

Comparing Low-density Lipoprotein Cholesterol Population Estimates Using Different Predictive Equations: National Health and Nutrition Examination Survey, 2015–2018

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Abstract

Background—Since 1972, low-density lipoprotein cholesterol (LDL-C) has been calculated by the Friedewald equation, which estimates very low-density lipoprotein cholesterol as triglycerides divided by 5 and is accurate only for triglycerides <400 mg/dL. The Martin equation, published in 2013 (for triglycerides <400 mg/dL), replaced 5 with a factor varying over an array of non-high-density lipoprotein cholesterol and triglyceride levels. This array was extended in 2021 for triglycerides 400–<800 mg/dL. In 2020, the Sampson equation, accurate for triglycerides <800 mg/dL, was developed using multiple least squares regression. This report compares LDL-C as calculated by the Friedewald, Martin, and Sampson equations in a nationally representative sample of adults with triglycerides <400 mg/dL across the distribution of clinical cut points for LDL-C (<70 mg/dL, 70–<100 mg/dL, 100–<160 mg/dL, 160–<190 mg/dL, and ≥190 mg/dL) to assess the impact of equation choice on national estimates.

Methods—Using data on 4,461 adults in the 2015–2018 National Health and Nutrition Examination Survey, classification agreement into the LDL-C categories used for clinical management across the three equations was assessed using kappa statistics for men and women overall and by demographic subgroups. A sensitivity analysis assessed classification agreement between the Martin and Sampson equations for adults with triglycerides <800 mg/dL.

Results—During 2015–2018, 9.8%–10.0% of adults age 20 and older had LDL-C levels <70 mg/dL (Friedewald: 10.0%, Martin: 9.8%, Sampson: 9.8%). Less than 3% had LDL-C ≥190 mg/dL (Friedewald: 2.3%, Martin: 2.4%, Sampson: 2.6%). Very good agreement between the equations was seen in all subgroups (kappa >0.8).

Conclusions—The three equations for LDL-C produce similar U.S. population-level percent distributions for adults age 20 and older across LDL-C categories.

Keywords: Friedewald • Martin • Sampson • demographic subgroup • Cohen's kappa statistic • National Health and Nutrition Examination Survey (NHANES)

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Introduction

Serum low-density lipoprotein cholesterol (LDL-C) is a clinically important biomarker associated with plaque formation and atherosclerotic cardiovascular disease (hardening of arteries) (1). Using predictive equations to estimate LDL-C has been a common practice for reducing costs in clinical laboratories because direct assay measurements by the gold-standard ultracentrifugation method are time intensive and expensive (1). The Friedewald equation, introduced in 1972, estimates LDL-C by subtracting the sum of high-density lipoprotein cholesterol (HDL-C) and very low-density lipoprotein cholesterol from total cholesterol (2); it has been a globally recognized formula for estimating LDL-C in clinical practice for decades. However, limitations of the Friedewald equation, which include a fixed factor of 5 to estimate very low-density lipoprotein cholesterol,

$$VLDL-C = \frac{\text{triglyceride}}{5}$$

have been discussed widely (1,3,4). The Friedewald equation has been shown to underestimate LDL-C for blood biospecimens with high triglyceride

levels (≥ 150 mg/dL) and low LDL-C levels (< 100 mg/dL) (5).

Many estimation equations have been developed to address limitations of the Friedewald equation. Two equations that repeatedly demonstrate accuracy compared with ultracentrifugation are the Martin (5) and Sampson (6) equations. The Martin equation replaced the fixed factor of 5 with an adjustable factor that varies over non-HDL-C and triglyceride strata (5). Like the Friedewald equation, the original Martin equation is accurate only for triglyceride levels < 400 mg/dL. In 2020, Sampson et al. (6) aimed to design a more accurate equation for adults with low LDL-C or high triglycerides by developing the first accurate equation for triglyceride levels up to 800 mg/dL. They created this multiple least squares regression equation using data from a sample of 8,656 patients who visited the National Institutes of Health Clinical Center between January 1, 1976, and June 2, 1999 (6). The variable factors for the Martin equation were extended in 2021 to include triglyceride levels from 400 to 799 mg/dL (7).

New cholesterol management guidelines were released in 2018 by the American College of Cardiology and American Heart Association Task Force on Clinical Practice Guidelines with aims to lower the risk of atherosclerotic cardiovascular disease through cholesterol management (8). These guidelines recommended lipid-lowering medications for adults with severe primary hypercholesterolemia (LDL-C level > 190 mg/dL) and intensifying the medications if the patient's LDL-C level remained above 100 mg/dL. A target threshold of LDL-C < 70 mg/dL was recommended in patients at very high risk of atherosclerotic cardiovascular disease, which includes a history of multiple, major atherosclerotic cardiovascular disease events (for example, heart attack or stroke) or one major atherosclerotic cardiovascular disease event and multiple high-risk conditions. An LDL-C level of ≥ 160 mg/dL is a risk-enhancing factor (8).

The 2018 guidelines support using LDL-C as calculated by the original Martin equation for prescribing lipid-lowering medications and to improve

accuracy over the Friedewald equation for LDL-C < 70 mg/dL. In a subsequent report, the American College of Cardiology stressed the need for further testing of the Sampson equation in patients with low LDL-C and elevated triglycerides (9). Recently, the Martin equation with extended factors for LDL-C levels up to 800 mg/dL has been shown to be the most accurate equation for people with high triglyceride levels and low LDL-C (7).

Since 2018, many studies have compared the effectiveness of the Friedewald, Martin, and Sampson equations at the individual level in specific clinical populations as compared with direct assay measurement (10). Fewer have examined differences between the equations on nationally representative population-level estimates (11). This report evaluates and presents the extent of agreement in population-level LDL-C estimates based on the Friedewald, Martin, and Sampson equations when classifying adults into the LDL-C categories typically used for clinical management and surveillance. Weighted percent distributions of LDL-C categories are presented overall and by sex, age, and race and Hispanic origin using 2015–2018 National Health and Nutrition Examination Survey (NHANES) data.

Methods

NHANES, conducted by the National Center for Health Statistics (NCHS), is a cross-sectional survey representative of the U.S. civilian noninstitutionalized population (12). NHANES became a continuous survey in 1999 and releases data in 2-year cycles. Survey sampling is based on a stratified, multistage, area probability sampling method (13). NHANES includes a home interview and a health examination at a mobile examination center (MEC). Participants in the examination component were randomly assigned to a morning, afternoon, or evening session and only the morning session participants were asked to fast for at least 8 hours before their examination. Examination response rates for adults age 20 and older were 58.1% in 2015–2016 and 49.8% in 2017–2018. This analysis used data

from NHANES 2015–2018. Data are also available for 2017–March 2020, but because there were no significant trends in cholesterol levels after 2013–2014 (14), the analysis combined two full 2-year survey cycles to obtain adequate sample sizes for subdomain estimates.

Adult participants self-reported their race and Hispanic origin. Analyses were limited to the race and Hispanic-origin groups for which estimates were statistically reliable, including Asian non-Hispanic (subsequently, Asian), Black non-Hispanic (subsequently, Black), White non-Hispanic (subsequently, White), and Hispanic. People who were categorized as other race non-Hispanic (including multiracial) were included in the analysis of the entire population but are not shown separately. The survey was approved by the NCHS Ethics Review Board. Written informed consent was obtained from adult participants.

Laboratory methods

During 2015–2018, NHANES directly measured values of total cholesterol, triglycerides, and HDL-C using standardized procedures. Venous blood biospecimens were collected in the MEC from NHANES participants and processed using a standardized protocol. After processing, serum biospecimens were stored frozen at -30°C until they were shipped on dry ice to the contracted laboratory for analysis (15). During 2015–2018, total cholesterol and triglycerides were measured using coupled enzymatic reactions, and HDL-C was measured using a two-step colorimetric endpoint reaction method. All three analytes were measured using the Roche/Hitachi Cobas 6000 at the University of Minnesota's Advanced Research & Diagnostic Laboratory with Cobas 6000 system reagents (16–18). Total cholesterol and HDL-C were obtained on examined people regardless of fasting time, whereas triglycerides were obtained only on adults randomly assigned and examined in the morning and who reported fasting 8.5– < 24 hours before venipuncture (blood draw). Therefore, LDL-C estimates are available only for adults examined in the morning.

LDL-C values were calculated from measured total cholesterol and triglycerides. The equations are:

$$LDL-C \text{ (Friedewald)} = \text{total cholesterol} - \left(HDL-C + \frac{\text{triglyceride}}{5} \right)$$

$$LDL-C \text{ (Martin)} = \text{total cholesterol} - \left(HDL-C + \frac{\text{triglyceride}}{\text{adjustable factor}} \right)$$

where the adjustable factor varies over a two-dimensional array of non-HDL-C and triglyceride levels (5,7), and

$$LDL-C \text{ (Sampson)} = \frac{\text{total cholesterol}}{0.948} - \frac{HDL-C}{0.971} - \left(\frac{\text{triglyceride}}{8.56} + \frac{\text{non-HDL-C} \cdot \text{triglyceride}}{2,140} - \frac{\text{triglyceride}^2}{16,100} \right) - 9.44$$

where $\text{non-HDL-C} = \text{total cholesterol} - HDL-C$.

Statistical methods

Weighted percent distributions of LDL-C estimates across the LDL-C categories used for clinical management (<70 mg/dL, 70–<100 mg/dL, 100–<160 mg/dL, 160–<190 mg/dL, and ≥190 mg/dL) were estimated for each equation overall, by sex and age, and by sex and race and Hispanic origin for adults with triglycerides <400 mg/dL. As a sensitivity analysis, estimates based on the Martin and Sampson equations were calculated for adults with triglycerides <800 mg/dL.

Cohen's kappa statistic serves as a correlation measure that assesses inter-rater reliability, specifically evaluating the agreement between two raters (in this case, two equations) in categorizing data into mutually exclusive groups. Here, Cohen's kappa statistic (19) was used to assess classification agreement into the LDL-C categories used for clinical management for participants with triglycerides <400 mg/dL (Friedewald compared with Martin, Friedewald compared with Sampson, and Martin compared with Sampson) and for participants with triglycerides <800 mg/dL (Martin compared with Sampson) for each sex–age category and each sex–race–Hispanic-origin category. The extent of agreement was determined by using the table by Landis and Koch (20). Values between 0.61 and 0.80 indicated good agreement and values between 0.81 and 1.00 indicated very good agreement. The kappa statistic was used instead of traditional significance testing so the full distribution across categories would be considered when comparing equations. Using kappa statistics also avoided issues of multiple comparisons that could have been a concern with so many subdomains.

Morning fasting sample weights, which account for unequal probability of selection, adjust for nonresponse, and were calibrated to 2015–2016 and 2017–2018 U.S. Census Bureau American Community Survey's civilian noninstitutionalized population totals, were used for all estimates (21). Stratification and clustering, in addition to weighting, were incorporated in estimating standard errors through Taylor series linearization (22). All statistical analyses were performed using SAS version 9.4 (23) and SUDAAN version 11 (24). Percent distributions were produced using PROC DESCRIPT and kappa estimates were produced using PROC CROSSTAB. The reliability of the estimated percentages was determined using the NCHS data presentation standards for proportions (25).

In the NHANES 2015–2018 sample, 10,739 adults age 20 and older were examined; 5,139 were examined in the morning and, of those, 4,561 fasted 8.5–<24 hours before venipuncture and had a fasting subsample weight greater than zero. An additional 51 adults had missing values for triglycerides, cholesterol, and direct HDL. This left a final sample of 4,461 adults with nonmissing triglyceride levels <400 mg/dL, an additional 37 adults with triglyceride levels of at least 400 mg/dL and up to 800 mg/dL, and 12 adults with triglyceride levels >800 mg/dL. The percentage

of missing outcomes due to missing values or extreme triglyceride levels was 2.2% in the main sample.

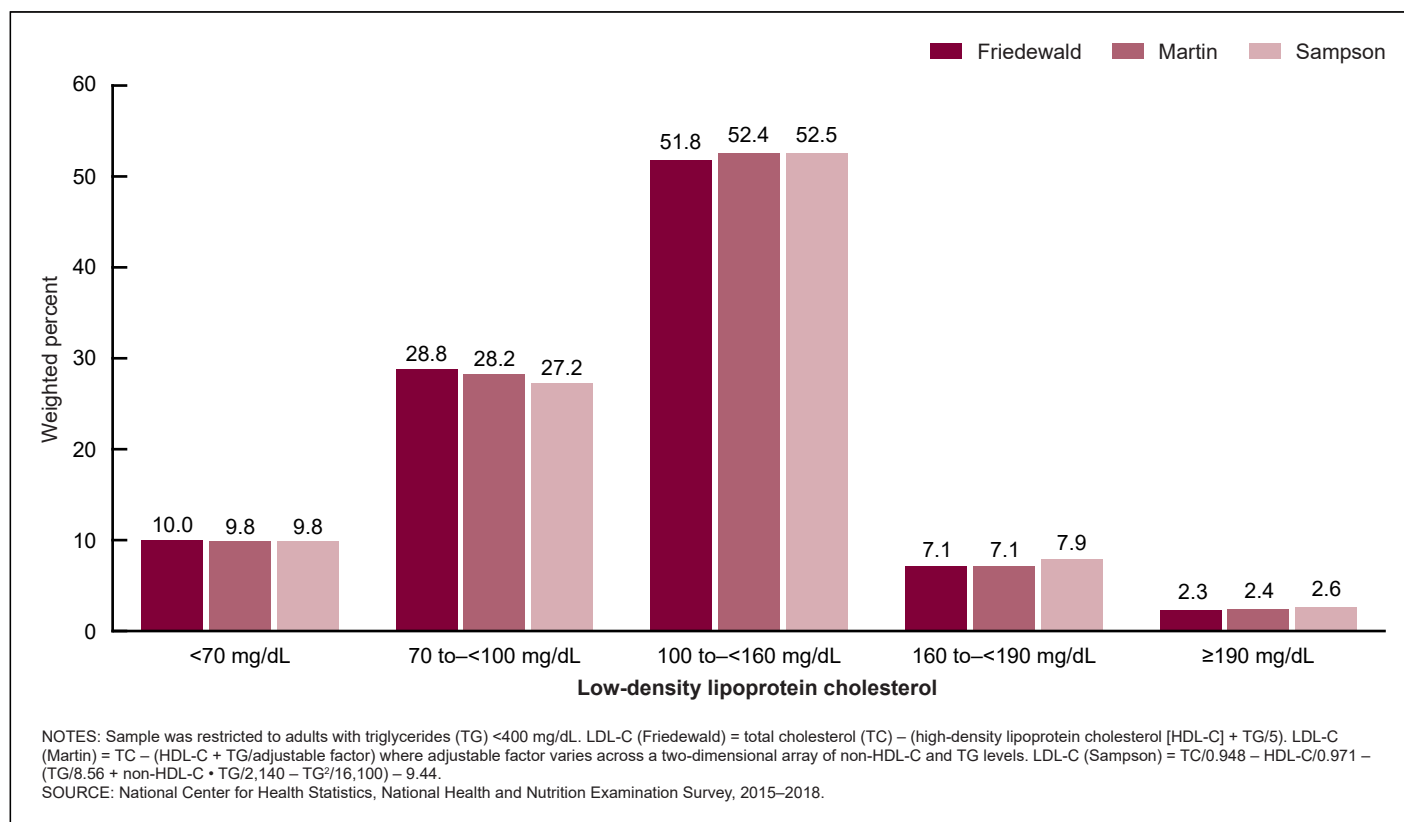
Results

The weighted distributions of LDL-C for participants with triglycerides <400 mg/dL are presented by equation in the Figure. During 2015–2018, 9.8%–10.0% of adults had LDL-C levels <70 mg/dL (Friedewald: 10.0%, Martin: 9.8%, Sampson: 9.8%) and 27.2%–28.8% had levels of 70–<100 mg/dL (Friedewald: 28.8%, Martin: 28.2%, Sampson: 27.2%). Just over one-half had levels 100–<160 mg/dL (Friedewald: 51.8%, Martin: 52.4%, Sampson: 52.5%). At the upper end of the distribution, 7.1%–7.9% had levels of 160–<190 mg/dL (Friedewald: 7.1%, Martin: 7.1%, Sampson: 7.9%), and less than 3% had levels ≥190 mg/dL (Friedewald: 2.3%, Martin: 2.4%, Sampson: 2.6%).

Table 1 shows the weighted means and weighted distributions across LDL-C categories for men overall, by age group, and by race and Hispanic origin for participants with triglycerides <400 mg/dL using each equation. Absolute differences in mean estimates across subgroups ranged from 0.4 mg/dL between Friedewald and Martin for men ages 20–39 to 2.39 mg/dL between Friedewald and Sampson for Asian men. The absolute differences between estimated percentages were all less than four percentage points when comparing Friedewald and Martin, Friedewald and Sampson, and Martin and Sampson across the distribution of LDL-C categories. Within age groups, the largest absolute difference (2.6%) in estimated percentages was seen between Friedewald and Sampson for men ages 40–59 with LDL-C 70–<100 mg/dL. Within race and Hispanic-origin groups, the largest absolute difference (3.6%) in estimated percentages was seen between Friedewald and Martin for Black men with LDL-C 100–<160 mg/dL. Among men with LDL-C <70mg/dL, the largest absolute difference (2.4%) was between Friedewald and Martin for those age 60 and older.

Table 2 presents the same estimates for women. Absolute differences in mean

Figure. Prevalence of low-density lipoprotein cholesterol levels among adults age 20 and older, by predictive equations: United States, 2015–2018



estimates across subgroups ranged from 0.1 mg/dL between Friedewald and Martin for all women to 2.48 mg/dL between Martin and Sampson for Black women. Within age groups, the largest absolute difference in estimated percentages (2.7%) was seen between Friedewald and Martin for women age 60 and older with LDL-C 100–<160 mg/dL. Within race and Hispanic-origin groups, the largest absolute difference in estimated percentages (2.2%) was seen between Martin and Sampson for Black women with LDL-C 70–<100 mg/dL. Among women with LDL-C <70 mg/dL, the largest absolute difference in estimated percentages (2.2%) was observed between Friedewald and Martin among those ages 20–39.

Based on the kappa statistics presented in Table 3, very good agreement (kappa = 0.81–1.00) between Friedewald and Martin, Friedewald and Sampson, and Martin and Sampson was seen overall and for all subgroups. However, the lower limit of the 95% confidence intervals for Friedewald compared with Martin were in the good

agreement (kappa = 0.61–0.80) range for men ages 40–59 (lower limit of kappa = 0.75) and Asian men (lower limit of kappa = 0.78). The observed kappa statistics for Friedewald compared with Martin were consistently lower than for Friedewald compared with Sampson and Martin compared with Sampson.

Table 4 shows the weighted means and weighted distributions across LDL-C categories for adults with triglycerides <800 mg/dL using the Martin and Sampson equations. The distribution of LDL-C based on the Martin equation was like that based on the Sampson equation for triglycerides <800 mg/dL. Absolute differences in mean estimates across subgroups ranged from 0.09 to 1.75 among men and from 1.01 to 2.42 for women. Absolute differences between estimated percentages based on the two equations were all less than three percentage points, with most less than one percentage point. Based on the kappa statistics presented in Table 5, very good agreement (kappa = 0.81–1.00) was observed between the Martin estimates and the Sampson estimates for

triglycerides <800 mg/dL. The lowest kappa statistic for men was 0.87 (Asian men). The lowest kappa statistic for women was 0.90 (ages 40–59). The lowest 95% confidence limit was 0.82 (Asian men).

Discussion

LDL-C estimated by the Friedewald, Martin, and Sampson equations showed similar results in U.S. adults age 20 and older during 2015–2018. Overall, 9.8%–10.0% of adults age 20 and older had LDL-C levels <70 mg/dL and less than 3% of adults age 20 and older had LDL-C levels >190 mg/dL, regardless of equation used. Across the distribution of LDL-C categories used for clinical management, no substantial differences (more than four percentage points) were observed between the three equations in adults with triglycerides <400 mg/dL or between the Martin and Sampson equations in adults with triglycerides <800 mg/dL. Kappa statistics confirmed very good agreement for adults overall, by sex and age, and by sex and race

and Hispanic origin in both triglyceride groups (<400 mg/dL and <800 mg/dL). That is, while differences in LDL-C estimates among the three equations may be important in clinical settings, they have minimal impact on population-level cholesterol surveillance.

It is well known that the equations perform differently for varying levels of triglycerides (11,26,27). Therefore, the small sample size of participants with triglycerides 400–<800 mg/dL (24 men and 13 women) could explain the lack of difference between the Martin and Sampson equations for participants with triglycerides <800 mg/dL. However, while important in clinical practice at the individual level, the impact is negligible at the population level because such a small proportion of the population has elevated triglyceride levels.

Observed variation between equations could be due to individual level mathematical variations. As an example, for a given adult, the Friedewald and Martin equations will be equal when the Martin adjustment factor is 5. The further this factor is from 5, the greater the difference between the LDL-C values calculated from these equations. Similar reasoning could be used to compare equation parameter values that make the Sampson equation equal to the Friedewald equation or the Sampson equation equal to the Martin equation.

The NHANES 2015–2018 sample is nationally representative. In contrast, clinical trial participants are often not randomly selected and are therefore not representative of the United States as a whole or of specific subpopulations. Several high-quality, randomized controlled trials and clinical trials have compared the Friedewald and Martin equations (10,28). These studies showed that LDL-C values estimated by the Friedewald equation tended to be lower than those estimated by the Martin equation, thus implying that the Friedewald equation could underestimate LDL-C levels and consequently overestimate LDL-C goal attainment, a threshold of <70 mg/dL for those at very high risk of atherosclerotic cardiovascular disease (8). At the population level, this could lead to a higher percentage with LDL-C <70 mg/dL based on Friedewald

estimates as compared with Martin estimates. The results in Table 1 show consistently lower mean Friedewald estimates compared with mean Martin estimates for men (in all but one age and race and Hispanic-origin group), and likewise, higher percentages in the <70 mg/dL category based on Friedewald as compared with Martin. However, the magnitudes of these differences are very small. This pattern was not observed for women.

In 2023, Wang et al. (11) studied differences between the three equations using NHANES 2017–March 2020 data. Their analysis stratified by sex and triglyceride levels. For triglycerides <149 mg/dL, their findings were consistent with those presented here in that the three estimates were close to one another. For higher triglyceride levels, they observed larger differences between estimates.

The main strength of this report is that it is based on a nationally representative survey with standardized sample collection and processing methods and is one of the first studies to compare LDL-C estimates from the Friedewald, Martin, and Sampson equations by sex and age and by sex and race and Hispanic origin. Because race and ethnicity variables are not available in many clinical laboratory data sets, this is a unique feature of the report.

Some limitations to this study exist. This report does not address how LDL-C values estimated by the Friedewald, Martin, or Sampson equations compare with LDL-C levels directly measured through beta-quantification, the gold standard. This analysis used samples from fasting participants; thus, performance for nonfasting triglyceride levels was not assessed. Finally, the distributions of LDL-C, as estimated by the Martin and Sampson equations for participants with triglyceride levels <800 mg/dL, are based on a small sample.

These results from NHANES 2015–2018 show very good agreement among LDL-C estimates calculated using the Friedewald, Martin, and Sampson equations. Distributions across the LDL-C categories typically used for clinical management were similar in the U.S. civilian noninstitutionalized population of adults overall, by sex and

age, and by sex and race and Hispanic origin.

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Table 1. Weighted mean and percent distribution of low-density lipoprotein cholesterol values calculated for men age 20 and older with triglyceride levels less than 400 mg/dL, by predictive equation and selected characteristics: United States, 2015–2018

Characteristic and estimating equation	Mean LDL-C	Standard error	LDL cholesterol level									
			<70 mg/dL		70–<100 mg/dL		100–<160 mg/dL		160–<190 mg/dL		≥190 mg/dL	
			Percent	Standard error	Percent	Standard error	Percent	Standard error	Percent	Standard error	Percent	Standard error
Total ¹ (n = 2,129)												
Friedewald ²	111.53	1.19	10.8	1.14	27.9	1.35	51.8	1.58	7.2	0.86	2.2	0.42
Martin ³	112.60	1.21	9.9	1.05	27.9	1.56	52.4	1.60	7.5	0.75	2.4	0.48
Sampson ⁴	113.44	1.23	10.5	1.14	26.0	1.40	52.8	1.51	8.0	0.79	2.6	0.44
Age group ¹												
20–39 (n = 644):												
Friedewald ²	110.36	1.58	9.9	1.97	31.4	2.45	49.8	2.56	7.0	1.50	1.9	0.54
Martin ³	110.76	1.63	9.2	1.96	32.0	2.66	49.7	2.52	7.3	1.38	1.8	0.52
Sampson ⁴	111.87	1.64	9.5	1.97	29.6	2.71	51.0	2.69	7.7	1.43	2.3	0.65
40–59 (n = 680):												
Friedewald ²	120.21	1.62	6.0	1.26	20.0	1.85	61.7	2.44	9.3	1.45	3.0	0.91
Martin	121.91	1.64	5.8	1.24	19.3	2.50	62.1	2.54	9.5	1.16	3.4	*1.12
Sampson ⁴	122.48	1.63	6.3	1.34	17.4	2.01	62.5	2.83	10.3	1.13	3.4	0.92
60 and older (n = 805):												
Friedewald ²	102.13	2.31	18.3	2.49	33.1	2.86	42.0	3.51	4.9	1.27	1.7	0.76
Martin ³	103.31	2.34	15.9	2.39	33.4	2.86	43.7	3.44	5.3	1.28	1.7	0.76
Sampson ⁴	104.15	2.37	17.3	2.48	32.1	2.70	43.0	3.42	5.7	1.36	1.8	0.76
Race and Hispanic origin												
Non-Hispanic:												
Asian (n = 271):												
Friedewald ²	115.24	3.19	9.1	1.64	27.7	3.02	50.0	2.78	10.9	2.39	2.2	*1.06
Martin ³	117.28	3.06	9.2	2.23	24.9	3.17	52.1	3.43	11.6	2.63	2.2	*1.06
Sampson ⁴	117.63	3.15	9.1	1.66	24.7	3.07	52.2	3.47	10.5	2.73	3.5	*1.20
Black (n = 445):												
Friedewald ²	111.82	2.21	11.0	1.95	28.0	1.96	51.6	2.79	7.0	1.20	2.4	0.65
Martin ³	111.18	2.18	12.4	2.28	28.7	2.18	48.0	2.63	9.0	1.23	1.8	0.57
Sampson ⁴	112.99	2.24	11.7	2.13	27.1	1.99	50.1	2.96	8.6	1.32	2.6	0.67
White (n = 753):												
Friedewald ²	110.36	1.65	11.8	1.65	28.9	2.02	50.1	2.55	7.2	1.23	2.1	0.62
Martin ³	111.56	1.68	10.3	1.53	29.2	2.33	51.0	2.56	7.1	1.02	2.4	0.72
Sampson ⁴	112.34	1.69	11.4	1.65	26.6	2.00	51.4	2.48	8.3	1.11	2.3	0.65
Hispanic (n = 553):												
Friedewald ²	115.56	1.95	8.0	1.43	26.2	2.39	56.2	2.22	7.3	1.24	2.4	0.70
Martin ³	117.05	1.94	7.1	1.50	25.4	2.61	57.2	2.12	7.7	1.23	2.5	0.70
Sampson ⁴	117.64	1.97	7.6	1.37	24.7	2.65	57.1	2.36	7.5	1.09	3.1	0.82

¹Includes data for race and Hispanic-origin groups not shown separately.

²Low-density lipoprotein cholesterol (LDL-C) (Friedewald) = total cholesterol (TC) – (high-density lipoprotein cholesterol [HDL-C] + triglycerides [TG]/5).

³LDL-C (Martin) = TC – (HDL-C + TG/adjustable factor) where the adjustable factor varies across a two-dimensional array (360 cells) of non-HDL-C (TC – HDL-C) 6 columns) and TG levels (60 rows).

⁴LDL-C (Sampson) = (TC/0.948) – (HDL-C/0.971) – (TG/8.56 + (non-HDL-C • TG/2,140) – TG²/16,100) – 9.44.

NOTES: Estimated percentages are based on the morning fasting sample weights, which account for unequal probability of selection, adjust for nonresponse and calibrate to the 2015–2016 and 2017–2018 U.S. Census Bureau's American Community Survey's civilian noninstitutionalized population totals. Percentages may not sum to 100 due to rounding. Standard errors estimated by Taylor series linearization, which incorporates stratification and clustering in addition to weighting into the estimation procedure. See Table 4 for distribution of LDL-C values for extended Martin and Sampson equation estimates limited to participants with TG <800mg/dL.

SOURCE: National Center for Health Statistics, National Health and Nutrition Examination Survey, 2015–2018.

Table 2. Weighted mean and percent distribution of low-density lipoprotein cholesterol values for women age 20 and older with triglyceride levels less than 400 mg/dL, by predictive equation and selected characteristics: United States, 2015–2018

Characteristic and estimating equation	Mean LDL-C	Standard error	LDL cholesterol level									
			<70 mg/dL		70–<100 mg/dL		100–<160 mg/dL		160–<190 mg/dL		≥190 mg/dL	
			Percent	Standard error	Percent	Standard error	Percent	Standard error	Percent	Standard error	Percent	Standard error
Total ¹ (n = 2,332)												
Friedewald ²	112.17	1.16	9.2	0.99	29.6	1.32	51.8	1.91	7.0	0.88	2.3	0.41
Martin ³	112.27	1.15	9.8	0.87	28.5	1.29	52.5	1.89	6.7	0.84	2.5	0.45
Sampson ⁴	113.90	1.18	9.2	0.90	28.4	1.34	52.1	1.90	7.7	0.92	2.6	0.45
Age group ¹												
20–39 (n = 737):												
Friedewald ²	101.71	1.59	12.8	1.78	38.6	2.27	43.9	2.27	2.9	0.84	1.8	0.64
Martin ³	101.10	1.65	15.0	1.82	37.6	2.05	43.0	2.19	2.6	0.77	1.8	0.64
Sampson ⁴	102.71	1.65	13.5	1.75	37.2	2.18	44.4	2.31	3.0	0.83	1.9	0.65
40–59 (n = 782):												
Friedewald ²	121.55	1.61	4.3	1.05	20.8	2.55	62.1	3.24	10.8	1.79	2.0	0.51
Martin ³	121.78	1.60	4.5	1.16	20.0	2.36	62.7	3.25	10.5	1.84	2.2	0.60
Sampson ⁴	123.58	1.63	4.2	1.09	19.7	2.52	62.0	3.21	12.0	1.92	2.2	0.55
60 and older (n = 813):												
Friedewald ²	113.60	2.09	10.8	1.80	29.3	2.40	49.1	2.24	7.6	1.44	3.3	0.70
Martin ³	114.37	2.04	9.7	1.77	27.7	2.51	51.8	2.45	7.2	1.41	3.6	0.83
Sampson ⁴	115.84	2.12	9.9	1.79	28.1	2.20	49.7	2.36	8.4	1.60	3.9	0.80
Race and Hispanic origin												
Non-Hispanic:												
Asian (n = 307):												
Friedewald ²	110.24	1.87	10.4	2.54	29.8	2.68	50.5	2.81	8.3	1.27	1.0	0.49
Martin ³	110.10	2.02	10.4	2.09	29.4	2.74	51.2	2.73	8.1	1.39	1.0	0.49
Sampson ⁴	111.86	1.96	10.6	2.27	28.1	2.48	51.5	2.89	8.7	1.49	1.1	0.50
Black (n = 506):												
Friedewald ²	109.75	1.95	11.0	1.60	34.4	2.93	45.0	2.09	6.9	0.91	2.7	0.82
Martin ³	108.16	1.96	10.8	1.45	35.4	2.62	45.1	2.26	6.2	0.95	2.6	0.82
Sampson ⁴	110.64	2.01	11.0	1.62	33.2	2.82	45.9	2.13	6.8	1.06	3.2	0.91
White (n = 758):												
Friedewald ²	112.80	1.55	8.9	1.42	29.3	1.80	52.1	2.79	7.3	1.31	2.5	0.56
Martin ³	113.05	1.52	9.7	1.24	27.7	1.84	52.9	2.81	6.9	1.22	2.8	0.60
Sampson ⁴	114.65	1.56	9.0	1.30	28.0	1.86	52.5	2.81	7.9	1.35	2.7	0.62
Hispanic (n = 666):												
Friedewald ²	109.84	1.58	9.9	1.50	29.2	3.28	53.6	2.72	5.3	1.19	2.0	0.62
Martin ³	110.47	1.63	9.9	1.26	28.6	2.59	54.1	2.72	5.4	1.11	2.0	0.62
Sampson ⁴	111.65	1.63	8.9	1.38	29.0	3.08	53.0	2.57	6.9	1.26	2.1	0.61

¹Includes data for race and Hispanic-origin groups not shown separately.

²Low-density lipoprotein cholesterol (LDL-C) (Friedewald) = total cholesterol (TC) – (high-density lipoprotein cholesterol [HDL-C] + triglycerides [TG]/5).

³LDL-C (Martin) = TC – (HDL-C + TG/adjustable factor) where the adjustable factor varies across a two-dimensional array (360 cells) of non-HDL-C (TC – HDL-C) 6 columns) and TG levels (60 rows).

⁴LDL-C (Sampson) = (TC/0.948) – (HDL-C/0.971) – (TG/8.56 + (non-HDL-C * TG/2,140) - TG²/16,100) – 9.44.

NOTES: Estimated percentages are based on the morning fasting sample weights, which account for unequal probability of selection, adjust for nonresponse and calibrate to the 2015–2016 and 2017–2018 U.S. Census Bureau's American Community Survey's civilian noninstitutionalized population totals. Percentages may not sum to 100 due to rounding. Standard errors estimated by Taylor series linearization, which incorporates stratification and clustering in addition to weighting into the estimation procedure. See Table 4 for distribution of LDL-C values for extended Martin and Sampson equation estimates limited to participants with TG <800mg/dL.

SOURCE: National Center for Health Statistics, National Health and Nutrition Examination Survey, 2015–2018.

Table 3. Kappa statistic agreement scores between estimates from pairs of predictive equations among adults age 20 and older with triglyceride levels less than 400 mg/dL, by predictive equation and selected characteristics: United States, 2015–2018

Characteristic	Friedewald ¹ compared with Martin ²			Friedewald ¹ compared with Sampson ³			Martin ² compared with Sampson ³		
	Kappa ⁴	95% confidence interval		Kappa ⁴	95% confidence interval		Kappa ⁴	95% confidence interval	
		Lower limit	Upper limit		Lower limit	Upper limit		Lower limit	Upper limit
Men									
Total ⁵	0.87	0.85	0.89	0.92	0.90	0.94	0.91	0.89	0.93
Age group ⁵									
20–39.....	0.87	0.84	0.91	0.91	0.87	0.95	0.92	0.89	0.95
40–59.....	0.82	0.75	0.88	0.91	0.86	0.96	0.88	0.83	0.93
60 and older.....	0.91	0.87	0.95	0.94	0.91	0.97	0.94	0.91	0.98
Race and Hispanic origin									
Non-Hispanic:									
Asian.....	0.84	0.78	0.90	0.92	0.87	0.97	0.87	0.82	0.91
Black.....	0.87	0.83	0.91	0.93	0.90	0.96	0.90	0.86	0.94
White.....	0.87	0.83	0.90	0.92	0.89	0.95	0.92	0.89	0.95
Hispanic.....	0.88	0.84	0.93	0.92	0.88	0.95	0.92	0.87	0.96
Women									
Total ⁵	0.91	0.88	0.93	0.94	0.92	0.96	0.92	0.90	0.94
Age group ⁵									
20–39.....	0.90	0.87	0.93	0.96	0.94	0.98	0.93	0.90	0.96
40–59.....	0.90	0.86	0.94	0.94	0.91	0.97	0.91	0.87	0.94
60 and older.....	0.91	0.87	0.95	0.92	0.88	0.96	0.91	0.88	0.95
Race and Hispanic origin									
Non-Hispanic:									
Asian.....	0.88	0.83	0.93	0.94	0.90	0.98	0.91	0.86	0.96
Black.....	0.90	0.87	0.93	0.96	0.93	0.98	0.90	0.87	0.93
White.....	0.90	0.87	0.94	0.94	0.92	0.97	0.92	0.89	0.95
Hispanic.....	0.91	0.88	0.94	0.94	0.91	0.96	0.92	0.89	0.95

¹Low-density lipoprotein cholesterol (LDL-C) (Friedewald) = total cholesterol (TC) – (high-density lipoprotein cholesterol [HDL-C] + triglycerides [TG]/5).

²LDL-C (Martin) = TC – (HDL-C + TG/adjustable factor) where the adjustable factor varies across a two-dimensional array (360 cells) of non-HDL-C (TC – HDL-C) 6 columns) and TG levels (60 rows).

³LDL-C (Sampson) = (TC/0.948) – (HDL-C/0.971) – (TG/8.56 + (non-HDL-C * TG/2,140) - TG²/16,100) – 9.44.

⁴Estimated kappa statistics are based on the morning fasting sample weights, which account for unequal probability of selection, adjust for nonresponse, and calibrate to the 2015–2016 and 2017–2018 U.S. Census Bureau's American Community Survey's civilian noninstitutionalized population totals.

⁵Includes data for race and Hispanic-origin groups not shown separately.

NOTES: LDL-C is low-density lipoprotein cholesterol; TC is total cholesterol; HDL-C is high-density lipoprotein cholesterol; TG is triglycerides; non-HDL-C = TC – HDL-C.

SOURCE: National Center for Health Statistics, National Health and Nutrition Examination Survey, 2015–2018.

Table 4. Weighted mean and percent distribution of low-density lipoprotein cholesterol values calculated for adults age 20 and older with triglyceride levels less than 800 mg/dL, by predictive equation and selected characteristics: United States, 2015–2018

Characteristic and estimating equation	Mean LDL-C	Standard error	LDL cholesterol level									
			<70 mg/dL		70–<100 mg/dL		100–<160 mg/dL		160–<190 mg/dL		≥190 mg/dL	
			Percent	Standard error	Percent	Standard error	Percent	Standard error	Percent	Standard error	Percent	Standard Error
Men												
Total ¹ (n = 2,153):												
Extended Martin ²	112.91	1.23	9.8	1.01	27.6	1.53	52.6	1.59	7.6	0.78	2.4	0.50
Sampson ³	113.49	1.22	10.5	1.09	26.0	1.36	52.8	1.51	8.1	0.82	2.6	0.45
Age group ¹ :												
20–39 (n = 652):												
Extended Martin ²	111.20	1.58	9.0	1.93	31.5	2.60	50.3	2.51	7.2	1.37	1.9	0.53
Sampson ³	112.03	1.59	9.3	1.94	29.5	2.70	51.2	2.65	7.6	1.41	2.4	0.65
40–59 (n = 692):												
Extended Martin ²	122.38	1.74	5.8	1.22	19.0	2.47	62.0	2.46	9.9	1.38	3.3	1.10
Sampson ³	122.62	1.68	6.3	1.31	17.2	2.01	62.5	2.80	10.7	1.33	3.4	0.91
60 and older (n = 809):												
Extended Martin ²	103.13	2.29	16.2	2.34	33.2	2.8	43.7	3.34	5.2	1.26	1.7	0.75
Sampson ³	103.82	2.31	17.5	2.42	32.4	2.74	42.7	3.40	5.7	1.35	1.8	0.75
Race and Hispanic origin												
Non-Hispanic:												
Asian (n = 273):												
Extended Martin ²	118.50	3.78	9.2	2.23	24.8	3.12	51.5	3.47	11.5	2.58	3.1	*1.44
Sampson ³	118.59	3.71	9.1	1.70	24.5	3.01	51.6	3.63	10.4	2.65	4.4	*1.54
Black (n = 446):												
Extended Martin ²	111.30	2.22	12.4	2.28	28.7	2.20	47.9	2.62	9.2	1.31	1.8	0.57
Sampson ³	113.05	2.26	11.7	2.12	27.0	2.01	50.2	2.97	8.6	1.32	2.6	0.67
White (n = 762):												
Extended Martin ²	111.90	1.68	10.3	1.47	28.7	2.27	51.4	2.53	7.3	1.10	2.3	0.71
Sampson ³	112.41	1.67	11.3	1.58	26.6	1.91	51.4	2.47	8.4	1.18	2.3	0.64
Hispanic (n = 562):												
Extended Martin ²	117.19	1.92	7.0	1.48	25.0	2.57	58.0	2.16	7.6	1.22	2.5	0.68
Sampson ³	117.46	1.92	7.4	1.36	24.7	2.63	57.4	2.35	7.4	1.09	3.1	0.80
Women												
Total ¹ (n = 2,345):												
Extended Martin ²	112.42	1.18	9.8	0.89	28.5	1.29	52.4	1.84	6.8	0.85	2.6	0.48
Sampson ³	113.97	1.2	9.3	0.90	28.3	1.35	52.0	1.86	7.7	0.92	2.7	0.48
Age group ¹ :												
20–39 (n = 739):												
Extended Martin ²	101.04	1.65	15.1	1.82	37.6	2.03	42.9	2.19	2.6	0.77	1.8	0.64
Sampson ³	102.60	1.66	13.6	1.77	37.2	2.18	44.3	2.31	3.0	0.83	1.9	0.65
40–59 (n = 791):												
Extended Martin ²	122.20	1.52	4.5	1.15	20.0	2.36	62.4	3.11	10.7	1.84	2.5	0.66
Sampson ³	123.83	1.55	4.3	1.08	19.5	2.53	61.7	3.08	12.0	1.93	2.5	0.63
60 and older (n = 815):												
Extended Martin ²	114.38	2.04	9.7	1.77	27.7	2.51	51.9	2.45	7.2	1.41	3.6	0.83
Sampson ³	115.84	2.12	9.9	1.79	28.0	2.19	49.8	2.36	8.4	1.60	3.9	0.80
Race and Hispanic origin												
Non-Hispanic:												
Asian (n = 308)												
Extended Martin ²	110.22	2.08	10.3	2.09	29.3	2.76	51.1	2.66	8.3	1.42	1.0	0.50
Sampson ³	111.93	1.98	10.6	2.26	28.0	2.51	51.6	2.93	8.7	1.49	1.1	0.50
Black (n = 508)												
Extended Martin ²	108.43	1.96	10.7	1.46	35.2	2.60	45.0	2.18	6.5	1.01	2.6	0.82
Sampson ³	110.85	2.01	10.9	1.63	33.0	2.79	45.8	2.07	7.1	1.11	3.2	0.91
White (n = 762)												
Extended Martin ²	113.23	1.58	9.7	1.24	27.7	1.84	52.7	2.73	6.9	1.23	3.0	0.66
Sampson ³	114.75	1.6	9.1	1.29	27.9	1.87	52.4	2.74	7.8	1.35	2.9	0.68
Hispanic (n = 672):												
Extended Martin ²	110.51	1.64	10.1	1.35	28.3	2.58	54.3	2.71	5.3	1.10	2.0	0.61
Sampson ³	111.52	1.63	9.1	1.46	28.9	3.08	53.1	2.58	6.8	1.24	2.1	0.61

Table 4. Weighted mean and percent distribution of low density lipoprotein cholesterol values calculated for adults age 20 and older with triglyceride levels less than 800 mg/dL, by predictive equation and selected characteristics: United States, 2015–2018–Con.¹Includes data for race and Hispanic-origin groups not shown separately.²Low-density lipoprotein cholesterol (LDL-C) (Martin) = total cholesterol (TC) – (high-density lipoprotein cholesterol [HDL-C] + triglycerides [TG]/adjustable factor) where the adjustable factor varies across a two-dimensional array (600 cells) of non-HDL-C (TC – HDL-C) (6 columns) and TG levels (100 rows).³LDL-C (Sampson) = (TC/0.948) – (HDL-C/0.971) – (TG/8.56 + (non-HDL-C * TG/2,140) – TG²/16,100) – 9.44.

NOTES: Estimated percentages are based on the morning fasting sample weights, which account for unequal probability of selection, adjust for nonresponse and calibrate to the 2015–2016 and 2017–2018 U.S. Census Bureau American Community Survey's civilian noninstitutionalized population totals. Percentages may not sum to 100 due to rounding. Standard errors estimated by Taylor series linearization, which incorporates stratification and clustering in addition to weighting into the estimation procedure.

SOURCE: National Center for Health Statistics, National Health and Nutrition Examination Survey, 2015–2018.

Table 5. Kappa statistic agreement scores between estimates from the extended Martin and Sampson equations, among adults age 20 and older with triglyceride levels less than 800 mg/dL, by selected characteristics: United States, 2015–2018

		Extended Martin ¹ compared with Sampson ²	
Characteristic	Kappa ³	95% confidence interval	
		Lower limit	Upper limit
Men			
Total ⁴	0.91	0.89	0.93
Age group ⁴			
20–39	0.91	0.88	0.95
40–59	0.88	0.83	0.93
60 and older	0.94	0.90	0.97
Race and Hispanic origin			
Non-Hispanic:			
Asian	0.87	0.82	0.91
Black	0.90	0.86	0.94
White	0.91	0.88	0.94
Hispanic	0.91	0.87	0.95
Women			
Total ⁴	0.92	0.90	0.94
Age group ⁴			
20–39	0.93	0.90	0.96
40–59	0.90	0.87	0.94
60 and older	0.91	0.88	0.95
Race and Hispanic origin			
Non-Hispanic:			
Asian	0.91	0.86	0.95
Black	0.90	0.87	0.93
White	0.92	0.89	0.95
Hispanic	0.92	0.89	0.95

¹Low-density lipoprotein cholesterol (LDL-C) (Martin) = total cholesterol (TC) – (high-density lipoprotein cholesterol [HDL-C] + triglycerides [TG]/adjustable factor) where the adjustable factor varies across a two-dimensional array (600 cells) of non-HDL-C (TC – HDL-C) (6 columns) and TG levels (100 rows).²LDL-C (Sampson) = (TC/0.948) – (HDL-C/0.971) – (TG/8.56 + (non-HDL-C * TG/2,140) – TG²/16,100) – 9.44.³Estimated kappa statistics are based on the morning fasting sample weights, which account for unequal probability of selection, adjust for nonresponse and calibrate to the 2015–2016 and 2017–2018 U.S. Census Bureau's American Community Survey's civilian noninstitutionalized population totals.⁴Includes data for race and Hispanic-origin groups not shown separately.

SOURCE: National Center for Health Statistics, National Health and Nutrition Examination Survey, 2015–2018.

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