic and nonallergic inflammation, we also tested for interactions of atopy with cholesterol in the outcomes.

METHODS**Study population**

Data were obtained from the NHANES 2005 to 2006, which was designed to assess the health and nutritional status of the civilian, noninstitutionalized US population. Details may be found online at <http://www.cdc.gov/nchs/>. The NHANES classifies participants into 5 main racial/ethnic groups: non-Hispanic white (NHW), non-Hispanic black (NHB), MA, other Hispanic, and other/multirace. Because of the heterogeneity of the other Hispanic and other/multirace categories (non-Mexican Hispanics, Asians, Native Americans, multiracial), we included them in analysis of the overall population but did not analyze them separately. Low-density lipoprotein cholesterol (LDL-C) was measured only in participants who were asked to fast for ≥ 8.5 hours ($n = 3026$), of whom 250 did not meet the fasting requirements. By contrast, TC and HDL-C were measured in fasting and nonfasting participants ($n = 7360$). Fasting time (time since consumption of anything other than water) was recorded in this combined study population, permitting assignment of fasting duration to individual cholesterol measurements. Non-HDL-C (ie, TC minus HDL-C) has comparable or better predictive value than LDL-C for CVD,^{21,22} and both fasting and nonfasting non-HDL-C are predictive of CVD.²³ Thus, all analyses were based on TC and HDL-C measured in a combined fasting and nonfasting study population.

Clinical outcomes

Doctor-diagnosed current asthma was assessed by questionnaire. Patients with current asthma were defined as participants who answered in the affirmative to the questions, "Has a doctor ever told you that you had asthma?" and "Do you still have asthma?" For assessment of wheezing, participants were first asked, "Have you had wheezing or whistling in your chest at any time in the past 12 months?" If they answered yes, they were then asked, "In the past 12 months, how many times have you gone to the doctor's office or the hospital emergency room for attacks of wheezing or whistling?" Wheezing requiring medical attention in the past 12 months (hereafter referred to as *medical wheeze*) was defined as 1 or more episodes in response to the second question.

Serum cholesterol measurement

Serum TC and HDL-C were measured by using a Roche Hitachi 717 or 912 (Roche, Indianapolis, Ind). For TC, coupled enzymatic reactions were used involving cholesteryl ester hydrolase, cholesterol oxidase, and peroxidase, followed by phenazine absorbance detection. HDL-C measurement was by the Roche/Boehringer-Mannheim Diagnostics direct HDL method. Non-HDL-C was derived by subtracting HDL-C from TC.

Covariates

Covariates were obtained from questionnaire, laboratory analyses (IgE, serum cotinine, serum C-reactive protein [CRP]), and physical examination (height, weight). Atopy was defined as ≥ 1 detectable (≥ 0.35 kU/L) serum allergen-specific IgE to a panel of 19 allergens: *Alternaria alternata*, *Aspergillus fumigatus*, Bermuda grass (*Cynodon dactylon*), birch (*Betula verrucosa*), cat dander, cockroach (*Blattella germanica*), dog dander, dust mite (*Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*), egg white, milk, mouse urine proteins, oak (*Quercus alba*), peanut (*Arachis hypogaea*), ragweed (*Ambrosia elatior*), rat urine proteins, Russian thistle (*Salsola kali*), rye grass (*Lolium perenne*), and shrimp (*Pandalus borealis*). IgE was measured with the Pharmacia Diagnostics ImmunoCAP 1000 System (Kalamazoo, Mich). Cotinine was measured by isotope dilution-HPLC/atmospheric pressure chemical ionization tandem mass spectrometry. CRP was measured by latex-enhanced nephelometry. Body mass index (BMI) is weight in kilograms divided by height in meters squared.

Statistical analyses

Relationships between serum cholesterol and asthma/wheeze were examined in stratified bivariate and logistic regression analyses. For each outcome, mean cholesterol values were compared for participants with and without that outcome for the total population and by race/ethnicity by using the *t* test. Odds ratios (ORs) for the associations between serum cholesterol concentrations and current asthma (dependent variable) and medical wheeze (dependent variable) were estimated with logistic regression per 1-SD increase of each cholesterol subtype. The weighted SDs for TC (39.1 mg/dL), non-HDL-C (39.3 mg/dL), and HDL-C (14.4 mg/dL) were determined for the overall NHANES 2005 to 2006 population for which these values were available ($n = 7360$). Covariates in fully adjusted models included age, sex, race/ethnicity (total population only), householder education, BMI, log-transformed cotinine, CRP, and number of hours fasting before blood draw. Associations in participants with and without atopy were compared by using multiplicative interaction terms in logistic models. Separate models were run by race/ethnicity and for each cholesterol subtype. The interaction between serum cholesterol and race in the outcomes was tested. All analyses were adjusted for the NHANES complex sampling design by using SAS statistical software (version 9.1.3; Cary, NC) survey procedures (SURVEYFREQ, SURVEYMEAN, SURVEYREG) according to NHANES analysis specifications. Statistical significance was $P \leq .05$ (main effects) or $\leq .10$ (interactions).

RESULTS

Table I shows the features of 7005 subjects aged ≥ 6 years in the NHANES 2005 to 2006 for whom data were available for the respiratory questionnaire, serum TC and HDL-C, and other covariates as shown. The mean (SEM) prevalences of current asthma and medical wheeze were 8.7% (0.5%) and 6.6% (0.5%). Of those participants reporting current asthma, 36.5% reported medical wheeze, and of those reporting medical wheeze, 48.6% reported current asthma (see this article's Table E1 in the Online Repository at www.jacionline.org). Among racial/ethnic groups, the mean prevalence of self-reported physician-diagnosed current asthma was lowest in MAs (4.5% in MAs; 9.9% in NHBs, $P < .001$; 9.1% in NHWs, $P < .001$). The prevalence of wheeze episodes over the preceding 12 months requiring medical attention

TABLE I. Characteristics of study population by race/ethnicity*

	Total population‡ n = 7005 (SE)†	MA n = 1739 (SE)†	NHB n = 1841 (SE)†	NHW n = 2897 (SE)†	P values§
Age (y)	40.0 (0.8)	31.5 (0.6)	36.6 (0.9)	42.3 (0.9)	<.001
Age (%)					
6-17 y	17.1 (0.6)	24.7 (0.2)	19.8 (0.4)	15.1 (0.7)	<.001
18-39 y	32.5 (1.1)	44.6 (0.5)	36.8 (0.9)	29.6 (0.9)	
≥40 y	50.4 (1.2)	30.8 (0.4)	43.4 (0.9)	55.3 (2.0)	
Sex (%)					
Male	49.0 (0.5)	52.7 (0.5)	46.4 (0.9)	49.5 (1.6)	.07
Female	51.0 (0.6)	47.3 (0.5)	53.6 (1.1)	50.5 (1.4)	
Education (%)					
<9th grade	6.3 (0.6)	34.3 (0.5)	4.4 (0.1)	2.8 (0.4)	<.001
9th to <12th grade	11.5 (1.1)	19.1 (0.2)	19.7 (0.5)	9.2 (1.1)	
High school—GED	25.2 (1.1)	20.6 (0.3)	24.7 (0.5)	26.2 (1.5)	
Some college	31.2 (1.0)	19.7 (0.3)	35.4 (0.7)	32.2 (1.2)	
College graduate	25.8 (2.1)	6.4 (0.1)	15.8 (0.4)	29.7 (2.1)	
BMI (kg/m ²)	27.2 (0.2)	26.9 (0.2)	28.8 (0.3)	27.2 (0.3)	<.001
BMI (%)					
Underweight or normal	50.0 (1.6)	47.0 (0.5)	41.2 (0.9)	51.1 (1.3)	<.01
Overweight (BMI 85% to 94%)	22.6 (0.7)	26.0 (0.3)	22.4 (0.4)	22.5 (1.2)	
Obese (BMI ≥ 95%)	27.4 (1.3)	27.0 (0.3)	36.4 (0.8)	26.5 (1.5)	
Serum cotinine (ng/mL)	0.37 (0.04)	0.12 (0.02)	0.68 (0.17)	0.40 (0.06)	<.001
Smoking status (%)					
Never smoked	57.3 (1.4)	69.1 (0.7)	67.1 (1.5)	52.5 (2.1)	<.001
Former smoker	21.4 (0.8)	15.1 (0.2)	13.2 (0.2)	24.7 (0.9)	
Current smoker	21.3 (0.9)	15.8 (0.2)	19.8 (0.4)	22.7 (1.1)	
CRP (mg/dL)	0.38 (0.01)	0.42 (0.04)	0.44 (0.02)	0.38 (0.02)	.04
Fasting time (h)	7.0 (0.1)	7.9 (0.2)	7.5 (0.2)	6.9 (0.1)	<.001
TC (mg/dL)	191.9 (0.7)	188.5 (1.4)	184.3 (0.7)	193.4 (0.7)	<.001
HDL-C (mg/dL)	54.5 (0.3)	51.4 (0.7)	57.6 (0.3)	54.4 (0.4)	<.001
Non-HDL-C (mg/dL)	137.4 (0.8)	137.1 (1.6)	126.7 (0.8)	139.0 (0.9)	<.001
Current asthma (%)	8.7 (0.5)	4.5 (0.8)	9.9 (0.7)	9.1 (0.5)	<.001
Medical wheeze (%)	6.6 (0.5)	2.8 (0.5)	5.3 (0.6)	7.2 (0.7)	<.001
Atopy (%)	44.8 (1.2)	46.7 (1.6)	57.8 (1.6)	41.7 (1.3)	<.001
Total IgE (kU/L)	139.7 (6.3)	194.3 (18)	260.1 (26)	106.8 (6.9)	<.001

Medical wheeze denotes wheeze episodes requiring medical attention. Atopy was defined as ≥1 detectable allergen-specific IgE value.

*Mean values unless otherwise specified.

†SE of the mean or percent.

‡Total population also includes other/multirace.

§P value result from χ^2 test of homogeneity or ANOVA test of main effect for 3 race/ethnicity groups as appropriate.

||Geometric mean reported because log(cotinine) is used as a covariate in the adjusted logistic regression models.

was also lowest in MAs (2.8% in MAs; 5.3% in NHBs, $P = .005$; 7.2% in NHWs, $P < .001$). Mean HDL-C was lowest among MAs, whereas MA non-HDL-C and TC were intermediate between that of NHBs and NHWs. Serum cotinine was lowest among MAs and highest among NHBs.

To explore relationships between current asthma and serum cholesterol, we first compared mean serum cholesterol values between subjects with and without current asthma (Table II). TC and non-HDL-C were both significantly lower in patients with asthma than in subjects without asthma in the overall population. On racial/ethnic stratification, the reduced TC and non-HDL-C were specific to MA patients with asthma ($P < .001$ for both). By contrast, among NHBs and NHWs, TC and non-HDL-C were not significantly different between subjects with and without asthma. HDL-C was not significantly different between patients with asthma and subjects without asthma in the overall population or in any racial/ethnic stratum.

As with asthma, among MAs, mean TC and non-HDL-C were both lower in those subjects with than in those without medical

wheeze ($P < .001$ for TC; $P < .05$ for non-HDL-C; Table III). TC was also reduced among wheezing NHBs, albeit more modestly.

The relationships between serum cholesterol and current asthma were next analyzed by multivariate logistic regression (Table IV). In the overall population, after adjustment for covariates, including age, race/ethnicity, sex, householder education, BMI, serum CRP, log-transformed serum cotinine, and number of hours fasting, the OR per 1-SD increase for current asthma diagnosis was 0.92 (95% CI, 0.86-0.98) for TC, and 0.91 (95% CI, 0.85-0.98) for non-HDL-C. On racial/ethnic stratification, these significant inverse relationships in the overall population between TC and asthma, and non-HDL-C and asthma, were determined largely to reflect striking inverse relationships specific to MAs (TC, adjusted OR, 0.62, 95% CI, 0.48-0.80, race/ethnicity interaction, $P = .007$; non-HDL-C, adjusted OR, 0.62, 95% CI, 0.48-0.79, race/ethnicity interaction, $P = .02$). Calculated ORs were essentially unchanged when CRP was left out of the model (data not shown). No significant relationship was found between any cholesterol variable and asthma in NHBs or NHWs, nor

TABLE II. Mean serum cholesterol among participants with and without current asthma by race/ethnicity

	Total population‡ Mean (SEM) n Overall n = 7005	MA Mean (SEM) n Overall n = 1739	NHB Mean (SEM) n Overall n = 1841	NHW Mean (SEM) n Overall n = 2897
TC (mg/dL)				
Current asthma, yes	188.5 (1.4) 623	171.4 (4.5) 102	182.6 (3.2) 201	192.0 (1.7) 274
Current asthma, no	192.2 (0.7)* 6382	189.3 (1.4)† 1637	184.5 (0.7) 1640	193.6 (0.7) 2623
HDL-C (mg/dL)				
Current asthma, yes	54.5 (0.9) 623	51.6 (1.1) 102	58.0 (1.5) 201	54.4 (1.2) 274
Current asthma, no	54.5 (0.3) 6382	51.3 (0.7) 1637	57.5 (0.4) 1640	54.4 (0.3) 2623
Non-HDL-C (mg/dL)				
Current asthma, yes	133.9 (1.6) 623	119.8 (4.5) 102	124.6 (3.4) 201	137.6 (2.1) 274
Current asthma, no	137.7 (0.8)* 6382	137.9 (1.5)† 1637	127.0 (0.8) 1640	139.2 (0.9) 2623

SEM = Standard error of the mean.

**P* value <.05 for *t* test of null hypothesis that mean cholesterol levels are equal comparing participants with current asthma with those without current asthma.†*P* value <.001 for *t* test of null hypothesis that mean cholesterol levels are equal comparing participants with current asthma with those without current asthma.

‡Total population also includes other/multirace.

TABLE III. Mean serum cholesterol among participants with and without wheeze requiring medical attention by race/ethnicity

	Total population‡ Mean (SEM) n Overall n = 7005	MA Mean (SEM) n Overall n = 1739	NHB Mean (SEM) n Overall n = 1841	NHW Mean (SEM) n Overall n = 2897
TC (mg/dL)				
Wheeze	192.5 (2.5) 394	167.7 (4.8) 60	175.9 (3.6) 99	197.1 (3.4) 203
No wheeze	191.8 (0.7) 6611	189.1 (1.4)† 1679	184.8 (0.7)* 1742	193.2 (0.7) 2694
HDL-C (mg/dL)				
Wheeze	53.6 (0.9) 394	52.8 (2.3) 60	53.6 (1.5) 99	53.8 (1.0) 203
No wheeze	54.6 (0.3) 6611	51.3 (0.7) 1679	57.8 (0.3)* 1742	54.5 (0.4) 2694
Non-HDL-C (mg/dL)				
Wheeze	139.0 (2.3) 394	114.9 (6.7) 60	122.3 (3.5) 99	143.2 (3.2) 203
No wheeze	137.3 (0.8) 6611	137.8 (1.6)* 1679	127.0 (0.8) 1742	138.7 (0.8) 2694

SEM = Standard error of the mean.

**P* value <.05 for *t* test of null hypothesis that mean cholesterol levels are equal comparing participants with wheeze with those without wheeze.†*P* value <.001 for *t* test of null hypothesis that mean cholesterol levels are equal comparing participants with wheeze with those without wheeze.

‡Total population also includes other/multirace.

TABLE IV. Associations between current asthma and serum cholesterol from logistic regression analysis

	TC*		HDL-C*		Non-HDL-C*	
	Unadjusted OR (95% CI)	Adjusted OR§ (95% CI)	Unadjusted OR (95% CI)	Adjusted OR§ (95% CI)	Unadjusted OR (95% CI)	Adjusted OR§ (95% CI)
Total population†	0.92 (0.87-0.98)	0.92 (0.86-0.98)	1.00 (0.92-1.10)	1.02 (0.91-1.15)	0.92 (0.86-0.99)	0.91 (0.85-0.98)
MA‡	0.63 (0.49-0.82)	0.62 (0.48-0.80)	1.02 (0.85-1.21)	0.95 (0.76-1.19)	0.64 (0.50-0.81)	0.62 (0.48-0.79)
NHB‡	0.96 (0.82-1.12)	0.98 (0.85-1.14)	1.02 (0.88-1.20)	1.06 (0.92-1.24)	0.94 (0.80-1.11)	0.95 (0.81-1.12)
NHW‡	0.97 (0.90-1.03)	0.97 (0.91-1.04)	1.00 (0.89-1.13)	1.01 (0.88-1.17)	0.97 (0.89-1.05)	0.97 (0.90-1.05)

*OR and 95% CI for each cholesterol-specific SD change. SDs (TC, 39.1 mg/dL; non-HDL-C, 39.3 mg/dL; HDL-C, 14.4 mg/dL) were determined for the total NHANES 2005 to 2006 population for which serum cholesterol was measured (*n* = 7360).

†From unadjusted model (current asthma=cholesterol) and fully adjusted model including age, race/ethnicity, sex, householder education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

‡Fully adjusted model does not include race/ethnicity.

§Adjusted racial/ethnic interaction *P* = .007 for TC, *P* = .33 for HDL-C, and *P* = .02 for non-HDL-C.

between HDL-C and asthma in MAs. Similar results for non-HDL-C were found, albeit with wider CIs, in an analysis limited to the fasting study subpopulation (*n* = 2776), in which the LDL-C-asthma relationship was also examined (see this article's [Table E2](#) in Online Repository at www.jacionline.org). No statistically significant interaction by atopy was found for the 3 cholesterol measures in the relationship to asthma (see this article's [Table E3](#) in the Online Repository at www.jacionline.org). The adjusted relationships between TC, non-HDL-C, HDL-C, and current

asthma for the different racial/ethnic groups, as modeled by logistic regression using serum cholesterol values measured in the NHANES 2005 to 2006, are depicted in [Fig 1](#). To explore further the cholesterol-asthma relationship in the overall population, we performed analyses stratified by age, sex, smoking status, and BMI category (see this article's [Tables E4-E7](#) in the Online Repository at www.jacionline.org). Of interest among these analyses was an interaction with sex observed in the HDL-C-asthma and non-HDL-C-asthma relationships ([Table E5](#)). We also

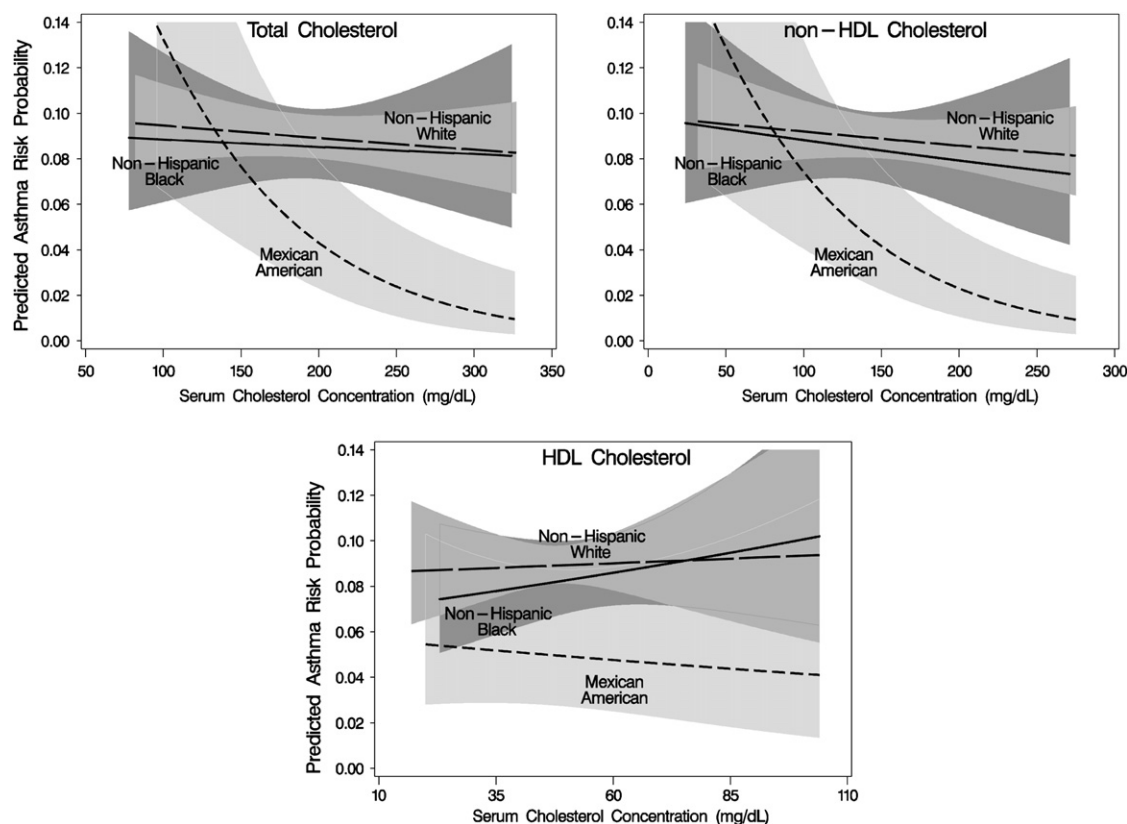


FIG 1. Predicted probability of current asthma for racial/ethnic categories in the NHANES 2005 to 2006 in relation to serum values of TC, non-HDL-C, and HDL-C. Logistic regression curves are adjusted for age, sex, household education, BMI, serum CRP, serum cotinine, and hours fasting. Range for each figure is limited to overall mean $\pm$ 3.5 SDs. 95% CIs are shown with shading.

TABLE V. Associations between wheeze requiring medical attention and serum cholesterol from logistic regression analysis

	TC*		HDL-C*		Non-HDL-C*	
	Unadjusted OR (95% CI)	Adjusted OR§ (95% CI)	Unadjusted OR (95% CI)	Adjusted OR§ (95% CI)	Unadjusted OR (95% CI)	Adjusted OR§ (95% CI)
Total population†	1.02 (0.92-1.12)	0.99 (0.88-1.10)	0.94 (0.84-1.06)	0.97 (0.86-1.09)	1.04 (0.94-1.14)	1.00 (0.90-1.10)
MA‡	0.57 (0.43-0.76)	0.57 (0.43-0.75)	1.10 (0.82-1.47)	1.07 (0.75-1.53)	0.55 (0.35-0.86)	0.53 (0.33-0.85)
NHB‡	0.79 (0.66-0.96)	0.80 (0.70-0.93)	0.78 (0.64-0.96)	0.79 (0.62-1.02)	0.89 (0.74-1.05)	0.88 (0.78-0.99)
NHW‡	1.09 (0.95-1.24)	1.08 (0.94-1.24)	0.96 (0.85-1.08)	1.00 (0.88-1.13)	1.10 (0.98-1.24)	1.08 (0.96-1.22)

*OR and 95% CI for each cholesterol-specific SD change. SDs (TC, 39.1 mg/dL; non-HDL-C, 39.3 mg/dL; HDL-C, 14.4 mg/dL) were determined for the total NHANES 2005 to 2006 population for which serum cholesterol was measured (n = 7360).

†From unadjusted model (wheeze = cholesterol) and fully adjusted model including age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

‡Fully adjusted model does not include race/ethnicity.

§Adjusted racial/ethnic interaction $P < .001$ for TC, $P = .12$ for HDL-C, and $P < .001$ for non-HDL-C.

analyzed the cholesterol-asthma relationship by using clinically relevant cut-points for the 3 cholesterol measures (see this article's Table E8 in the Online Repository at www.jacionline.org).

We next tested for an independent relationship between serum cholesterol and medical wheeze. As shown in Table V, among MAs, the adjusted OR for wheeze per 1-SD increase of TC was 0.57 (95% CI, 0.43-0.75), and that per 1-SD increase of non-HDL-C was 0.53 (95% CI, 0.33-0.85), indicating that TC and non-HDL-C are inversely related to medical wheeze. A similar, albeit more modest, relationship was found between TC and wheeze, and non-HDL-C and wheeze, among NHBs, but not among NHWs (race/ethnicity interaction $P < .001$ for both TC and non-HDL-C). An inverse relationship between non-HDL-C

and wheeze was also found for MAs and NHBs in an analysis limited to the fasting study subpopulation; similar findings were noted in an analysis using LDL-C (see this article's Table E9 in the Online Repository at www.jacionline.org). No statistically significant interaction by atopy was found for the 3 cholesterol measures in the wheeze outcome (see this article's Table E10 in the Online Repository at www.jacionline.org). Analyses of the cholesterol-wheeze relationship stratified by age, sex, smoking status, and BMI category appear as this article's Tables E11 to E14 in the Online Repository at www.jacionline.org. The cholesterol-wheeze relationship analyzed by using clinically relevant cholesterol cut-points appears in this article's Table E15 in the Online Repository at www.jacionline.org.

DISCUSSION

Dyslipidemia affects inflammation,¹⁻⁴ and emerging studies suggest that cholesterol trafficking and inflammation are coupled in the lung.⁸⁻¹⁰ Given this, we tested for a relationship between serum cholesterol and asthma, an inflammatory lung disease, in the NHANES 2005 to 2006, a large, nationally representative survey. We report that, contrary to their risk factor status for CVD, TC and non-HDL-C are inversely related to current asthma in the overall US population, and that this phenomenon chiefly reflects a relationship that is specific to MAs. TC and non-HDL-C were also inversely related to wheeze requiring medical attention in MAs and NHBs. These relationships are independent of both obesity (BMI), an established asthma risk factor,²⁴ and CRP, an inflammatory biomarker, and are not modified by atopy.

To our knowledge, this is the first study to investigate a connection between cholesterol and asthma in a national survey, and the first to identify a factor that may possibly contribute to the reduced prevalence and morbidity of asthma in MAs. The few previous investigations of serum cholesterol and asthma have differed substantially in design and methodology. Al-Shawwa et al¹¹ reported that TC was positively associated with asthma, but this single-center study included only 189 NHW children. Picado et al¹² found no difference in serum cholesterol between 121 controls and 118 patients with asthma at a single center, but did not stratify by race/ethnicity. In a nested case-control study of 1537 adults in Germany, Schafer et al¹³ found no significant relationship between serum cholesterol and asthma. In the current study, a very large sample size revealed significant interracial/ethnic differences in the cholesterol-asthma relationship in the US population. Although modest, statistically nonsignificant relationships were found in NHWs and NHBs, a striking relationship was observed in MAs.

Although Hispanics are the fastest growing minority in the United States and are projected to be 24.4% of the US population by 2050,²⁵ asthma in Hispanics has been understudied,^{26,27} leading to its identification as an urgent research priority.²⁸ Consistent with our findings, others have reported lower asthma prevalence in MAs than in NHWs and NHBs.¹⁴⁻¹⁷ This low prevalence remains unexplained, especially in the face of heightened asthma risk factors among MAs, such as obesity and low socioeconomic status.^{14,15,29} Of interest, among Hispanics, asthma prevalence and severity vary dramatically by subgroup. Whereas MAs have the lowest asthma prevalence in the United States, Puerto Ricans have the highest prevalence³⁰ and higher disease severity than MAs.³¹ Because of the complexity and extremity of the asthma phenotype among Hispanics, study of this population provides an opportunity to dissect novel determinants of asthma that may also have generalizable significance to other populations.

Several reports have indicated that MAs have increased dyslipidemia and inflammation, yet attenuated disease manifestations of cholesterol dysregulation, suggesting that a distinct dyslipidemia-inflammation-disease axis may characterize this population. Like us, other national surveys have found reduced HDL-C in MAs.³² Also reported are higher cardiovascular risk in MAs than NHWs,³³ higher rates of metabolic syndrome in Hispanics than in NHWs and NHBs,³⁴ and higher levels of circulating cytokines in MAs.^{6,35} Despite increased dyslipidemia and inflammation, MAs have an attenuated risk relationship between metabolic syndrome and atherosclerosis,^{6,34,36} and, in fact, reduced CVD.¹⁸⁻²⁰ Collectively, this literature suggests that MAs

have a distinct lipid-inflammation set-point and may have a distinct relationship between dyslipidemia and lipid-related inflammatory disease.

Although our analysis was cross-sectional, there is some cellular and animal model evidence to suggest that non-HDL-C, and, in particular LDL, the major lipoprotein component of the non-HDL fractions, may reduce asthma risk. LDL is taken up by the lung³⁷ and induces functional responses in lung-resident cells. LDL suppresses cellular responsiveness to TGF- β ,³⁸ a pivotal asthma mediator; inhibits histamine release from human lung mast cells³⁹; and inhibits histamine effect.⁴⁰ In mice, dyslipidemia is associated with dampened airway inflammation (Fessler MB, unpublished data, May 2009). However, whether LDL was causal in the current study or was a marker of other causal mediators such as oxidized LDL is uncertain. Of interest, oxidized LDL, which is elevated in MAs compared with NHWs,⁴¹ is a Toll-like receptor 4 stimulus, and Toll-like receptor 4 stimulation dampens asthmatic phenotypes in rodent models.⁴² Moreover, oxidized LDL phospholipids impair, and HDL restores, dendritic cell differentiation and antigen presentation to T cells,⁴³ immunologic events critical to asthma.

Our study had limitations. Because the NHANES is cross-sectional, the causality and directionality of the cholesterol-asthma relationship is uncertain. Despite the multiple adjustments we made, the possibility of unmeasured confounders remains. Given the multiple, nonprespecified comparisons made in our secondary, stratified analyses (Tables E2-E15), these findings are best viewed as exploratory and hypothesis-generating. We performed our analyses with combined fasting and nonfasting cholesterol values; this notwithstanding, the fasting time in our study population had tight variation, was very close to the ≥ 8 -hour fast traditionally imposed for fasting serum lipid measurement, and was adjusted for in the regressions. Moreover, on stratification by fasting status (8.5-hour cutpoint), we found no significant interactions of fasting with either TC or non-HDL-C in the asthma or wheeze outcomes (data not shown). We were unable to adjust for nonprescription medication use because of nonavailability of these data. Two trials have reported that statins do not affect clinical asthma outcomes.^{44,45} Consistent with this, we found no significant interactions between statin use and any of the cholesterol measures in either the asthma or wheeze outcome (data not shown). The effect of inhaled and oral glucocorticoids on serum lipids is somewhat controversial, although a large analysis of NHANES III reported no differences in TC, LDL-C, or HDL-C between glucocorticoid users and nonusers among participants <60 years old.⁴⁶ Finally, we did not address diet. Multiple nutritional factors, including antioxidants, fruits, minerals, and fatty acids have been variably associated with altered risk for asthma and allergy.⁴⁷ As non-HDL-C—raising westernized diets are generally low in antioxidants, fruit, and some minerals, these reportedly asthma-protective factors are not likely to confound the cholesterol-asthma relationship we report. Nevertheless, future studies may be warranted, especially given likely interracial/ethnic differences in dietary composition.

Several clinical questions arise. Do cholesterol-reducing therapies modify asthma risk differentially among MAs, NHWs, and NHBs? Do changes in asthma severity temporally affect serum cholesterol, and, if so, does cholesterol track with exacerbation and treatment response? Do other metabolic syndrome components interact with serum cholesterol to modify asthma risk? In

MA subjects with respiratory symptoms, do serum cholesterol levels have good predictive value in diagnosis of asthma?

In conclusion, serum TC and non-HDL-C were negatively associated with asthma and wheeze in MAs in this cross-sectional analysis. To our knowledge, this is the first report of a putative protective biological factor that may distinguish asthma in MAs from that in other racial/ethnic groups. If independently confirmed, we speculate that these findings may have implications for the treatment of dyslipidemia in MAs, and may also provide new insights into basic mechanisms of asthma pathogenesis and treatment relevant to additional populations.

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Key messages

- Asthma is inversely related to serum TC and non-HDL-C in the US population, chiefly reflecting a relationship among MAs.
- The cholesterol-asthma relationship is independent of BMI and serum CRP, and similar among atopic and non-atopic subjects.

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TABLE E1. Prevalence of current asthma versus medical wheeze:
unweighted counts and weighted percentages

		Medical wheeze			
Frequency	Row %	Column %	No	Yes	Total
Current asthma	No		6198	184	6382
			96.3	3.7	
			94.1	51.4	
	Yes		413	210	623
			63.5	36.5	
			5.9	48.6	
Total			6611	394	7005

Values in each cell, descending vertically, are unweighted frequency, weighted percentage that the cell frequency represents of row total, and weighted percentage that the cell frequency represents of column total.

TABLE E2. Associations between current asthma and serum cholesterol from logistic regression in fasting population

Characteristic	Non-HDL-C		LDL-C	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
All	0.82 (0.62-1.07)	0.81 (0.64-1.04)	0.85 (0.71-1.02)	0.86 (0.73-1.02)
MA	0.58 (0.32-1.05)	0.61 (0.30-1.23)	0.73 (0.58-0.91)	0.78 (0.59-1.03)
NHB	0.93 (0.58-1.50)	0.89 (0.54-1.45)	0.92 (0.68-1.25)	0.91 (0.67-1.23)
NHW	0.88 (0.66-1.17)	0.91 (0.72-1.15)	0.87 (0.72-1.05)	0.89 (0.75-1.05)

OR and 95% CI for each cholesterol-specific standard deviation (SD) change. SDs (non-HDL-C, 65.0 mg/dL, n = 2831; LDL-C, 34.9 mg/dL, n = 2776). Unadjusted model: current asthma = cholesterol. Adjusted model includes age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

TABLE E3. Atopy-stratified associations between current asthma and serum cholesterol from logistic regression

Characteristic	TC		HDL-C		Non-HDL-C	
	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
Atopy						
Yes	0.95 (0.87-1.05)	0.96 (0.86-1.07)	1.06 (0.91-1.24)	1.12 (0.94-1.33)	0.93 (0.84-1.04)	0.92 (0.83-1.03)
No	0.88 (0.76-1.02)	0.81 (0.68-0.97)	0.96 (0.85-1.08)	0.93 (0.79-1.09)	0.90 (0.78-1.03)	0.83 (0.70-0.99)

OR and 95% CI for each cholesterol-specific SD change. SDs (TC, 39.1 mg/dL; non-HDL-C, 39.3 mg/dL; HDL-C, 14.4 mg/dL). Unadjusted model: current asthma = cholesterol. Adjusted model includes age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

*Adjusted atopy interaction *P* values are *P* = .38 for TC, *P* = .24 for HDL-C, and *P* = .71 for non-HDL-C.

TABLE E4. Age-stratified associations between current asthma and serum cholesterol by logistic regression

Characteristic	TC		HDL-C		Non-HDL-C	
	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
Age (y)						
6-17	0.98 (0.73-1.31)	0.93 (0.68-1.27)	0.91 (0.75-1.11)	0.98 (0.81-1.19)	1.02 (0.77-1.37)	0.93 (0.72-1.21)
18-39	0.95 (0.80-1.12)	0.93 (0.79-1.10)	1.00 (0.84-1.19)	1.04 (0.81-1.32)	0.95 (0.78-1.16)	0.92 (0.75-1.13)
≥40	0.95 (0.81-1.12)	0.93 (0.79-1.09)	1.03 (0.91-1.15)	1.03 (0.89-1.19)	0.94 (0.80-1.11)	0.92 (0.78-1.07)

OR and 95% CI for each cholesterol-specific SD change. SDs (TC, 39.1 mg/dL; non-HDL-C, 39.3 mg/dL; HDL-C, 14.4 mg/dL). Unadjusted model: current asthma = cholesterol. Adjusted model includes age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

*Adjusted age interaction *P* values are *P* = 1.00 for TC, *P* = .78 for HDL-C, and *P* = .99 for non-HDL-C.

TABLE E5. Sex-stratified associations between current asthma and serum cholesterol from logistic regression

Characteristic	TC		HDL-C		Non-HDL-C	
	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
Gender						
Male	0.82 (0.71-0.94)	0.85 (0.72-1.01)	1.11 (0.98-1.25)	1.15 (1.00-1.33)	0.80 (0.72-0.88)	0.82 (0.72-0.94)
Female	0.97 (0.84-1.12)	0.96 (0.83-1.12)	0.87 (0.75-1.01)	0.95 (0.82-1.11)	1.03 (0.89-1.19)	0.98 (0.84-1.14)

OR and 95% CI for each cholesterol-specific SD change. SDs (TC, 39.1 mg/dL; non-HDL-C, 39.3 mg/dL; HDL-C, 14.4 mg/dL. Unadjusted model: current asthma = cholesterol. Adjusted model includes age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

*Adjusted sex interaction *P* values are *P* = .19 for TC, *P* = .02 for HDL-C, and *P* = .03 for non-HDL-C.

TABLE E6. Smoking status–stratified associations between current asthma and serum cholesterol by logistic regression

Characteristic	TC		HDL-C		Non-HDL-C	
	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
Smoking status						
Never	0.91 (0.82-1.01)	0.94 (0.84-1.05)	1.03 (0.89-1.18)	1.09 (0.92-1.28)	0.90 (0.81-1.00)	0.91 (0.82-1.00)
Former	1.00 (0.77-1.30)	0.99 (0.77-1.27)	1.02 (0.86-1.22)	0.99 (0.78-1.26)	0.99 (0.76-1.30)	1.00 (0.77-1.29)
Current	0.87 (0.71-1.07)	0.76 (0.64-0.90)	0.90 (0.79-1.02)	0.95 (0.80-1.12)	0.92 (0.76-1.11)	0.78 (0.66-0.92)

OR and 95% CI for each cholesterol-specific SD change. SDs (TC, 39.1 mg/dL; non-HDL-C, 39.3 mg/dL; HDL-C, 14.4 mg/dL. Unadjusted model: current asthma = cholesterol. Adjusted model includes age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

*Adjusted smoking status interaction *P* values are *P* = .86 for TC, *P* = .31 for HDL-C, and *P* = .83 for non-HDL-C.

TABLE E7. BMI category–stratified associations between current asthma and serum cholesterol by logistic regression

Characteristic	TC		HDL-C		Non-HDL-C	
	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
BMI category						
Underweight or normal	0.86 (0.76-0.98)	0.90 (0.77-1.06)	1.02 (0.89-1.17)	1.01 (0.86-1.18)	0.85 (0.75-0.95)	0.89 (0.76-1.05)
Overweight (BMI 85% to 94%)	0.88 (0.70-1.12)	0.92 (0.73-1.16)	1.22 (1.03-1.44)	1.19 (1.00-1.42)	0.82 (0.65-1.02)	0.86 (0.69-1.08)
Obese (BMI ≥95%)	0.95 (0.80-1.12)	0.93 (0.79-1.10)	1.09 (0.91-1.30)	0.99 (0.78-1.26)	0.92 (0.78-1.10)	0.93 (0.79-1.10)

OR and 95% CI for each cholesterol-specific SD change. SDs (TC, 39.1 mg/dL; non-HDL-C, 39.3 mg/dL; HDL-C, 14.4 mg/dL. Unadjusted model: current asthma = cholesterol. Adjusted model includes age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

*Adjusted BMI category interaction *P* values are *P* = .87 for TC, *P* = .41 for HDL-C, and *P* = .77 for non-HDL-C.

TABLE E8. Associations between current asthma and serum cholesterol from logistic regression based on cholesterol cut-points*

Characteristic	TC		HDL-C		Non-HDL-C	
	Unadjusted OR (95% CI)	Adjusted OR† (95% CI)	Unadjusted OR (95% CI)	Adjusted OR† (95% CI)	Unadjusted OR (95% CI)	Adjusted OR† (95% CI)
All	0.87 (0.74-1.02)	0.88 (0.74-1.05)	0.96 (0.73-1.24)	0.94 (0.71-1.24)	0.76 (0.59-0.98)	0.76 (0.59-0.99)
MA	0.42 (0.25-0.70)	0.44 (0.24-0.81)	1.33 (0.67-2.65)	1.16 (0.60-2.26)	0.51 (0.29-0.90)	0.60 (0.33-1.07)
NHB	0.93 (0.65-1.34)	0.98 (0.66-1.44)	1.15 (0.56-2.37)	1.24 (0.56-2.75)	0.71 (0.50-1.02)	0.70 (0.45-1.08)
NHW	0.95 (0.79-1.15)	0.99 (0.78-1.24)	0.85 (0.61-1.17)	0.81 (0.58-1.14)	0.85 (0.64-1.11)	0.86 (0.65-1.13)

OR and 95% CI for each cholesterol-specific SD change. Unadjusted model: current asthma = cholesterol. Adjusted model includes age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

*Cut-points are 200 mg/dL (TC), 160 mg/dL (non-HDL-C), and 40 mg/dL (HDL-C).

†Adjusted racial/ethnic interaction *P* values are *P* = .04 for TC, *P* = .70 for HDL-C, and *P* = .24 for non-HDL-C.

TABLE E9. Associations between medical wheeze and serum cholesterol from logistic regression in fasting population

Characteristic	Non-HDL-C		LDL-C	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
All	0.93 (0.69-1.25)	0.82 (0.59-1.14)	0.95 (0.79-1.15)	0.91 (0.75-1.11)
MA	0.23 (0.12-0.42)	0.18 (0.06-0.58)	0.42 (0.30-0.58)	0.42 (0.25-0.71)
NHB	0.60 (0.34-1.07)	0.52 (0.28-0.96)	0.74 (0.52-1.05)	0.71 (0.50-1.01)
NHW	1.08 (0.70-1.67)	0.98 (0.62-1.54)	1.02 (0.79-1.33)	0.99 (0.76-1.28)

OR and 95% CI for each cholesterol-specific SD change. SDs (non-HDL-C, 65.0 mg/dL, n = 2831; LDL-C, 34.9 mg/dL, n = 2776). Unadjusted model: medical wheeze = cholesterol. Adjusted model includes age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

TABLE E10. Atopy-stratified associations between medical wheeze and serum cholesterol from logistic regression

Characteristic	TC		HDL-C		Non-HDL-C	
	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
Atopy						
Yes	1.00 (0.85-1.17)	1.00 (0.84-1.19)	0.93 (0.76-1.14)	0.93 (0.75-1.14)	1.02 (0.87-1.20)	1.02 (0.87-1.20)
No	1.04 (0.89-1.21)	0.96 (0.80-1.15)	0.98 (0.85-1.13)	1.01 (0.88-1.16)	1.04 (0.89-1.22)	0.96 (0.80-1.13)

OR and 95% CI for each cholesterol-specific SD change. SDs (TC, 39.1 mg/dL; non-HDL-C, 39.3 mg/dL; HDL-C, 14.4 mg/dL).

Unadjusted model: medical wheeze = cholesterol. Adjusted model includes age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

*Adjusted atopy interaction *P* values are *P* = .84 for TC, *P* = .75 for HDL-C, and *P* = .93 for non-HDL-C.

TABLE E11. Age-stratified associations between medical wheeze and serum cholesterol by logistic regression

Characteristic	TC		HDL-C		Non-HDL-C	
	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
Age (y)						
6-17	1.02 (0.69-1.49)	0.94 (0.61-1.43)	1.14 (0.86-1.51)	1.16 (0.85-1.59)	0.95 (0.69-1.31)	0.86 (0.60-1.25)
18-39	0.99 (0.80-1.21)	0.97 (0.77-1.21)	0.88 (0.72-1.08)	0.88 (0.73-1.06)	1.03 (0.81-1.31)	1.00 (0.78-1.29)
≥ 40	1.06 (0.86-1.30)	1.03 (0.83-1.29)	0.93 (0.80-1.08)	0.92 (0.80-1.06)	1.08 (0.90-1.31)	1.06 (0.86-1.29)

OR and 95% CI for each cholesterol-specific SD change. SDs (TC, 39.1 mg/dL; non-HDL-C, 39.3 mg/dL; HDL-C, 14.4 mg/dL). Unadjusted model: medical wheeze = cholesterol. Adjusted model includes age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

*Adjusted age interaction *P* values are *P* = .92 for TC, *P* = .11 for HDL-C, and *P* = .59 for non-HDL-C.

TABLE E12. Sex-stratified associations between medical wheeze and serum cholesterol from logistic regression

Characteristic	TC		HDL-C		Non-HDL-C	
	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
Sex						
Male	0.92 (0.75-1.11)	0.98 (0.79-1.22)	1.06 (0.84-1.35)	1.06 (0.84-1.33)	0.90 (0.74-1.10)	0.96 (0.77-1.20)
Female	1.08 (0.93-1.26)	1.01 (0.85-1.19)	0.81 (0.68-0.97)	0.89 (0.75-1.06)	1.16 (1.00-1.34)	1.05 (0.89-1.23)

OR and 95% CI for each cholesterol-specific SD change. SDs (TC, 39.1 mg/dL; non-HDL-C, 39.3 mg/dL; HDL-C, 14.4 mg/dL. Unadjusted model: medical wheeze = cholesterol. Adjusted model includes age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

*Adjusted sex interaction *P* values are *P* = .28 for TC, *P* = .09 for HDL-C, and *P* = .12 for non-HDL-C.

TABLE E13. Smoking status–stratified associations between medical wheeze and serum cholesterol by logistic regression

Characteristic	TC		HDL-C		Non-HDL-C	
	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
Smoking status						
Never	1.01 (0.86-1.19)	1.05 (0.87-1.27)	0.84 (0.70-1.02)	0.89 (0.71-1.11)	1.07 (0.93-1.24)	1.09 (0.94-1.27)
Former	1.16 (0.80-1.68)	1.12 (0.81-1.55)	0.79 (0.52-1.22)	0.74 (0.45-1.23)	1.23 (0.86-1.75)	1.18 (0.87-1.62)
Current	0.90 (0.74-1.11)	0.80 (0.66-0.98)	1.21 (1.08-1.35)	1.19 (1.07-1.32)	0.83 (0.66-1.04)	0.73 (0.59-0.92)

OR and 95% CI for each cholesterol-specific SD change. SDs (TC, 39.1 mg/dL; non-HDL-C, 39.3 mg/dL; HDL-C, 14.4 mg/dL. Unadjusted model: medical wheeze = cholesterol. Adjusted model includes age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

*Adjusted smoking status interaction *P* values are *P* = .41 for TC, *P* = .002 for HDL-C, and *P* = .08 for non-HDL-C.

TABLE E14. BMI category–stratified associations between medical wheeze and serum cholesterol by logistic regression

Characteristic	TC		HDL-C		Non-HDL-C	
	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
BMI category						
Underweight or normal	0.87 (0.78-0.99)	0.91 (0.77-1.07)	1.08 (0.96-1.22)	1.14 (1.00-1.30)	0.83 (0.73-0.95)	0.84 (0.72-0.98)
Overweight (BMI 85% to 94%)	0.98 (0.74-1.29)	0.99 (0.74-1.33)	0.95 (0.75-1.20)	0.81 (0.68-0.96)	0.99 (0.74-1.33)	1.05 (0.78-1.41)
Obese (BMI ≥95%)	1.13 (0.96-1.34)	1.10 (0.94-1.29)	0.88 (0.71-1.10)	0.75 (0.54-1.02)	1.16 (0.98-1.38)	1.16 (0.98-1.38)

OR and 95% CI for each cholesterol-specific SD change. SDs (TC, 39.1 mg/dL; non-HDL-C, 39.3 mg/dL; HDL-C, 14.4 mg/dL). Unadjusted model: medical wheeze = cholesterol. Adjusted model includes age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

*Adjusted BMI interaction *P* values are *P* = .06 for TC, *P* = .07 for HDL-C, and *P* = .01 for non-HDL-C.

TABLE E15. Associations between medical wheeze and serum cholesterol from logistic regression based on cholesterol cut-points*

Characteristic	TC		HDL-C		Non-HDL-C	
	Unadjusted OR (95% CI)	Adjusted OR† (95% CI)	Unadjusted OR (95% CI)	Adjusted OR† (95% CI)	Unadjusted OR (95% CI)	Adjusted OR† (95% CI)
All	1.11 (0.83-1.48)	1.06 (0.78-1.45)	0.72 (0.49-1.05)	0.74 (0.51-1.07)	1.13 (0.86-1.49)	1.08 (0.83-1.42)
MA	0.29 (0.13-0.66)	0.33 (0.15-0.72)	0.77 (0.41-1.46)	0.67 (0.34-1.31)	0.24 (0.09-0.62)	0.29 (0.13-0.62)
NHB	0.72 (0.42-1.25)	0.74 (0.47-1.14)	1.00 (0.39-2.56)	1.11 (0.39-3.18)	0.67 (0.33-1.37)	0.65 (0.34-1.22)
NHW	1.26 (0.92-1.72)	1.25 (0.88-1.77)	0.70 (0.49-0.99)	0.72 (0.52-1.00)	1.28 (0.97-1.70)	1.25 (0.93-1.69)

OR and 95% CI for each cholesterol-specific SD change. Unadjusted model: medical wheeze = cholesterol. Adjusted model includes age, race/ethnicity, sex, household education, BMI, serum CRP, log-transformed serum cotinine, and hours fasting.

*Cut-points are 200 mg/dL (TC), 160 mg/dL (non-HDL-C), and 40 mg/dL (HDL-C).

†Adjusted racial/ethnic interaction *P* values are *P* = .001 for TC, *P* = .93 for HDL-C, and *P* = .007 for non-HDL-C.