International Journal of Biochemistry, Bioinformatics and Biotechnology Studies, 10(1) 1-10, 2026
Print ISSN: 2397-7728(Print)
Online ISSN: 2397-7736(Online)
Website: https://www.eajournals.org/
Publication of the European Centre for Research Training and Development -UK

Evaluation of LDL-cholesterol estimation formulas (Friedewald, Martin–Hopkins and Sampson) compared to direct dosing in a Senegalese adult population

Thiam Souleymane[1,2], Ba R[1,2], Agossou HHM[1], Dia FKST[1], Soumah IY[1], Diedhiou F[1], Samba A[1,3], Coly NF[1,4], Diouf NN[5], Doupa D[6], Ndiaye A[1], Cisse F[1,2], Diatta A[5], Diallo F[1].

[1] FMPO Medical Biochemistry Laboratory, UCAD, Senegal
[2] Laboratory of Biochemistry, Dalal Jamm Hospital
[3] Laboratory of Medical Biology, Abass Ndao Hospital
[4] Department of Biochemistry, Iba Der Thiam University of Thiès
[5] Department of Biochemistry, Assane Seck University in Ziguinchor
[6] Department of Biochemistry, Gaston Berger University in Saint-Louis

doi:s https://doi.org/10.37745/ijbbbs.15/vol10n1110 Published January 20, 2026

Citation: Souleymane T, Ba R., Agossou HHM, Dia FKST, Soumah IY, Diedhiou F, Samba A., Coly NF, Diouf NN, Doupa D, Ndiaye A, Cisse F., Diatta A., Diallo F. (2026) Evaluation of LDL-cholesterol estimation formulas (Friedewald, Martin–Hopkins and Sampson) compared to direct dosing in a Senegalese adult population, *International Journal of Biochemistry, Bioinformatics and Biotechnology Studies*, 10(1) 1-10

Abstract: *LDL-C calculation formulas are proposed to overcome the difficulty of standardizing the dosage but also its cost. However, a performance evaluation is required for each to determine the best formula used for the best estimate of LDL-C. This study was conducted to compare the 3 calculation formulas in comparison to the direct LDL-C test. It is a retrospective and analytical study conducted at the biochemistry laboratory of CHN Dalal Jamm. The study population includes patients with a lipid profile prescription, who met the required pre-analytical conditions. The LDL-c concentration was determined in parallel for each patient with the Friedewald, Martin-Hopkins, and Sampson-NIH formula, as well as the direct test method. The study included 119 patients with a mean age of 54±14 years, with a predominance of female (male ratio of 0.63). Statistically significant correlations and negative biases were observed between the LDL-c calculation methods (Friedewald (r=0.902; bias = -0.255), Martin-Hopkins (r=0.895; bias = -0.239), Sampson-NIH (r=0.901; bias = -2.255)) and the direct test method. LDL values were underestimated by the various calculation formulas, in particular for triglyceride levels < 1.5 g/l and LDL values ≥ 1.89 g/L. Sampson's formula showed better overall agreement at 63.87% and a lower downward reclassification rate at 32.77% compared to direct doses. Sampson's formula seems more accurate in estimating LDL-C in our population compared to Friedewald and Martin's formula.*

Keywords: LDL-cholesterol estimation formulas, Friedewald, Martin–Hopkins, Sampson, direct dosing, Senegalese adult population

INTRODUCTION

LDL cholesterol (LDL-C) is considered one of the main risk factors for cardiovascular disease, mainly due to its causal link to atherosclerotic cardiovascular disease (VADD). It is estimated that high LDL-C is responsible for up to 4.3 million deaths per year, or 7.7% of deaths worldwide [1,]. A reduction in LDL-C of 80 mg/dL, or 2 mmol/L, can decrease the risk of VAD by 40 to 50%, and recent clinical guidelines have adopted combination therapeutic approaches to reduce LDLC levels [4,5]. Given the causal link between LDL-C and VACM, it is important for laboratories to have accurate methods to determine LDL-C levels. This requires direct measures which unfortunately lack standardization [6]. Despite the existence of several methods for direct analysis of LDL-C concentration, many clinical laboratories use LDL-C estimation for its simplicity and the absence of associated costs; Friedewald's formula is the most commonly used calculation [7]. Friedewald's equation is generally accurate for the average patient, but underestimates LDL-C at lower levels (especially LDL-C<150 mg/dL, leading to missed prevention opportunities for more aggressive lipid control [8]. The use of indirect calculation formulas is an alternative proposed by several authors [8-11].

However, most calculation formulas do not consider the inter-individual variability of the TG/VLDL-C ratio, which is very important when estimating LDL-C[12]. The Martin-Hopkins formula, developed on results based on the analysis of more than 1,350,000 patients from the very large lipid study database, proposes a specific adjustable factor based on triglyceride and non-HDL-C levels [8,13,14]. Similarly, in 2020, Sampson et al proposed a new formula developed in patients that has triglyceride levels of up to 800 mg/dl [15]. The authors also report an equivalence to other calculation formulas for normolipidemic patients [15]. Good laboratory practices require a study of the transferability of data from other populations before they are implemented in the laboratory. This study aims to evaluate the best LDL-C calculation formula (Friedewald, Matin-Hopkins and Sampson-NIH) in a Senegalese adult population by comparing it with the direct LDL-C assay method.

MATERIALS AND METHODS

We conducted a retrospective study at the Laboratory of Biochemistry at Dalal Jamm National Hospital Center during the year 2024. The study population consisted of patients recruited at the laboratory for the determination of lipid profile (total cholesterol, LDL-C, HDL-C and Triglycerides). Young patients, pregnant women, and patients on lipid-lowering therapy were not included. Blood samples were taken by venipuncture from subjects fasting for at least 12 hours in dry 5 ml Vacutainer vacuum tubes (Becton Dickinson®). After centrifugation at 3500 rpm for five minutes in a non-refrigerated centrifuge. Total cholesterol and triglycerides were

measured by enzymatic methods and HDL-C, and LDL-C were measured by direct method adapted on the ARCHITECT ci4100 automaton (Abbott Diagnostics, Chicago, Illinois, USA). The concentration of LDL-c was also determined for each patient using the Friedewald formula in mg/dl (LDL C=CH. T-HDL C-TG/5), Martin-Hopkins formula [LDLC= non-HDL C)–(TG/AF)], where AF is an adjustable factor, and Sampson-NIH Sampson equation [LDL C=TC/0.948 – HDL-C/0.971 - (TG/8.56 + TG×non-HDL-C/2140 - TG2/16100) - 9.44].

The adjustment factor for Martin/Hopkins was calculated based on TG and high-density lipoprotein-unbound cholesterol (non-HDLC) levels derived from a 180-cell stratification table [12]. For the correlation between direct LDL cholesterol (LDL D), Friedewald's LDL cholesterol (LDL F) and Martin Hopkins LDL cholesterol (LDL M), we used the Spearman rank correlation coefficient and linear regression (R^2). Scatter plots with Pearson correlation coefficient calculations were made to evaluate the correlation between the equations. Estimated LDL C values were classified according to clinically relevant thresholds of 70, 70-99, 100-189 and ≥ 189 mg/dL. The classification agreement between LDL C estimates was examined by cross-tabulations by LDL-C categories, in order to study the impact of the reclassification. The discordance was then assessed according to the proportion of subjects reclassified to a higher (up) or lower (down) level.

RESULTS

Our study included 119 patients with a mean age of 54±14.3 years with extremes of 21 and 89 years. There is a female predominance at 61.3% with a sex ratio (M/F) of 0.63.

Table I shows the overall results of the study with the mean values of the various lipid parameters that are within normal limits (TC=2.04±0.55 g/L), HDL-C=0.56±0.16 g/L, TG=1.05±0.95 g/L and LDL-D=1.53±0.6 g/L). There are pathological upper extremes, especially for triglycerides with a value of 7.03 g/L. The average values of the different calculation formulas are lower than the direct assay with 1.27±0.50g/L for Friedewald, 1.27±0.51 g/L for Martin-Hopkins and 1.29±0.51 Sampson-NIH.

Table 1: Descriptive statistical values of lipid parameters

Settings	Minimum	Maximum	Mean ± SD
LDL-F (g/L)	0.39	3.34	1.27±0,50
LDL-M (G/L)	0.37	3,33	1.27±0.51
LDL-S (g/L)	0.37	3 .35	1.29±0.51
LDL-D (g/L)	0.30	3.57	1.53±0.6
CT (G/L)	0.94	4.29	2.04±0.55
HDL-C (g/L)	0,10	0.99	0.56±0.16
TG (g/L)	0.27	7.03	1.05±0*.95

LDL-F: LDL calculated with Friedewlad; LDL-M: LDL calculated with Martin-Hopkins; LDL-S: LDL calculated with Sampson-NIH; LDL-D: LDL determined by direct assay; TC: Total cholesterol; HDL-C: HDL cholesterol; TG: triglycerides.

A good correlation was found between the direct LDL-C assay and the calculation formulas with a better coefficient for the Friedewald formula (Figure 1).

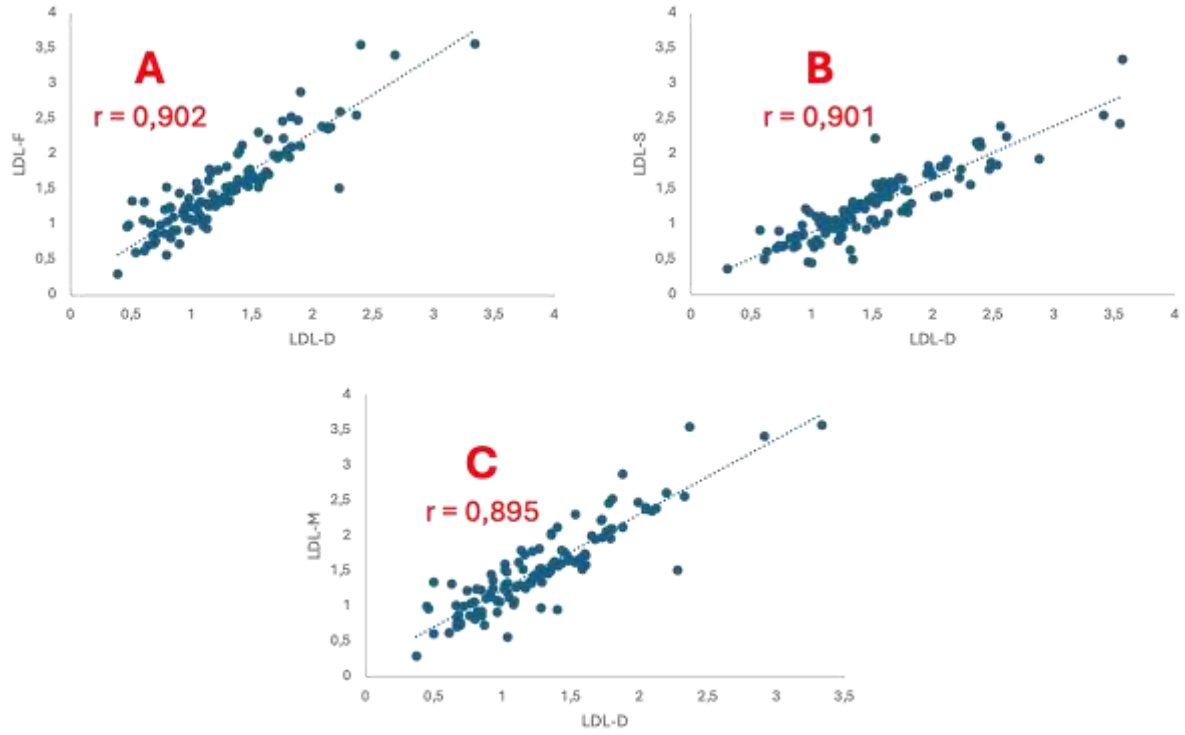

Figure 1: Correlation between direct LDL and calculation formulas with A: Friedewald, B=Sampson and C=Martins

For all formulas, we found a negative bias with respect to the direct LDL assay with values of -0.255 (-0.77 – 0.26), -0.255 (-0.79 – 0.27) and -0.239 (-0.76 – 0.29) respectively for Friedewald, Martin-Hopkins and Sampson-NIH (Figure 2).

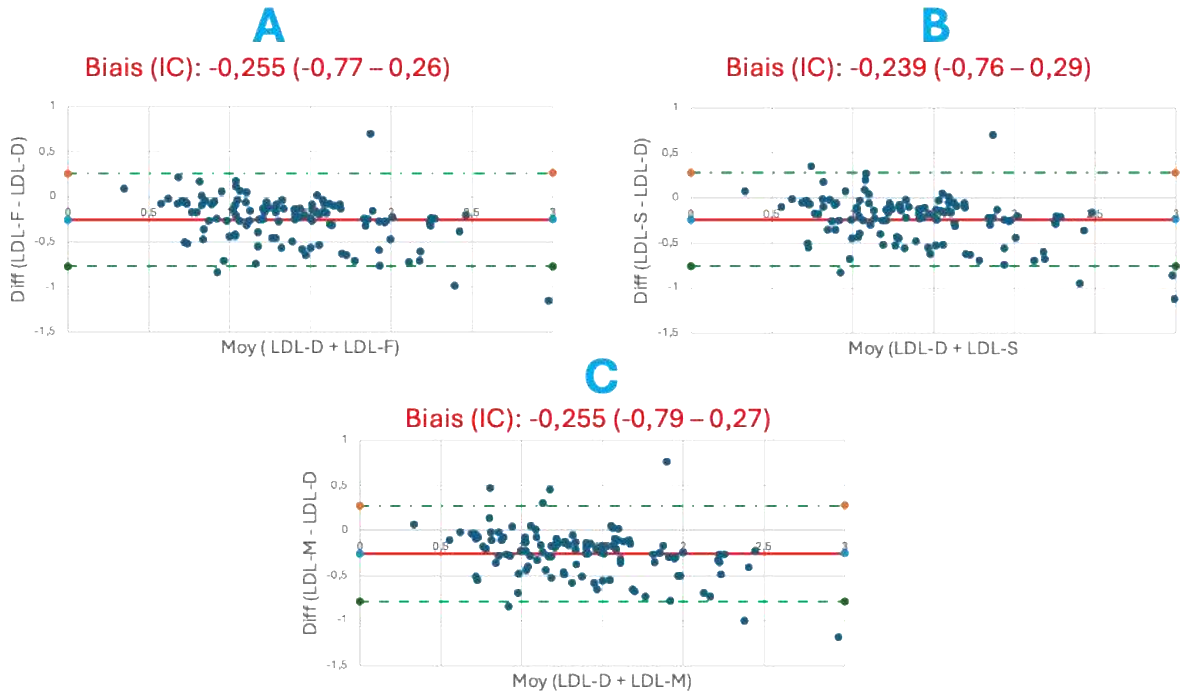

Figure 2: Bland-Altman diagram between direct LDL and Friedewald (A), Sampson (B) and Martins (B)

The calculation of LDL-C by the four methods (direct assay, Friedewald, Martin Hopkins and Sampson) was carried out considering the triglyceride level in order to assess the impact of the latter on the estimate. In patients with triglycerides < 1.5 g/L (n=105) and LDL value < 0.7 g/L, the distributions were different for direct dosing and calculation formulations. However, there is a downward reclassification from LDL-C above 0.7 g/L, especially for range 1 - 1.89 g/L, with 28.1% for Friedewald and Martin-Hopkins and 26.6% for Sampson (Table II).

For triglycerides between 1.5 and 2 g/L (n=3), perfect agreement between the four methods was observed in all ranges except for LDL values > to 1.89 g/L where all formulas underestimated the calculation.

Finally, for triglycerides ≥ 2 g/L (n = 11), the best agreement was obtained between the direct method and Martin-Hopkins with 60% (n=3/5) for values between 1 and 1.89 g/L and 67% (n=2/3) for values greater than 2 g/L (Table II)

Table II: Distribution of LDL values according to triglyceridemia.

			LDL (g/l)				Eff
			< 0.7	0.7 – 0.99	1 – 1.89	≥ 1.89	
TRIG (g/l)	< 1.5	LDL-D	3 (2.9)	15 (14.3)	64 (61)	23 (21.9)	105
		LDL-F	12 (11.4)	24 (22.9)	59 (56.2)	10 (9.5)	
		LDL-M	15 (14.3)	21 (20)	61 (58.1)	8 (7.6)	
		LDL-S	12 (11.4)	23 (21.9)	60 (57.1)	10 (9.5)	
	1.5 - 2	LDL-D	0	0	2 (66.7)	1 (33.3)	3
		LDL-F	0	0	3 (100)	0	
		LDL-M	0	0	3 (100)	0	
		LDL-S	0	0	3 (100)	0	
	≥ 2	LDL-D	1 (9.1)	2 (18.2)	5 (45.5)	3 (27.3	11
		LDL-F	1	2 (18.2)	6 (54.5)	2 (18.2)	
		LDL-M	0	1 (9.1)	7 (63.6)	3 (27.3	
		LDL-S	0	2 (18.2)	7 (63.6)	2 (18.2)	

The comparison between direct LDL and that estimated by the Friedewald formula shows agreement in 74 patients (74/119=62%). However, there was an upward reclassification of Friedewald of 3.36% (n=4/199) and a downward reclassification of 34.5% (n=41/119). For LDL values ≥ 1.89 g/l, 59.3% of the samples were reclassified in the range 1 – 1.89 g/l (Table III).

Table III: Direct and Friedewald LDL Comparison

		LDL-D				Total
		< 0.7	0.7 – 0.99	1 – 1.89	≥ 1.89	
LDL-F	< 0.7	3 (75)	5 (29.4)	5 (7)	0	13
	0,7 – 0,99	1 (25)	10 (58.8)	15 (21.1)	0	26
	1 – 1.89	0	2 (11.8)	50 (70.4)	16 (59.3)	68
	≥ 1.89	0	0	1 (1.4)	11 (40.7)	12
Total		4	17	71	27	119

Table IV shows a 59.6% agreement (n=71/119) between the direct LDL-C assay and the Martin-Hopskin formula. An upward reclassification of 3.36% (n=4/119) and a downward reclassification of 36.97% (n=44/119) were found between the Matin-Hopskin formula. The best agreement was for LDL values < 0.7 g/L (75%). For LDL values ≥ 1.89 g/l, 63% of the samples were reclassified in the range 1 – 1.89 g/l

Table IV: Comparison of LDL by direct assay and Martin Hopkins

		LDL-D				Total
		< 0.7	0.7 – 0.99	1 – 1.89	≥ 1.89	
LDL-M	< 0.7	3 (75)	8 (47.1)	4 (5.6)	0	15
	0.7 – 0.99	0	7 (41.2)	15 (21.1)	0	22
	1 – 1.89	1 (25)	2 (11.8)	51 (71.8)	17 (63)	71
	≥ 1.89	0	0	1 (1.4)	10 (37)	11
Total		4	17	71	27	119

The comparison between the direct assay and the Sampson-NIH formula shows a concordance of 63.87% (n=76/119) with an overestimation of LDL-C of 3.36% (n=4/119) and an overestimation of 32.77% (n=39/119). Agreement is important for low concentrations (<0.70 g/L, 75%) with an upward reclassification of 25%. 29.4% of the samples were downgraded to the range 0.7 – 0.99. For LDL values ≥ 1.89 g/l, 59.3% of the samples were reclassified in the range 1 – 1.89 g/l.

Table IV: Comparison of LDL by direct assay and Sampson-NIH

		LDL-D				Total
		< 0.7	0.7 – 0.99	1 – 1.89	≥ 1.89	
LDL-S	< 0.7	3 (75)	5 (29.4)	4 (5.6)	0	12
	0.7 – 0.99	1 (25)	10 (58.8)	14 (19.7)	0	25
	1 – 1.89	0	2 (11.8)	52 (73.2)	16 (59.3)	70
	≥ 1.89	0	0	1 (1.4)	11 (40.7)	12
Total		4	17	71	27	119

DISCUSSION

Measuring LDL-C is of great interest in medical practice, especially during therapeutic decisions, prevention and monitoring of cardiovascular risk factors. The guidelines of several learned societies are based on LDL-C thresholds for the prevention of cardiovascular risk [16,17]. However, several studies have reported that Friedewald's formula tends to underestimate LDL-C, especially in patients with hypertriglyceridemia (TG ≥ 150 mg/dL) or diabetes [18]. To compensate for these imitations, other formulas have been proposed such as Martin-Hopkins and Sampson-NIH. Thus, the objective of our study was to evaluate the best formula for calculating LDL-C in our population compared to the direct assay method.

Our population consisted of patients with a mean age of 54 ± 14.3 years (21 – 89 years), with a predominance of women of 61.3%. The mean LDL-C concentrations determined by the Friedewald and Martins–Hopkins equations (1.27 ± 0.50 g/L) were slightly lower than those obtained by the Sampson formula (1.29 ± 0.51 g/L) and direct measurement (1.53 ± 0.60 g/L). All estimation equations showed a negative bias (Friedewald and Martin with a bias = -0.255 and Sampson a bias = -0.239), reflecting an underestimation of LDL-C compared to the direct measurement. In addition, strong correlation was found especially with the formula of Friedewald (r=0.902) and Sampson (r=0.901). The weakest correlation with the direct method was found with the Martin-Hopkins formula (r=0.895). Silva et al reported lower correlations for LDL-C values < 70 mg/dl (Friedewald (R2=0.680), Martin (R2=0652) and Sampson (R2=0.778)) [18]. Alpdemir et al also reported in their study population better correlation with Sampson's formula (r=0.905). [19]

It also appears from our study that the Sampson formula had the best overall agreement (63.9%), followed by Friedewald (62%) and Martins–Hopkins (59.6%). These results contrast with those of d'Alpdemir et al who report a higher agreement for Martin Hopkins (81.4%), compared to Sampson (62.9%) and Friedewald (49.9%) [19]. According to Zafrir et al, the Martin and Sampson equations showed a high proportion of upward reclassification, 10.8% and 7.5%, respectively, and a low proportion of downward reclassification, 0.7% and 0.2%, respectively, for LDL values <0.7 g/L compared to the Friedewald equation.[11]

In our study, contrary to the data in the literature, the Sampson formula was found to be more accurate than the Martins–Hopkins formula, suggesting contextual variability in the performance of LDL-C estimation equations. However, several studies, including those of Seth S. Martin [20] and Cátia Ferrinho [10], have shown that the Martin–Hopkins formula offers better accuracy for low LDL-C concentrations (<70 mg/dL), especially in patients with high triglycerides. Ferrinho et al observed an 87.5% concordance for Martins–Hopkins versus 75% for Friedewald when direct LDL-C was <55 mg/dL, highlighting its value in avoiding LDL-C underestimation and the risk of undertreatment in patients at high cardiovascular risk [10].

CONCLUSION

The calculation formulas were overall satisfactory with regard to the direct dosing.
However, our results indicate better performance for the Sampson formula followed by the Friedewald formula.

REFERENCES

[1] F. J. Neumann *et al.*, "2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes: The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)," *Eur Heart J*, vol. 41, no. 3, pp. 407–477, Jan. 2020, doi: 10.1093/EURHEARTJ/EHZ425.

[2] D. K. Arnett *et al.*, "2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines," *J Am Coll Cardiol*, vol. 74, no. 10, pp. 1376–1414, Sep. 2019, doi: 10.1016/J.JACC.2019.03.009;PAGEGROUP:STRING:PUBLICATION.

[3] C. Mattiuzzi, F. Sanchis-Gomar, and G. Lippi, "Worldwide burden of LDL cholesterol: Implications in cardiovascular disease," *Nutrition, Metabolism and Cardiovascular Diseases*, vol. 30, no. 2, pp. 241–244, Feb. 2020, doi: 10.1016/J.NUMECD.2019.09.008.

[4] A. Cieza, K. Causey, K. Kamenov, S. W. Hanson, S. Chatterji, and T. Vos, "Global estimates of the need for rehabilitation based on the Global Burden of Disease study 2019: a systematic analysis for the Global Burden of Disease Study 2019," *The Lancet*, vol. 396, no. 10267, pp. 2006–2017, Dec. 2020, doi: 10.1016/S0140-6736(20)32340-0.

[5] C. Baigent *et al.*, "Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials.," *Lancet*, vol. 376, no. 9753, pp. 1670–1681, Nov. 2010, doi: 10.1016/S0140-6736(10)61350-5.

[6] M. R. Langlois *et al.*, "Quantifying atherogenic lipoproteins for lipid-lowering strategies: Consensus-based recommendations from EAS and EFLM," *Clin Chem Lab Med*, vol. 58, no. 4, pp. 496–517, Apr. 2020, doi: 10.1515/CCLM-2019-1253/XML.

[7] F. Mach *et al.*, "2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)," *Eur Heart J*, vol. 41, no. 1, pp. 111–188, Jan. 2020, doi: 10.1093/EURHEARTJ/EHZ455.

[8] S. S. Martin *et al.*, "Comparison of Low-Density Lipoprotein Cholesterol Assessment by Martin/Hopkins Estimation, Friedewald Estimation, and Preparative Ultracentrifugation: Insights From the FOURIER Trial," *JAMA Cardiol*, vol. 3, no. 8, pp. 749–753, Aug. 2018, doi: 10.1001/JAMACARDIO.2018.1533.

[9] E. T. Bairaktari, K. I. Seferiadis, and M. S. Elisaf, "Evaluation of methods for the measurement of low-density lipoprotein cholesterol," *J Cardiovasc Pharmacol Ther*, vol. 10, no. 1, pp. 45–54, Mar. 2005, doi: 10.1177/10742484050100106;WEBSITE:WEBSITE:SAGE;WGROUP:STRING:PUBLICATION.

[10] C. Ferrinho, A. C. Alves, M. Bourbon, and S. Duarte, "Applicability of Martin-Hopkins formula and comparison with Friedewald formula for estimated low-density lipoprotein cholesterol in e_COR study population," *Revista Portuguesa de Cardiologia (English Edition)*, vol. 40, no. 10, pp. 715–724, Oct. 2021, doi: 10.1016/J.REPCE.2021.07.001.

[11] B. Zafrir, W. Saliba, and M. Y. Flugelman, "Comparison of Novel Equations for Estimating Low-Density Lipoprotein Cholesterol in Patients Undergoing Coronary

Angiography," *J Atheroscler Thromb*, vol. 27, no. 12, pp. 1359–1373, Dec. 2020, doi: 10.5551/JAT.57133.

[12] S. S. Martin *et al.*, "Comparison of a Novel Method vs the Friedewald Equation for Estimating Low-Density Lipoprotein Cholesterol Levels From the Standard Lipid Profile," *JAMA*, vol. 310, no. 19, pp. 2061–2068, Nov. 2013, doi: 10.1001/JAMA.2013.280532.

[13] M. Kang, J. Kim, S. Y. Lee, K. Kim, J. Yoon, and H. Ki, "Martin's Equation as the Most Suitable Method for Estimation of Low-Density Lipoprotein Cholesterol Levels in Korean Adults," *Korean J Fam Med*, vol. 38, no. 5, pp. 263–269, Sep. 2017, doi: 10.4082/KJFM.2017.38.5.263.

[14] J. W. Meeusen, A. J. Lueke, A. S. Jaffe, and A. K. Saenger, "Validation of a Proposed Novel Equation for Estimating LDL Cholesterol," *Clin Chem*, vol. 60, no. 12, pp. 1519–1523, Dec. 2014, doi: 10.1373/CLINCHEM.2014.227710.

[15] M. Sampson *et al.*, "A New Equation for Calculation of Low-Density Lipoprotein Cholesterol in Patients with Normolipidemia and/or Hypertriglyceridemia," *JAMA Cardiol*, vol. 5, no. 5, pp. 540–548, May 2020, doi: 10.1001/JAMACARDIO.2020.0013.

[16] F. Mach *et al.*, "2019 ESC/EAS guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk," *Atherosclerosis*, vol. 290, no. 1, pp. 140–205, Nov. 2019, doi: 10.1016/J.ATHEROSCLEROSIS.2019.08.014.

[17] S. M. Grundy *et al.*, "2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines," *J Am Coll Cardiol*, vol. 73, no. 24, pp. e285–e350, Jun. 2019, doi: 10.1016/J.JACC.2018.11.003.

[18] V. B. Silva, C. Chaves, J. C. Oliveira, and I. Palma, "Comparison of the accuracy of the Friedewald, Martin, and Sampson formulas to estimate very low levels of low-density lipoprotein cholesterol," *Endokrynol Pol*, vol. 74, no. 2, pp. 203–210, 2023, doi: 10.5603/EP.A2023.0025.

[19] M. Alpdemir, M. F. Alpdemir, and M. Şeneş, "Comparison of Friedewald, Martin/Hopkins, and Sampson formulae with direct LDL measurement in hyperlipidaemic and normolipidaemic adults in a Turkish population," *J Med Biochem*, vol. 43, no. 5, p. 671, 2024, doi: 10.5937/JOMB0-46549.

[20] S. S. Martin *et al.*, "Comparison of a novel method vs the Friedewald equation for estimating low-density lipoprotein cholesterol levels from the standard lipid profile," *JAMA*, vol. 310, no. 19, pp. 2061–2068, Nov. 2013, doi: 10.1001/JAMA.2013.280532.