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)

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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
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)\textsuperscript{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, Scheffé 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

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Male</td>
<td>N</td>
<td>Mean</td>
<td>L</td>
<td>U</td>
<td>Mean</td>
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<tr>
<td>12-15 yr</td>
<td>1092</td>
<td>84.6</td>
<td>82.6</td>
<td>86.6</td>
<td>84.7</td>
<td>81.1</td>
</tr>
<tr>
<td>16-19 yr</td>
<td>1025</td>
<td>88.2</td>
<td>86.2</td>
<td>90.3</td>
<td>89.2</td>
<td>85.7</td>
</tr>
<tr>
<td>20-24 yr</td>
<td>720</td>
<td>98.9</td>
<td>96.4</td>
<td>101.3</td>
<td>102.8</td>
<td>98.4</td>
</tr>
<tr>
<td>25-29 yr</td>
<td>704</td>
<td>111.6</td>
<td>109.1</td>
<td>114.1</td>
<td>120.1</td>
<td>115.7</td>
</tr>
<tr>
<td>30-34 yr</td>
<td>783</td>
<td>116.4</td>
<td>114.0</td>
<td>118.7</td>
<td>118.9</td>
<td>114.6</td>
</tr>
<tr>
<td>35-39 yr</td>
<td>793</td>
<td>120.9</td>
<td>118.5</td>
<td>123.2</td>
<td>121.0</td>
<td>116.9</td>
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<tr>
<td>40-44 yr</td>
<td>961</td>
<td>119.8</td>
<td>117.6</td>
<td>121.9</td>
<td>121.5</td>
<td>117.8</td>
</tr>
<tr>
<td>45-49 yr</td>
<td>1107</td>
<td>118.9</td>
<td>116.9</td>
<td>120.9</td>
<td>121.6</td>
<td>118.4</td>
</tr>
<tr>
<td>50-54 yr</td>
<td>1325</td>
<td>114.4</td>
<td>112.6</td>
<td>116.2</td>
<td>118.9</td>
<td>116.0</td>
</tr>
<tr>
<td>55-59 yr</td>
<td>1509</td>
<td>109.1</td>
<td>107.4</td>
<td>110.8</td>
<td>115.0</td>
<td>111.9</td>
</tr>
<tr>
<td>60-64 yr</td>
<td>2161</td>
<td>102.5</td>
<td>101.1</td>
<td>103.9</td>
<td>102.9</td>
<td>100.5</td>
</tr>
<tr>
<td>65-69 yr</td>
<td>1851</td>
<td>96.0</td>
<td>94.5</td>
<td>97.6</td>
<td>96.2</td>
<td>93.7</td>
</tr>
<tr>
<td>70-74 yr</td>
<td>1828</td>
<td>93.8</td>
<td>92.3</td>
<td>95.4</td>
<td>97.4</td>
<td>94.9</td>
</tr>
<tr>
<td>75-80 yr</td>
<td>3385</td>
<td>91.6</td>
<td>90.4</td>
<td>92.7</td>
<td>95.8</td>
<td>94.0</td>
</tr>
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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...
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
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

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


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