Trends in Low-Density Lipoproteins Cholesterol (LDL-C) in US Aged 12 to 80 Years: Data from the 2007-2018 National Health and Nutrition Examination Survey (NHANES)

Inga Wang[1,*], Stephen Hou[2], Mohammad H Rahman[3], Xiaoyan Li[4], David Ritchie[5] and Antoinette L Spector[1]

[1]*Department of Rehabilitation Sciences & Technology, University of Wisconsin-Milwaukee, Milwaukee, WI, USA*

[2]*Department of Biomedical Sciences, University of Wisconsin-Milwaukee, Milwaukee, WI, USA*

[3]*Department of Biomedical Engineering / Mechanical Engineering, University of Wisconsin-Milwaukee, Milwaukee, WI, USA*

[4]*Department of Neurology, Medical College of Wisconsin, Milwaukee, WI, USA*

[5]*Department of Surgery, Kendall Regional Medical Center, Miami, FL, USA*

Abstract: *Background:* Elevated levels of low-density lipoprotein cholesterol (LDL-C) are associated with an increased risk of coronary heart disease.

Objectives: We described LDL-C distributions across the age span and compared the trends in three distinct cross-sectional surveys during 2007-2010, 2011-2014, and 2015-2018.

Methods: This is an observational study. Blood lipid measurements, taken from 40,977 noninstitutionalized participants, aged 12 to 80, were obtained from the National Health and Nutrition Examination Survey (NHANES) study.

Results: The LDL-C values changed by age and differed by sex. Mean LDL-C levels increased with age through middle age and then decreased with age. In males, mean LDL-C declined from 104.5 (95% CI, 103.6-105.3) in 2007-2010, to 100.5 (95% CI, 99.7-101.4) in 2011-2014, and 100.8 (95% CI, 99.9-101.7) in 2015-2018 ($p<0.001$ for linear trend). In females, mean LDL-C declined from 110.3 (95% CI, 109.5-111.1) in 2007-2010, to 108.3 (95% CI, 107.6-109.1) in 2011-2014, and 106.8 (95% CI, 105.9-107.7) in 2015-2018 ($p<0.001$ for linear trend).

Conclusions: Between 2007 and 2018, favorable trends in LDL-C levels were observed among noninstitutionalized residents in the US.

Keywords: Serum lipids, Aging, lipoprotein ratio, Cholesterol, Cardiovascular diseases.

1. INTRODUCTION

Cardiovascular diseases are the leading cause of global mortality and a major contributor to disability [1-3]. As such, several organizations such as the American College of Cardiology/American Heart Association (ACC/AHA) [4] and the European Association for Cardiovascular Prevention & Rehabilitation (EACPR) [5] have addressed the cardiovascular risk factors and provided guidelines on the primary prevention of cardiovascular disease. It is suggested that the most important way to reduce cardiovascular disease risks is to promote a healthy lifestyle throughout life (*e.g.*, healthy diet, physical activity, quitting smoking, controlling body weight) and avoid risk factors (*e.g.*, hypertension, hypercholesterolemia) [4-6].

Among the risk-enhancing factors, the low-density lipoprotein cholesterol (LDL-C) value is commonly used as an index. LDL-C has viewed as the main source of cholesterol buildup and blockage in the arteries, and is one of the predictors to estimate the 10-year risk of atherosclerotic cardiovascular disease (ASCVD), such as a heart attack or stroke [7, 8]. The level of other blood lipoproteins also has prognostic value [9]. While age and sex also affect cholesterol levels [10-13], generally LDL-C less than 100 mg/L is considered the healthy level (*i.e.*, optimal), while LDL-C ≥160 mg/dL is considered high and ≥190 mg/dL is very high. For individuals with multiple cardiovascular disease risk factors or are at intermediate risk, it is recommended that individuals have risk discussions with health professionals and initiate statin therapy to reduce LDL-C [4]. Previous studies have supported the association between LDL-C reduction and relative and absolute effects of statin treatment [14, 15], and that reducing LDL-C causes a corresponding risk reduction in

*Address correspondence to this author at the Department of Rehabilitation Sciences & Technology, University of Wisconsin-Milwaukee, Enderis Hall 955, 2400 E Hartford Ave, Milwaukee, WI 53211; Tel: (414) 251-7936;
Fax: (414) 229-5100; E-mail: wang52@uwm.edu

E-ISSN: 2309-6179/22

cardiovascular mortality and non-fatal myocardial infarction [5, 16].

The purpose of this study was to describe the distributions of LDL-C levels across the age of 12 to 80 years old and examine the trends in serum lipoprotein in noninstitutionalized US residents between 2007 and 2018. Data on the LDL-C can provide insight into current and future cardiovascular health.

2. MATERIALS AND METHODS

Study Design

This was an observational cross-sectional study. Data from the National Health and Nutrition Examination Survey (NHANES)[28] were extracted from the database. NHANES collected biological specimens (*e.g.*, blood, urine) in the mobile examination center for laboratory analysis to provide detailed information about participants' health and nutritional status. Serum LDL-C values were derived from study participants who aged 12 and above, were examined in the morning session only, and fasted at least 8.5 hours or more. LDL-C was calculated from measured values of total cholesterol (TC), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) according to the Friedewald calculation: LDL-C (in mg/dL) = [TC] – [HDL-C] – [TG/5]. All lipid analyses (blood tests) were analyzed according to a standardized protocol and can be found on the NHANES website (https://wwwn.cdc.gov/nchs/nhanes).

NHANES 2007-2018 Data

NHANES data has since been released in two-year cycles. Data from six NHANES data cycles were included in the analysis, including 2007-2008, 2009-2010, 2011-2012, 2013-2014, 2015-2016, and 2017-2018. Of the initial 109,220 data records, 67,498 participants were removed because they did not have LDL-C testing results. Because the Friedewald equation is not valid for TG results greater than 400 mg/dL [17, 18], additional 745 participants were removed. Hence, the final data included 40,977 participants for subsequent data analysis.

Because this study involved secondary analysis of de-identified data, the Institutional Review Board of the University of Wisconsin - Milwaukee determined that this study did not fall within the regulatory definition of research involving human subjects and did not require further IRB review.

Statistical Analyses

Age was categorized as 12-15, 16-19 (adolescent), 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-80 (adult) years. Based on the analytical guidelines, [29] each 2-year cycle, and any combination of 2-year cycles is a nationally representative sample. We categorized survey years as 2007-2010, 2011-2014, and 2015-2018.

A factorial 2 (sex: male vs female) x 3 (survey periods: 2007-2010, 2011-2014, and 2015-2018) x 14 (age group) general linear model (GLM) analysis was used to compare LDL-C measures and test the hypothesis that these independent variables should be used to stratify LDL-C measurements. The significant level for the overall comparisons was set at alpha = 0.05. For independent variables found to have a significant main or interactive effect on lipid measurements, Scheffe pairwise post-hoc comparisons were conducted. Hypotheses of no survey trends in LDL-C values over the three survey periods were tested. Descriptive statistics (including the mean and confidence interval) of the LDL-C were tabulated for relevant strata. All analyses were performed using the SPSS Statistics for Windows, Version 27.0. (Armonk, NY: IBM Corp).

3. RESULTS

Analytic Sample

The final data for analysis included 40,977 participants. Among them, 53.0% of the sample were females. The majority of the sample was non-Hispanic white (45.9%), followed by non-Hispanic black (21.1%), Mexican American (13.0%), other race including multi-racial (10.1%) and other Hispanic (9.9%). Data were balanced across each of the six, 2-year data collection cycles performed: 2007-2010: 36.1%, 2011-2014: 34.1% and 2015-2018: 29.8%.

Overall GLM

The main effects (sex, age group, survey periods) and the interaction terms were all significant ($p<0.001$). Subsequently, to assist in clinical interpretation of the LDL-C levels, we summarized LDL-C measures by sex and age group, and the linear trend of the survey years was tested for each age group.

LDL-C

The LDL-C values changed by age and differed by sex. Hence, Table **1** summarizes means and 95%

Table 1: Means and 95% Confidence Intervals of the LDL-C, Aged 12 to 80 Years, 2007-2018

LDL-C		NHANES 2007-2018			NHANES 2007-2010			NHANES 2011-2014			NHANES 2015-2018c			p-value for linear trend			overall p-value*
			95% CI			95% CI			95% CI			95% CI		2007-2010 to	2007-2010 to	2011-2014 to	2007 to 2018
Male	N	Mean	L	U	Mean	L	U	Mean	L	U	Mean	L	U	2011-2014	2015-2018	2015-2018	
12-15 yr	1092	84.6	82.6	86.6	84.7	81.1	88.2	85.9	82.5	89.4	83.3	79.9	86.7				0.367
16-19 yr	1025	88.2	86.2	90.3	89.2	85.7	92.8	87.4	83.7	91.2	88.0	84.6	91.4				0.664
20-24 yr	720	98.9	96.4	101.3	102.8	98.4	107.3	95.4	91.2	99.6	98.7	94.6	102.9	0.023			0.023
25-29 yr	704	111.6	109.1	114.1	120.1	115.7	124.5	108.1	103.7	112.5	107.0	102.8	111.2	0.003	<0.001		<0.001
30-34 yr	783	116.4	114.0	118.7	118.9	114.6	123.3	115.0	111.1	118.9	115.5	111.4	119.5				0.326
35-39 yr	793	120.9	118.5	123.2	121.0	116.9	125.2	121.8	117.8	125.8	119.8	115.8	123.9				0.820
40-44 yr	961	119.8	117.6	121.9	121.5	117.8	125.1	117.4	113.8	121.0	120.5	116.7	124.4				0.271
45-49 yr	1107	118.9	116.9	120.9	121.6	118.4	124.8	118.0	114.7	121.4	116.1	112.3	119.9				0.100
50-54 yr	1325	114.4	112.6	116.2	118.9	116.0	121.8	111.0	107.8	114.1	112.2	108.8	115.7	0.003	0.024		0.001
55-59 yr	1509	109.1	107.4	110.8	115.0	111.9	118.2	107.0	104.2	109.9	105.9	103.0	108.8	0.002	<0.001		<0.001
60-64 yr	2161	102.5	101.1	103.9	102.9	100.5	105.4	102.3	99.9	104.7	102.3	99.8	104.9				0.942
65-69 yr	1851	96.0	94.5	97.6	96.2	93.7	98.7	97.6	94.9	100.2	94.2	91.4	97.0				0.243
70-74 yr	1828	93.8	92.3	95.4	97.4	94.9	99.9	93.5	90.8	96.2	89.0	86.1	92.0		<0.001		<0.001
75-80 yr	3385	91.6	90.4	92.7	95.8	94.0	97.6	87.4	85.6	89.2	90.8	88.4	93.3	<0.001	0.002		<0.001
Female	N	Mean	L	U	Mean	L	U	Mean	L	U	Mean	L	U				
12-15 yr	944	86.2	84.0	88.3	88.7	84.6	92.8	87.0	83.4	90.6	83.4	79.9	87.0		0.032		0.023
16-19 yr	1033	91.6	89.5	93.7	92.0	88.1	95.8	92.8	89.3	96.4	90.2	86.9	93.6				0.399
20-24 yr	811	97.1	94.7	99.4	97.1	92.9	101.3	100.4	96.4	104.4	93.9	90.0	97.8			0.031	0.031
25-29 yr	850	101.8	99.6	104.1	105.3	101.2	109.4	102.1	98.1	106.1	98.8	95.1	102.5				0.056
30-34 yr	996	104.7	102.6	106.8	111.4	107.8	115.1	103.3	99.7	106.9	99.3	95.6	102.9	0.002	<0.001		<0.001
35-39 yr	1126	113.6	111.7	115.6	119.6	116.2	123.0	114.0	110.5	117.4	107.4	104.0	110.8		<0.001	0.025	<0.001
40-44 yr	1273	112.1	110.3	114.0	114.7	111.5	118.0	111.5	108.5	114.4	110.0	106.5	113.5				0.124
45-49 yr	1453	118.1	116.3	119.8	116.9	114.1	119.7	118.7	115.6	121.8	118.9	115.7	122.1				0.583
50-54 yr	1638	120.7	119.1	122.4	120.2	117.4	122.9	116.7	114.0	119.5	126.2	123.2	129.3		0.035	<0.001	<0.001
55-59 yr	1763	119.0	117.5	120.6	120.5	117.7	123.3	116.7	114.1	119.3	120.2	117.4	123.1				0.149
60-64 yr	2444	113.0	111.7	114.4	111.4	109.2	113.5	113.2	111.0	115.4	115.4	112.7	118.0		0.050		0.049
65-69 yr	1894	109.0	107.5	110.5	113.6	111.0	116.3	109.0	106.5	111.5	103.9	101.1	106.7		<0.001	0.050	<0.001
70-74 yr	2001	107.4	105.9	108.8	107.8	105.6	110.0	103.1	100.6	105.5	113.8	110.5	117.1		0.035	<0.001	<0.001
75-80 yr	3507	104.9	103.8	106.0	106.1	104.3	107.8	107.0	105.1	108.9	100.1	97.8	102.3		<0.001	<0.001	<0.001

Abbreviations: LDL-c = low-density lipoprotein cholesterol; CI = confidence interval; U = 95% CI upper limit; L = 95% CI lower limit.

For independent variables found to have a significant main effect on LDL-C values across 3 survey periods (*i.e.*, overall p-value), Scheffe pairwise post-hoc comparisons were conducted. Here, we listed p-values for linear trend if the p-value in the pairwise comparison was less than 0.05.

confidence intervals of the LDL-C by year (2007-2010, 2011-2014, and 2015-2018) and by sex (male and female). Figure **1** shows the trend trajectories of the observed LDL-C levels across the age of 12 to 80 years old, stratified by sex.

Overall, mean LDL-C levels increased with age during young adulthood and middle age and decreased with age later in life. Men showed higher mean LDL-C values than women for ages 20 to 49, with the greatest difference in their 30s: 116.4 mg/dL in men versus 104.7 mg/dL in women. In contrast, women

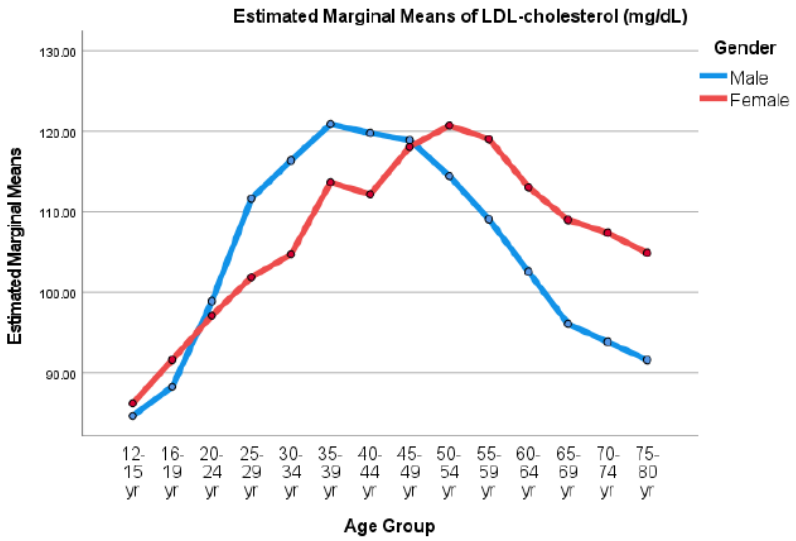


Figure 1: The trend trajectories of the observed LDL-C levels across the age of 12 to 80 years old, 2007-2018, stratified by sex.

consistently had higher values after midlife (age 50). For example, ages 65 to 69: 109.0 mg/dL in women versus 96.0 mg/dL in men.

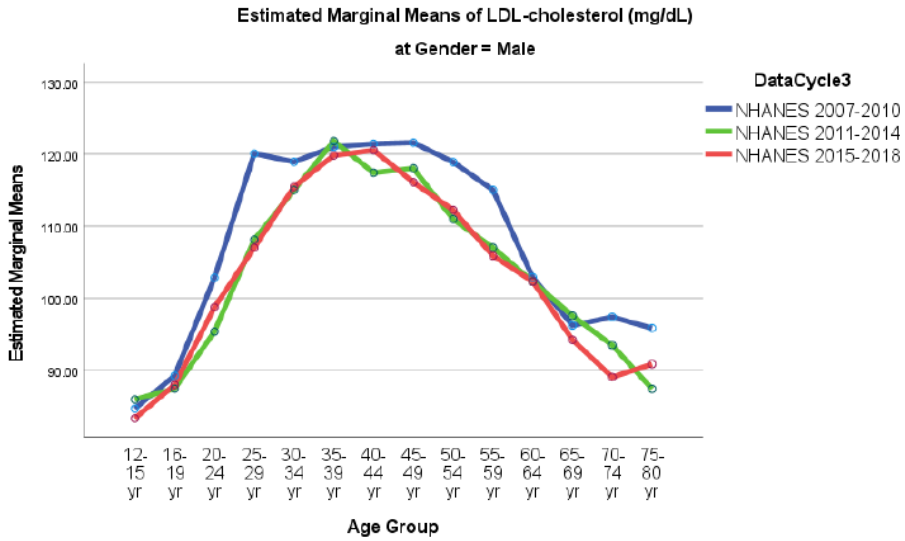
Figure **2** presents the trend trajectories of the observed LDL-C levels, stratified by sex and survey periods. In males, mean LDL-C declined from 104.5 (95% CI, 103.6-105.3) in 2007-2010, to 100.5 (95% CI, 99.7-101.4) in 2011-2014, and 100.8 (95% CI, 99.9-101.7) in 2015-2018 ($p<0.001$ for linear trend). In females, mean LDL-C declined from 110.3 (95% CI, 109.5-111.1) in 2007-2010, to 108.3 (95% CI, 107.6-109.1) in 2011-2014, and 106.8 (95% CI, 105.9-107.7) in 2015-2018 ($p<0.001$ for linear trend).

4. DISCUSSION

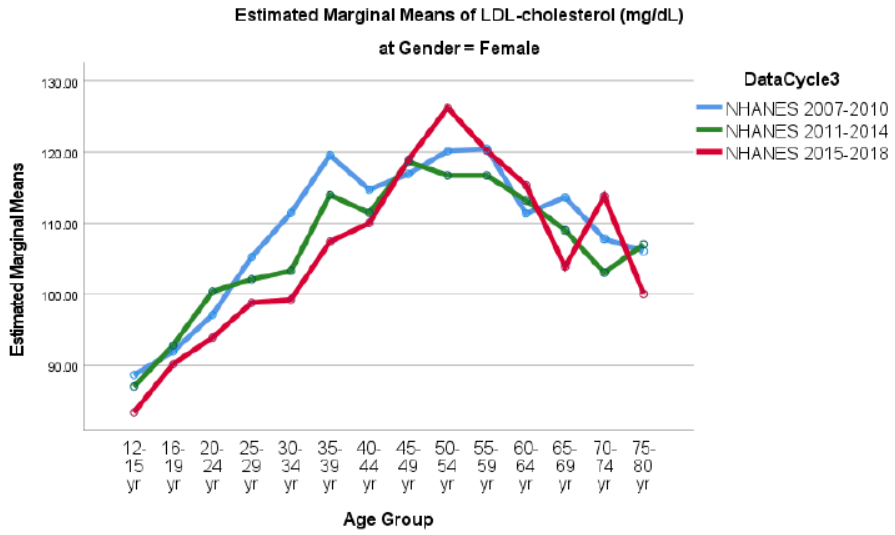
Cholesterol levels are important biomarkers associated with cardiovascular disease. In addition to predicting cardiovascular adverse events in patients with heart conditions [6], these parameters are cost-effective markers to monitor abnormalities in lipoprotein metabolism and various disorders. In this study, we examined the trends in LDL-C in more recent years between 2007 and 2018, and presented the trends in levels of lipids across the age span (12 to 80 years old).

Our results were consistent with some previous research that cholesterol levels increase with age during young adulthood and middle age and decline with age later in life [10, 12], and vary by sex [19]. Swiger *et al*. [19] described that men showed higher median LDL-C values than women for ages 20 to 59 and women consistently had higher values after midlife (age 60). On the other hand, our results indicated that men showed higher mean LDL-C values than women for ages 20 to 49, women consistently had higher values after midlife (age 50). Moreover, our reported mean LDL-values were consistently lower than their reported median values. The differences could be due to differences in the study sample, survey period (2009 to 2011 vs. 2007 to 2018), and data analytical procedures.

Like previous studies [10-12], our results further supported the favorable decreasing trends in LDL-C in the US population. In Carroll's study [12], the mean LDL-C levels in US adults decreased from 140 mg/dL (year 1976-1980) to 129 mg/dL (year 1988-1994) and 126 mg/dL (year 1999-2002) in males, and 136 mg/dL (year 1976-1980) to 124 mg/dL (year 1988-1994) and 120 mg/dL (year 1999-2002) in females. In contrast, the mean LDL-C levels in US youth (6 to 19 years old) remained relatively stable (91, 96, 89 mg/dL in boys, and 99, 95, 90 mg/dL in girls from 1988-1994, 1999-2002, and 2007-2010) [11]. As described by Perak *et al*., [13] it is important to understand the reasons for the favorable lipid trends observed to acknowledge public health successes (*e.g*., decrease in consumption of trans-fatty acids or other healthy lifestyle changes) and plan for future efforts (*e.g*., risk estimates and early intervention). It is of importance to monitor the short-term and long-term impact of the COVID-19 on lipid metabolisms. Several studies have shown that alteration in the lipid profile in patients with severe coronavirus disease 2019 and dyslipidemia is related to mortality in critical patients [20-24]. For instance, Fan *et al*. [25] described that, the LDL-C levels in COVID



(**A**) Male



(**B**) Female

Figure 2: The trend in three distinct cross-sectional surveys.

patients decreased significantly on admission, remained constantly low during the disease progression, and showed an irreversible and continuous decrease until death in non-surviving cases. While it is not directly related to LDL-C, Li *et al*. [22] reported that high C-reactive protein /HDL-C ratio is significantly associated with an increase in mortality and a poor prognosis. Hence, it may be of interest to monitor the longitudinal trend of the lipoprotein values after the COVID pandemic.

This study involves several limitations. First, this study included secondary data sources. The researchers were not in control of the data collection procedures. Missing values and data entry errors were not correctable. NHANES uses several quality assurance and quality control (QA/QC) protocols, which meet the 1988 Clinical Laboratory Improvement Act mandates, to monitor the quality of the analyses performed by the contract laboratories. Second, our analysis of trends was based on NHANES surveys. Data from other future surveys are needed to confirm the favorable trends. Third, the calculation of LDL-C using the Friedewald equation is valid when TG is less than or equal to 400 mg/dL. If TG > 400 mg/dL, it is suggested to measure the LDL-C directly, rather than calculating it. Hence, the results may be biased due to removing those participants from data analysis. Fourth, because of the lack of information on whether the participants had taken lipid-lowering medications, we

were unable to perform sub-group analysis and examine the effect on LDL-C levels. Last, several extraneous factors could influence cholesterol levels, such as lipid-lowering medications and race/ethnicity. We prioritized the maintenance of sample size within each stratum to achieve stable estimates of the LDL-C values. Future studies should endeavor to describe the lipid profile in US residents stratified by extraneous variables. Future studies are needed to fill the gaps in the fundamental knowledge of the factors that influence the changes in LDL-C levels across the age span.

5. CONCLUSION

Between 2007 and 2018, favorable trends in LDL-C levels were observed among noninstitutionalized residents in the US.

REFERENCES

[1] Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, *et al*. Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. J Am Coll Cardiol. 2020 Dec 22; 76(25): 2982-3021.

[2] Li Z, Lin L, Wu H, Yan L, Wang H, Yang H, *et al*. Global, Regional, and National Death, and Disability-Adjusted Life-Years (DALYs) for Cardiovascular Disease in 2017 and Trends and Risk Analysis From 1990 to 2017 Using the Global Burden of Disease Study and Implications for Prevention. Front Public Health. 2021; 9: 559751. https://doi.org/10.3389/fpubh.2021.559751

[3] Mensah GA, Brown DW. An overview of cardiovascular disease burden in the United States. Health Aff Proj Hope. 2007 Feb; 26(1): 38-48. https://doi.org/10.1377/hlthaff.26.1.38

[4] Arnett DK, Blumenthal RS, Albert MA, Michos ED, Buroker AB, Miedema MD, *et al*. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary. Circulation. 2019 Sep 10; 140(11): e563-95. https://doi.org/10.1161/CIR.0000000000000677

[5] Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, *et al*. 2016 European Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2016 Aug 1; 37(29): 2315-81. https://doi.org/10.1093/eurheartj/ehw106

[6] Broedl UC, Geiss HC, Parhofer KG. Comparison of Current Guidelines for Primary Prevention of Coronary Heart Disease. J Gen Intern Med. 2003 Mar; 18(3): 190-5. https://doi.org/10.1046/j.1525-1497.2003.20207.x

[7] Ferhatbegović L, Mršić D, Kušljugić S, Pojskić B. LDL-C: The Only Causal Risk Factor for ASCVD. Why Is It Still Overlooked and Underestimated? Curr Atheroscler Rep. 2022 May 28; https://doi.org/10.1007/s11883-022-01037-3

[8] Gluckman TJ, Kovacs RJ, Stone NJ, Damalas D, Mullen JB, Oetgen WJ. The ASCVD Risk Estimator App: From Concept to the Current State. J Am Coll Cardiol. 2016 Jan 26; 67(3): 350-2. https://doi.org/10.1016/j.jacc.2015.10.068

[9] Surguchov AP, Page GP, Smith L, Patsch W, Boerwinkle E. Polymorphic markers in apolipoprotein C-III gene flanking regions and hypertriglyceridemia. Arterioscler Thromb Vasc Biol. 1996 Aug; 16(8): 941-7. https://doi.org/10.1161/01.ATV.16.8.941

[10] Carroll MD, Kit BK, Lacher DA, Shero ST, Mussolino ME. Trends in lipids and lipoproteins in US adults, 1988-2010. JAMA. 2012 Oct 17; 308(15): 1545-54. https://doi.org/10.1001/jama.2012.13260

[11] Kit BK, Carroll MD, Lacher DA, Sorlie PD, DeJesus JM, Ogden C. Trends in serum lipids among US youths aged 6 to 19 years, 1988-2010. JAMA. 2012 Aug 8; 308(6): 591-600. https://doi.org/10.1001/jama.2012.9136

[12] Carroll MD, Lacher DA, Sorlie PD, Cleeman JI, Gordon DJ, Wolz M, *et al*. Trends in serum lipids and lipoproteins of adults, 1960-2002. JAMA. 2005 Oct 12; 294(14): 1773-81. https://doi.org/10.1001/jama.294.14.1773

[13] Perak AM, Ning H, Kit BK, de Ferranti SD, Van Horn LV, Wilkins JT, *et al*. Trends in Levels of Lipids and Apolipoprotein B in US Youths Aged 6 to 19 Years, 1999-2016. JAMA. 2019 May 21; 321(19): 1895-905. https://doi.org/10.1001/jama.2019.4984

[14] Byrne P, Demasi M, Jones M, Smith SM, O'Brien KK, DuBroff R. Evaluating the Association Between Low-Density Lipoprotein Cholesterol Reduction and Relative and Absolute Effects of Statin Treatment: A Systematic Review and Meta-analysis. JAMA Intern Med. 2022 May 1; 182(5): 474-81. https://doi.org/10.1001/jamainternmed.2022.0134

[15] Liu K, Wilkins JT, Colangelo LA, Lloyd-Jones DM. Does Lowering Low-Density Lipoprotein Cholesterol With Statin Restore Low Risk in Middle-Aged Adults? Analysis of the Observational MESA Study. J Am Heart Assoc. 2021 Jun; 10(11): e019695. https://doi.org/10.1161/JAHA.120.019695

[16] Ference BA, Yoo W, Alesh I, Mahajan N, Mirowska KK, Mewada A, *et al*. Effect of long-term exposure to lower low-density lipoprotein cholesterol beginning early in life on the risk of coronary heart disease: a Mendelian randomization analysis. J Am Coll Cardiol. 2012 Dec 25; 60(25): 2631-9. https://doi.org/10.1016/j.jacc.2012.09.017

[17] Dansethakul P, Thapanathamchai L, Saichanma S, Worachartcheewan A, Pidetcha P. Determining a new formula for calculating low-density lipoprotein cholesterol: data mining approach. EXCLI J. 2015 Mar 26; 14: 478-83.

[18] Martin SS, Blaha MJ, Elshazly MB, Toth PP, Kwiterovich PO, Blumenthal RS, *et al*. Comparison of a novel method vs the Friedewald equation for estimating low-density lipoprotein cholesterol levels from the standard lipid profile. JAMA. 2013 Nov 20; 310(19): 2061-8. https://doi.org/10.1001/jama.2013.280532

[19] Swiger KJ, Martin SS, Blaha MJ, Toth PP, Nasir K, Michos ED, *et al*. Narrowing sex differences in lipoprotein cholesterol subclasses following mid-life: the very large database of lipids (VLDL-10B). J Am Heart Assoc. 2014 Apr 22; 3(2): e000851. https://doi.org/10.1161/JAHA.114.000851

[20] Abu-Farha M, Thanaraj TA, Qaddoumi MG, Hashem A, Abubaker J, Al-Mulla F. The Role of Lipid Metabolism in COVID-19 Virus Infection and as a Drug Target. Int J Mol Sci. 2020 May 17; 21(10): 3544. https://doi.org/10.3390/ijms21103544

[21] Surma S, Banach M, Lewek J. COVID-19 and lipids. The role of lipid disorders and statin use in the prognosis of patients with SARS-CoV-2 infection. Lipids Health Dis. 2021 Oct 25; 20(1): 141. https://doi.org/10.1186/s12944-021-01563-0

[22] Li Y, Zhang Y, Lu R, Dai M, Shen M, Zhang J, *et al*. Lipid metabolism changes in patients with severe COVID-19. Clin Chim Acta Int J Clin Chem. 2021 Jun; 517: 66-73. https://doi.org/10.1016/j.cca.2021.02.011

[23] Wang G, Zhang Q, Zhao X, Dong H, Wu C, Wu F, *et al*. Low high-density lipoprotein level is correlated with the severity of COVID-19 patients: an observational study. Lipids Health Dis. 2020 Sep 7; 19(1): 204. https://doi.org/10.1186/s12944-020-01382-9

[24] Yue J, Xu H, Zhou Y, Liu W, Han X, Mao Q, *et al*. Dyslipidemia Is Related to Mortality in Critical Patients With Coronavirus Disease 2019: A Retrospective Study. Front Endocrinol. 2021; 12: 611526. https://doi.org/10.3389/fendo.2021.611526

[25] Fan J, Wang H, Ye G, Cao X, Xu X, Tan W, *et al*. Letter to the Editor: Low-density lipoprotein is a potential predictor of poor prognosis in patients with coronavirus disease 2019. Metabolism. 2020 Jun; 107: 154243. https://doi.org/10.1016/j.metabol.2020.154243

Received on 23-06-2022 Accepted on 13-08-2022 Published on 23-09-2022

DOI: https://doi.org/10.12974/2309-6179.2022.07.03