Faculty of Natural and Applied Sciences Journal of Scientific Innovations
Print ISSN: 2814-0877 e-ISSN: 2814-0923
www.fnasjournals.com
Volume 4; Issue 2; October 2023; Page No. 126-134.

MULTIPLE CORRELATIONS ANALYSISOF DIFFERENT CHOLESTEROL-REDUCING DRUGS

[*1]Ekeng, N.H., [2]Biu, E.O., &[3]George, N.R.
[1&3]Department of Mathematics/Statistics, Ignatius Ajuru University of Education, Port Harcourt, Nigeria.
[2]Department of Mathematics University of Port Harcourt, Choba Port Harcourt Nigeria

***Corresponding author email**: ekengh@yahoo.com

Abstract
In this research, multiple correlation analyses of different cholesterol-reducing drugs were examined. There have been several arguments by physicians as to which anti-cholesterol drugs are the best to administer. To solve this problem, four cholesterol-reducing drugs-statin, proprotein convertase subtilisin/kexin (PCSK) inhibitors, fibrates, and nicotinic acid were experimented. The result shows that the drugs are statistically significant and that combining statin and PCSK qlutubitor is the best combination to be administered to the patient.

Keywords: Correlations, Cholesterol, Drugs, Physicians, Patients

Introduction

According to Khera et al. (2011), cholesterol is a growing issue because of its impact on human health. Cigarette smoking, high blood pressure, and high blood cholesterol are the most clearly established risk factors that have been identified as being strongly associated with coronary heart disease (CHD) (Rohatgi et al., 2014). Total serum cholesterol level (SCL) is a major risk factor for CHD. Cholesterol is present in every cell of the body and has important natural functions when it comes to digesting foods, producing hormones, and generating vitamin D. A better understanding of lipoprotein production and removal, lipoprotein receptors, and apolipoproteins is needed because they are considered the most important factors in cholesterol (Layoun et al., 2017). Cholesterol is classified into two types: low-density lipoproteins (LDL) and high-density lipoproteins (HDL). Lipids are circulating as lipoproteins, consisting of unesterified cholesterol, triglycerides, phospholipids, and proteins. The major lipoproteins in the blood are chylomicrons, very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL). Each of these classes of lipoproteins transports cholesterol and triglycerides to their designated destinations. The level of cholesterol plays a vital role in the cardiovascular disease process. A high level of lipids, including cholesterol and triglycerides in the serum, which is also termed hyperlipidemia, leads to a higher risk of developing atherosclerotic cardiovascular disease (CVD). Cholesterol level measurement is from serum. Clinically, obtaining a lipid profile assists in screening, diagnosing, and managing diseases.

A non-fasting lipid test can be done anytime without fasting; a fasting lipid test requires a 12-hour fast except for water. Total and HDL cholesterol are measured directly from serum. Fasting LDL-C is still the standard for initiating lipid-lowering therapy, but there has been a heated debate over fasting or non-fasting lipid profiles among specialists. The rationale behind the discussion of fasting or non-fasting is that the triglyceride level can be affected by the last intake and the limitations of the Friedewald equation (Kolovou et al., 2005). Many current guidelines propose that no fasting LDL-C holds similar significance to that of fasting LDL-C (Nordestgaard et al., 2007). A fasting lipid panel is a strong recommendation for patients with type 2 diabetes, obesity, medications that may affect lipid levels, such as thiazides and beta blockers and excessive intake of alcohol (Herink & Ito, 2018). Cholesterol and triglycerides desirable levels are; Total cholesterol (below 200 mg/dl), LDL cholesterol (below 100 mg/dl), HDL cholesterol (at or above 60 mg/dl) and Triglycerides (below 150 mg/dl) (Duerden et al., 2015). A recommendation has been made that total SCL for adults should be below 200mg/dl and individuals with values between 200mg/dl to 239 mg/dl should be considered as borderlinehigh risk; those with values more than 240 mg/dl should be regarded as high risk for CHD 3, 9. Therefore, the recommended level for children is170mg/dl

Cite this article as:
Ekeng, N.H., Biu, E.O., & George, N.R.(2023). Multiple correlations analysis of different cholesterol-reducing drugs. *FNAS Journal of Scientific Innovations*,*4*(2), 126-134.

The National Health and Nutrition Examination Survey (NHANES) for 1999 to 2006 reports a 20% prevalence rate of dyslipidemia among adolescents with a statistically significant higher level of lipids in higher BMI adolescents (Ford et al., 2009). Among those adolescents with dyslipidemia, only 0.8% of them might need pharmacological treatment (Gooding et al., 2015). National Heart, Lung, and Blood Institute (NHLBI) expert panel in 2011 recommended that all children should be screened for dyslipidemia to identify children with familial hypercholesterolemia (FH). FH patients are at higher risk for morbidity and early mortality (JBS3 Board, 2014). A fasting lipid test is recommended for children with cardiovascular risks, such as hypertension, obesity, diabetes, and family history; a non-fasting lipid test is preferable for those without known cardiovascular risks (D'Agostino et al., 2008). According to Stamler et al. (1986), large clinical trials have shown that lowering LDL-C levels significantly reduces cardiovascular events and mortality rate; whereas, according to current consensus, HDL-C is not a target for primary prevention in coronary artery diseases (Gregg et al., 2005). Nevertheless, recent studies proposed the prognostic value of serum cholesterol efflux capacity in patients with coronary artery disease (Zhang et al., 2016). According to the 2018 Guideline on the Management of Blood Cholesterol, clinicians target at lowering LDL-C levels by more than 50% with maximally tolerated statin therapy. An individual who are already under statin therapy and remain at an increased LDL-C level (more than 70mg/dL); clinicians then initiate additional non-statin therapy such as PCSK9. Apart from statins and PCSK9 inhibitors, a doctor may prescribe selective cholesterol absorption inhibitors such as Fibrates and Nicotinic acid. The Framingham Heart Study states that the following cholesterol ratios roughly signal different degrees of heart disease risk: Men: 5.0 = average risk, 3.4 = half the average risk, 9.6 = twice the average risk and Women: 4.4 = average risk, 3.3 = half the average risk and 7.0 = twice the average risk and Children: 2.8 = average risk; 2.8 -3.3 = half average risk and 3.4 = twice the average risk. While men and women have the same blood test, their average HDL, LDL, and VLDL levels are typically different.

Management for atherosclerotic cardiovascular diseases and Evaluation for lipid-lowering therapy potentially diagnosis that; Dyslipidemias Primary disorders of lipid metabolism such as familial hypercholesterolemia (FH), chylomicronemia, familial combined hyperlipidemia, familiar dysbetalipoproteinemia classify according to Fredrickson phenotype (Fredrickson, 1971). Secondary dyslipidemia can result from diabetes mellitus, hypothyroidism, obstructive liver diseases, chronic renal failure, drugs that increase LDL-C including retinoids, cyclosporine A, and phenothiazines and drugs that decrease HDL-C including progestins, androgens, beta-blockers, and anabolic steroids. Based on the types of lipid abnormalities, dyslipidemias can be categorized into high total cholesterol (TC), High low-density lipoprotein cholesterol (LDL-C), High non-high-density lipoprotein cholesterol (non-HDL-C), High triglycerides (TG), and Low high-density lipoprotein cholesterol (HDL-C). Bhikhari and Chris (2017) studied the serum cholesterol level by racial and gender differences in terms of probability distributions.

The majority of people who are suffering from high levels of cholesterol have aimed to reduce to a target level, for instance, below 100mg/dl using native (herb) and English methods (Medication), yet no clear fact as to which method is the optimal. Also, randomized controlled clinical trials have not produced enough evidence to suggest treatment for a specific target. However, research has proven that certain health conditions such as kidney disease or chronic inflammation can increase the risk of high cholesterol and considering these factors will lead to a more personalized approach to the treatment and prevention of high cholesterol levels. In this research, the emphasis is based on the English way of reducing high cholesterol where many physicians have several arguments as to which particular drug or combination of drugs is suitable for this health issue. To solve this problem, different cholesterol-reducing drugs are tested and analysed to draw inferences to remedy the situation.

Aim and Objectives

This research aims to examine several anti-cholesterol drugs and the objectives are to:

(i) test the significant effects of the drugs.
(ii) examine whether the drugs are partially correlated.
(iii) elucidate the degree of multiple correlations existing between the drugs and make inferences.

This research will help physicians to know the right prescription of cholesterol-reducing drugs to be prescribed to people with this health challenge. It is also significant in terms of the interaction effect of the combined drugs. This will save many lives from the risk of side effects of taking drugs for the treatment of high cholesterol in humans.

Cite this article as:
Ekeng, N.H., Biu, E.O., & George, N.R.(2023). Multiple correlations analysis of different cholesterol-reducing drugs. *FNAS Journal of Scientific Innovations*,*4*(2), 126-134.

Materials and Methods

The material for this research as a form of data is obtained from the University of Calabar Teaching Hospital (UCTH). The source of data is secondary and the experiment was done for twenty (20) days considering three categories of clients (Men, Women and Children). The techniques used for the analysis to achieve the objectives of this research are discussed below.

One–way classification technique

This design is appropriate for experiments having homogeneous experimental materials and units where effects are easy to control. In this design, treatments (drugs) are assigned entirely at random to experimental units such that each unit has an equal chance of receiving any one drug. The data for this experiment would appear in the Table 1.

Table 1: Cholesterol level in a randomly selected person

Treatments (Drugs)				
1	2	3 . . .		k
y_{11}	y_{12}	y_{13} . . .		y_{1k}
y_{21}	y_{22}	y_{23} . . .		y_{2k}
-	-	-	-	-
-	-	-	-	-
y_{n1}	y_{n2}	y_{n3}		y_{nk}

The linear statistical model for the experiment is given by;

$$y_{ij} = \mu + \tau_j + \varepsilon_{ij} \begin{cases} j = 1,2,...,k \\ i = 1,2,\ldots,n \end{cases} \quad (1)$$

Where; y_{ij} is the i^{th} observation receiving j^{th} drug, μ is the grand mean of the drugs, τ_j is the j^{th} drug effect and ε_{ij} is a random error that is normally distributed with mean zero (0) and variance (σ^2). Two sources of variation are considered; variation between groups (drugs) and variation within groups (error). Here, the interest is to test the equality of k–drug effects. That is;

$H_0 : \tau_1 = \tau_2 = \ldots = \tau_k = 0$ and $H_1 : \tau_j \neq 0$ for at least one j.

The analysis of variance (ANOVA) consists of partitioning the total variability into its components parts as follows;

$$SS_{Total} = SS_{Drug} + SS_{Error} \quad (2)$$

The test procedure is summarized in Table 2 below:

Table 2: Analysis of variance for different drugs in reducing cholesterol level

Source of variation	Df	Sum of Squares	Mean Square	F – ratio
Drugs	$k-1$	SS_{Drug}	MS_{Drug}	$\frac{MS_{Drug}}{MS_{Error}}$

Cite this article as:
Ekeng, N.H., Biu, E.O., & George, N.R.(2023). Multiple correlations analysis of different cholesterol-reducing drugs. *FNAS Journal of Scientific Innovations*,*4*(2), 126-134.

Error	$N-k$	SS_{Error} MS_{Error}
Total	$N-1$	SS_{Total}

Partial correlation

Simple correlation for zero order between X_i X_j and. The simple correlation of zero order between combinations of two variables is given below;

$$r_{ij} = \frac{\sum X_i X_j}{\sqrt{\sum X_i^2 X_j^2}}, \quad i \neq j \; ij = 1,2,3,\ldots,n \tag{3}$$

The simple correlation between Statin and PCSK 9 Inhibitors

$$r_{12} = \frac{\sum x_1 x_2}{\sqrt{\sum x_1^2 \sum x_2^2}} \equiv r_{21} \tag{4}$$

The simple correlation between Statin and Fibrates

$$r_{13} = \frac{\sum x_1 x_3}{\sqrt{\sum x_1^2 \sum x_3^2}} \equiv r_{31} \tag{5}$$

Simple correlation between Statin and Nicotinic acid

$$r_{14} = \frac{\sum x_1 x_4}{\sqrt{\sum x_1^2 \sum x_4^2}} \equiv r_{41} \tag{6}$$

The simple correlation between PCSK 9 Inhibitors and Fibrates

$$r_{23} = \frac{\sum x_2 x_3}{\sqrt{\sum x_2^2 \sum x_3^2}} \equiv r_{32} \tag{7}$$

The simple correlation between PCSK 9 Inhibitors and Nicotinic acid

$$r_{24} = \frac{\sum x_2 x_4}{\sqrt{\sum x_2^2 \sum x_4^2}} \equiv r_{42} \tag{8}$$

Simple correlation between Fibrates and Nicotinic acid

$$r_{34} = \frac{\sum x_3 x_4}{\sqrt{\sum x_3^2 \sum x_4^2}} \equiv r_{43} \tag{9}$$

First-order partial correlation between the variables

This is a partial correlation between two variables keeping the third variable constant. The following is the partial correlation of three variables for this research:

1. Partial correlation between Statin and PCSK 9 Inhibitors keeping Fibrates constant

Cite this article as:
Ekeng, N.H., Biu, E.O., & George, N.R.(2023). Multiple correlations analysis of different cholesterol-reducing drugs. *FNAS Journal of Scientific Innovations*,*4*(2), 126-134.

$$r_{12.3} = \frac{r_{12} - r_{13}r_{23}}{\sqrt{1-r_{13}^2}\sqrt{1-r_{23}^2}} \equiv r_{21.3} \quad (10)$$

2. Partial correlation between Statin and PCSK 9 Inhibitors keeping Nicotinic acid constant

$$r_{12.4} = \frac{r_{12} - r_{14}r_{24}}{\sqrt{1-r_{14}^2}\sqrt{1-r_{24}^2}} \quad (11)$$

3. Partial correlation between Statin and Fibrates keeping Nicotinic acid constant

$$r_{13.4} = \frac{r_{13} - r_{14}r_{34}}{\sqrt{1-r_{14}^2}\sqrt{1-r_{34}^2}} \quad (12)$$

4. Partial correlation between Statin and Nicotinic acid keeping PCSK 9 Inhibitors constant

$$r_{14.2} = \frac{r_{14} - r_{12}r_{24}}{\sqrt{1-r_{12}^2}\sqrt{1-r_{24}^2}} \quad (13)$$

5. Partial correlation between Statin and Nicotinic acid keeping Fibrates constant

$$r_{14.3} = \frac{r_{14} - r_{13}r_{34}}{\sqrt{1-r_{13}^2}\sqrt{1-r_{34}^2}} \quad (14)$$

6. Partial correlation between PCSK 9 Inhibitors and Statin keeping Nicotinic acid constant

$$r_{21.4} = \frac{r_{21} - r_{24}r_{14}}{\sqrt{1-r_{24}^2}\sqrt{1-r_{14}^2}} \quad (15)$$

7. Partial correlation between PCSK 9 Inhibitors and Fibrates keeping Nicotinic acid constant

$$r_{23.4} = \frac{r_{23} - r_{24}r_{34}}{\sqrt{1-r_{24}^2}\sqrt{1-r_{34}^2}} \quad (16)$$

8. Partial correlation between PCSK 9 Inhibitors and Nicotinic acid keeping Fibrates constant

$$r_{24.3} = \frac{r_{24} - r_{23}r_{34}}{\sqrt{1-r_{23}^2}\sqrt{1-r_{34}^2}} \quad (17)$$

9. Partial correlation between Fibrates and Statin keeping PCSK 9 Inhibitors constant

$$r_{31.2} = \frac{r_{31} - r_{32}r_{12}}{\sqrt{1-r_{32}^2}\sqrt{1-r_{12}^2}} \quad (18)$$

10. Partial correlation between Fibrates and Nicotinic acid keeping PCSK 9 Inhibitors constant

Cite this article as:
Ekeng, N.H., Biu, E.O., & George, N.R.(2023). Multiple correlations analysis of different cholesterol-reducing drugs. *FNAS Journal of Scientific Innovations*,*4*(2), 126-134.

$$r_{34.2} = \frac{r_{34} - r_{32}r_{42}}{\sqrt{1-r_{32}^2}\sqrt{1-r_{42}^2}} \tag{19}$$

Second-order partial correlation coefficient in four variables

If X_1, X_2, X_3 and X_4 are four variables, then the second-order partial correlation coefficients kept two variables constant. For partial correlation in four variables, six partial correlation coefficients of second order are; $r_{12.34}$, $r_{13.24}$, $r_{14.23}$, $r_{23.14}$, $r_{24.13}$ and $r_{34.12}$. The formula and the interpretation in harmony with this research are shown below;

1. Partial correlation of Statin and PCSK 9 Inhibitors keeping Fibrates and Nicotinic acid constant.

$$r_{12.34} = \frac{r_{12.4} - r_{13.4}r_{23.4}}{\sqrt{1-r_{13.4}^2}\sqrt{1-r_{23.4}^2}} \tag{20}$$

2. Partial correlation of Statin and Fibrates keeping PCSK 9 Inhibitors and Nicotinic acid constant.

$$r_{13.24} = \frac{r_{13.4} - r_{12.4}r_{23.4}}{\sqrt{1-r_{12.4}^2}\sqrt{1-r_{23.4}^2}} \tag{21}$$

3. Partial correlation of Statin and Nicotinic acid keeping PCSK 9 Inhibitors and Fibrates constant.

$$r_{14.23} = \frac{r_{14.3} - r_{12.3}r_{24.3}}{\sqrt{1-r_{12.3}^2}\sqrt{1-r_{24.3}^2}} \tag{22}$$

4. Partial correlation of PCSK 9 Inhibitors and Fibrates keeping Statin and Nicotinic acid constant.

$$r_{23.14} = \frac{r_{23.4} - r_{12.4}r_{13.4}}{\sqrt{1-r_{12.4}^2}\sqrt{1-r_{13.4}^2}} \tag{23}$$

5. Partial correlation of PCSK 9 Inhibitors and Nicotinic acid keeping Statin and Fibrates constant.

$$r_{24.13} = \frac{r_{24.3} - r_{12.3}r_{14.3}}{\sqrt{1-r_{12.3}^2}\sqrt{1-r_{14.3}^2}} \tag{24}$$

6. Partial correlation of Fibrates and Nicotinic acid keeping Statin and PCSK 9 Inhibitors constant.

$$r_{34.12} = \frac{r_{34.2} - r_{13.2}r_{14.2}}{\sqrt{1-r_{13.2}^2}\sqrt{1-r_{14.2}^2}} \tag{25}$$

Cite this article as:
Ekeng, N.H., Biu, E.O., & George, N.R.(2023). Multiple correlations analysis of different cholesterol-reducing drugs. *FNAS Journal of Scientific Innovations*,*4*(2), 126-134.

Results

The data collected for different cholesterol-reducing drugs for the people taking the drugs are displayed in Table 1 below. The drugs are X_1 = Statin, X_2 = PCSK 9 Inhibitors, X_3 = Fibrates and X_4 = Nicotinic acid.

Table 1: Shows the data and its computations

x_1	x_2	x_3	x_4	x_1^2	x_2^2	x_3^2	x_4^2	x_1x_2	x_1x_3	x_1x_4	x_2x_3	x_2x_4	x_3x_4
18	16	19	20	324	256	361	400	288	342	360	304	320	380
19	14	14	17	361	196	196	289	266	266	323	196	238	238
15	15	17	14	225	225	289	196	225	255	210	255	210	238
18	13	15	18	324	169	225	324	234	270	324	195	234	270
17	13	16	13	289	169	256	169	221	272	221	208	169	208
19	14	18	11	361	196	324	121	266	342	209	252	154	198
16	16	16	14	256	256	256	196	256	256	224	256	224	224
15	16	18	19	225	256	324	361	240	270	285	288	304	342
18	15	18	18	324	225	324	324	270	324	324	270	270	324
19	15	17	16	361	225	289	256	285	323	304	255	240	272
14	17	16	15	196	289	256	225	238	224	210	272	255	240
15	13	15	14	225	169	225	196	195	225	210	195	182	210
16	12	15	15	256	144	225	225	192	240	240	180	180	225
15	19	18	16	225	361	324	256	285	270	240	342	304	288
13	18	17	20	169	324	289	400	234	221	260	306	360	340
18	16	15	18	324	256	225	324	288	270	324	240	288	270
19	15	19	17	361	225	361	289	285	361	323	285	255	323
17	15	18	14	289	225	324	196	255	306	238	270	210	252
20	16	16	13	400	256	256	169	320	320	260	256	208	208
14	14	17	16	196	196	289	256	196	238	224	238	224	272
335	**302**	**334**	**318**	**5691**	**4618**	**5618**	**5172**	**5039**	**5595**	**5313**	**5063**	**4829**	**5322**

The results obtained for equation (4) – (9), (10) – (19) and (20) – (25) are shown in the Table 2, Table 3 and Table 4 below;

Table 2: Simple correlation of zero order between combinations of two variables

γ_{12}	γ_{13}	γ_{14}	γ_{23}	γ_{24}	γ_{34}
0.0145	0.0132	0.0136	0.0133	0.0137	0.0135
1.45%	1.32%	1.36%	1.33%	1.37%	1.35%

Cite this article as:
Ekeng, N.H., Biu, E.O., & George, N.R.(2023). Multiple correlations analysis of different cholesterol-reducing drugs. *FNAS Journal of Scientific Innovations*,*4*(2), 126-134.

Table 3: First-order partial correlation coefficients keeping one variable constant

$\gamma_{12.3}$	$\gamma_{12.4}$	$\gamma_{13.4}$	$\gamma_{14.2}$	$\gamma_{14.3}$	$\gamma_{23.4}$	$\gamma_{24.3}$	$\gamma_{31.2}$	$\gamma_{34.2}$
0.0144	0.0143	0.0130	0.0134	0.0134	0.0131	0.0135	0.0130	0.0133
1.44%	1.43%	1.30%	1.34%	1.34%	1.31%	1.35%	1.30%	1.33%

Table 4: Second-order partial correlation coefficients keeping two variables constant

$\gamma_{12.32}$	$\gamma_{13.24}$	$\gamma_{14.23}$	$\gamma_{23.14}$	$\gamma_{24.13}$	$\gamma_{34.12}$
0.0141	0.0128	0.0132	0.0129	0.0133	0.0131
1.41%	1.28%	1.32%	1.29%	1.33%	1.31%

Table 5: ANOVA for different drugs

Model		Sum of Squares	Df	Mean Square	F	Sig.
1	Regression	238.862	4	59.715	4.355	.016[b]
	Residual	205.688	15	13.713		
	Total	444.550	19			

Discussion

Based on the analysis of the result above in Table 2, it shows that the drugs are positively correlated. The effect of combining x1 and x2 is higher than every other combination of the drug intake, the result also revealed that the side effect of taking x1 and x3 is minimal compared to others. Table 3 indicates that taking x1 and x3 relaxing x4 and taking x3 and x1 relaxing x2 produces the same function in the body. In comparing table 2 and table 3, it shows that taking x2 and x3 gives the same result as taking x3 and x4, relaxing x2. Also taking x3 and x4 is more or less like taking x2 and x4 relaxing x3. The same result is replicated in Table 4 for the patient that takes x2 and x4, relaxing x1 and x3 at the same time. However, the partial correlation of x1 and x3 with others gives a better result, followed by x2 and x3,x3 x4, and x2 x4, and x1 x4 and x1 x2 accordingly.

Conclusion

In consonance with the results, it shows that combining statin and PCSK inhibitor is the best cholesterol-reducing drug, followed by PCSK inhibitor and nicotinic acid, statin and nicotinic acid, fibrates and nicotinic acid, PCSK inhibitor and fibrates, and statin. Although, these drugs are statistically significant, necessary caution needs to be taken. The intake of these drugs should also be guided by the physician for optimum results.

References

Bhikhari, P. T., & Chris, P. T. (2017). A statistical study of serum cholesterol level by gender and race. *Journal Research of Health Science,* 17(3); 294 – 308.

D'Agostino, R. B., Vasan, R. S., Pencina, M. J., Wolf, P. A., Cobain, M., Massaro, J. M., &Kannel, W. B. (2008). General cardiovascular risk profile for use in primary care: the Framingham Heart Study. *Journal of Circulation, 117*(6); 743 - 53.

Duerden, M., O'Flynn, N., & Qureshi, N. (2015). Cardiovascular risk assessment and lipid modification: NICE guideline. *Br J Gen Pract,* 65(636); 378-80.

Ford, E. S., Li, C., Zhao, G., & Mokdad, A. H. (2009). Concentrations of low-density lipoprotein cholesterol and total cholesterol among children and adolescents. *Journal of Circulation, 119*(8); 1108 - 15.

Fredrickson, D. S. (1971). An international classification of hyperlipidemias and hyperlipoproteinemias. *Ann Intern Med*, 75(3); 471-2.

Gooding, H. C., Rodday, A. M., Wong, J. B., Gillman, M. W., Lloyd-Jones, D. M., Leslie, L. K., & de Ferranti, S. D. (2015). Application of pediatric and adult guidelines for treatment of lipid levels among us adolescents transitioning to young adulthood. *JAMA Pediatric*, *169*(6); 569 - 74.

Gregg, E. W., Cheng, Y. J., Cadwell, B. L., Imperatore, G., Williams, D. E., Flegal, K. M., Narayan, K. M., & Williamson, D. F.(2005). Secular trends in cardiovascular disease risk factors according to body mass index in US adults. *JAMA, 293*(15); 1868 - 1874.

Herink, M., & Ito, M. K. (2018). *Medication induced changes in lipid and lipoproteins.* In: Feingold KR, Anawalt B, Boyce A, Chrousos G, de Herder WW, Dhatariya K, Dungan K, Grossman A, Hershman JM, Hofland J, Kalra S, Kaltsas G, Koch C, Kopp P, Korbonits M, Kovacs CS, Kuohung W, Laferrère B, McGee EA, McLachlan R, Morley JE, New M, Purnell J, Sahay R, Singer F, Stratakis CA, Trence DL, Wilson DP, editors. Endotext [Internet]. MDText.com, Inc.; South Dartmouth (MA)

JBS3 Board. (2014). Joint British Societies' consensus recommendations for the prevention of cardiovascular disease (JBS3). Heart. Suppl 2:ii1-ii67.

Khera, A. V., Cuchel, M., de la Llera-Moya, M., Rodrigues, A., Burke, M. F., & Jafri, K, (2011). Cholesterol Efflux Capacity, High-Density Lipoprotein Function, and Atherosclerosis. *N Engl J Med*, *364*(2); 127 - 135.

Kolovou, G. D., Anagnostopoulou, K. K., Daskalopoulou, S. S., Mikhailidis, D. P., & Cokkinos, D. V. (2005). Clinical relevance of postprandial lipaemia. Curr Med Chem, 12(17);1931- 45.

Layoun, N., Hallit, S., Waked, M., Aoun, B. Z., Godin, I., &Dramaix, M. (2017). Predictors of readiness to quit stages and intention to quit cigarette smoking in 2 and 6 months in Lebanon. *Journal Research of Health Sciences, 17*(2); 358 – 379.

Nordestgaard, B. G., Benn, M., Schnohr, P., & Tybjaerg-Hansen, A. (2007). Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women. JAMA, 298(3); 299-308.

Rohatgi, A., Khera, A., Berry, J. D., Givens, E. G., Ayers, C. R., & Wedin, K. E. (2014). HDL Cholesterol Efflux Capacity and Incident Cardiovascular Events. *NEJM, 371*(1); 2383 - 2393.

Stamler, J., Wentworth, D., & Neaton, J.D. (1986). Relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded. Findings in 356,222 primary screenees of the Multiple Risk Factor Intervention Trial (MRFIT). *JAMA*, *256*(20); 2823 - 2828.

Zhang, J., Xu, J., Wang, J., Wu, C., Xu, Y., Wang, Y., Deng, F., Wang, Z., Chen, X., Wu, M., & Chen, Y. (2016). Prognostic usefulness of serum cholesterol efflux capacity in patients with coronary artery disease. *American Journal of Cardiology*, *117*(4); 508 - 514.