Primary Preventive Medication use and Risk of Atherosclerotic Cardiovascular Diseases Among Patients with Hypertension and Diabetes Attending Irrua Specialist Teaching Hospital, Irrua, Nigeria

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ABSTRACT

Introduction: Atherosclerotic cardiovascular diseases (ASCVD) constitute a significant health burden in Nigeria. Aspirin and Statin though effective, are not routinely used as primary preventive medication in those with increased risk of CVD. The study aimed to determine the association between the use of primary preventive medication (low-dose soluble aspirin and statin) on the risk of atherosclerotic cardiovascular diseases among patients with hypertension and diabetes attending Irrua Specialist Teaching Hospital (ISTH), Irrua, Nigeria.

Methodology: This was a descriptive cross-sectional study of 394 systematically selected adult patients aged 18 years and above, visiting the GOPD, who had hypertension or diabetes mellitus. Data was collected using a pretested questionnaire and the Cardiovascular risk was assessed using the Framingham 10-year Risk of General Cardiovascular Disease Score (FRS). Respondents were categorised as low risk (< 10%), intermediate risk (10 to 20%), and high risk (> 20%). Data were entered into an Excel worksheet (2007) and analysed with Stata version 16.

Results: The mean age of participants was 53.95±15.47 years. They were mostly females (55.3%), and civil servants (32.74%) with tertiary education (44.67%). The majority of the patients (42%) had a high risk of developing CVD in 10 years. There was a significant association between intake of aspirin (p=0.01 AOR 18.98, CI: 2.61-137.91) and statin (p=0.01 AOR 5.02, CI: 0.48-56.00) and reduced risk of CVD.

Conclusion: There was a high risk of developing CVD among the study participants. The use of low-dose aspirin/statin for primary prevention of CVD was associated with risk reduction with those not on low-dose aspirin and statin having a 6 and 14-fold increased risk of developing CVD respectively. Routine prescription of low-dose aspirin and/or statins is recommended for patients with hypertension and/or diabetes except those in whom the medications are contraindicated.

Keywords: Aspirin, Statin, Primary Preventive, Medications, Hypertension, Diabetes

INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of death worldwide caused mainly by atherosclerosis, a chronic inflammatory disease of the blood vessel that results in narrowing.[1-3] CVDs including hypertension, heart failure, and stroke have been on the increase over the past 20 years in Nigeria.[4-7] Non-communicable diseases account for about 29% of all deaths in Nigeria, of which 11% are from CVDs.[3] Atherosclerotic cardiovascular diseases (ASCVD) constitute a significant health burden in Nigeria. A lot of high-quality evidence abounds for primary preventive medication use against its development.[8-12]

Aspirin is an effective primary prevention medication for those with an increased risk of CVD.[9] The American Diabetes Association recommends use of aspirin as a primary prevention strategy in patients with diabetes who are at increased cardiovascular risk, including those who are older than 40 years or who have additional risk factors, such as family history of coronary heart disease, hypertension, smoking, dyslipidaemia, or albuminuria.[10] Aspirin reduces the

risk of major CVD events by 11 per cent with doses less than 100mg as effective as doses up to 650mg daily with the CVD benefit of Aspirin seen within the first 5 years of administration.[10]

Statins (or HMG-CoA reductase inhibitors) act by inhibiting the enzyme HMG-CoA reductase, which plays a major role in the production of cholesterol. High cholesterol levels have been associated with cardiovascular disease. Low-density lipoprotein (LDL) carriers of cholesterol play a key role in the development of atherosclerosis and coronary heart disease and statins are the most widely prescribed and evidenced-based lipid-lowering drugs in the world for lowering LDLc and reducing cardiovascular morbidity and mortality, both in primary and secondary prevention[13,14]

Five major guidelines on statin use for primary prevention of atherosclerotic cardiovascular disease (ASCVD) have been published since 2014: the National Institute for Health and Care Excellence (NICE; 2014), US Preventive Services Task Force (USPSTF; 2016), Canadian Cardiovascular Society (CCS; 2016), European Society of Cardiology/European Atherosclerosis Society (ESC/EAS; 2016), and American College of Cardiology/American Heart Association (ACC/AHA; 2018).[11,12]

Adults who are 40 to 75 years of age and are being evaluated for cardiovascular disease prevention should undergo a 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimation and have a clinician-patient risk discussion before they are started on pharmacological therapy, such as antihypertensive therapy, a statin, or aspirin.[15,16] There is high-quality evidence that aspirin, BP-lowering therapy, and statins reduce the risk of ASCVD events from 10% to 25% among individuals without prevalent ASCVD. There is also high-quality evidence that BP-lowering therapy and statins reduce the risk of all-cause mortality by 11% and 14%, respectively.[4,5,17-19]

Despite this evidence, much had not been done in our setting to ascertain those at risk of ASCVDs to be able to set up management strategies to meet the sustainable development goal target of 50% use of medications in primary prevention of ASCVD. This study would therefore fill that research gap by providing data on the ASCVD risk in our environment which will help us as clinicians institute preventive measures to reduce the risks in our patients and the populace. The study aimed to determine the association between the use of primary preventive medication (low-dose soluble aspirin and statin) on the risk of atherosclerotic cardiovascular diseases among patients with hypertension and diabetes attending Irrua Specialist Teaching Hospital (ISTH), Irrua, Nigeria.

MATERIALS AND METHODS

Location of The Study:

This study was carried out at the General Outpatient Department (GOPD) of Irrua Specialist Teaching Hospital (ISTH), Irrua, a semi-urban town in Edo State, Southern Nigeria. The General Outpatient Department (GOPD) runs every working day of the week, from 8 am to 4 pm. Local statistics from the Medical Records Unit of the department show that an average of 98 patients are seen per day which adds up to about 25,480 patients per year. Patients with hypertension and/or diabetes presenting to ISTH are first seen in the GOPD where over 70% of them are managed and the rest particularly those with complications requiring other specialists' attention are then referred mainly to the cardiologists, nephrologists and endocrinologists.

Study Design: This was a descriptive cross-sectional study.

Study Population: The study population comprised adult patients aged 18 years and above, visiting the GOPD, who had hypertension or diabetes mellitus.

Selection Criteria:

Inclusion Criteria:

- Newly diagnosed Hypertensive patients
- Previously diagnosed Hypertensive patients whether or not on treatment
- Newly diagnosed patients with Diabetes Mellitus
- Previously diagnosed Diabetes Mellitus patients whether or not on treatment

Exclusion Criteria:

- Critically ill patients who would not be able to participate.
- Patients with clinical evidence of cardiovascular diseases such as stroke, Congestive Cardiac Failure (CCF), Ischaemic Heart Disease/Myocardial Infarction (IHD/MI), Peripheral Vascular Disease (PVD) etc.

Sample Size Determination:

The sample size was calculated using William Cochran's formula and a prevalence of 37% of cardiovascular disease was reported by Adedapo in southwestern Nigeria.[11]

$n = Z^2pq/d^2$

Z is the standard normal deviation at a 95% confidence interval which is 1.96.

P= 37.0%

q= 1-p

d= degree of the desired accuracy usually set at 0.05

$$n = \frac{1.96 \times 1.96 \times 0.37 \times 0.63}{0.05 \times 0.05}$$

n= 358

With an anticipated 10% attrition, a total of 394 participants were recruited for the study.

Sampling Technique:

Subjects who met the selection criteria above were selected using systematic random sampling. Patients were addressed and enlightened about the study. The selection criteria were spelt out and those who consented were systematically selected. The sampling interval was determined to be 3. The first patient was selected by simple random sampling (balloting). Three ballot papers numbered 1 to 3 were mixed in a bag and one was randomly chosen. That determined the first patient to be seen. Thereafter, every third patient was selected until the required sample size was achieved.

Data Collection:

The sociodemographic characteristics including age and sex, as well as smoking habits, medical history including history of hypertension and diabetes and use of statins and low dose aspirin as well as duration were collected from the patient using the semi-structured questionnaire. Blood pressure was determined using an Omron Intellisence® digital sphygmomanometer. Blood samples were tested for Fasting blood sugar, HbA1C, and lipid profile (Total Cholesterol, Triglycerides, LDL-Cholesterol, and HDL-Cholesterol) using the enzymatic colourimetric method. The Cardiovascular risk was assessed using the Framingham 10-year Risk of General Cardiovascular Disease Score (FRS) based on the six coronary risk factors of age, gender, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure and smoking habits.[20] The 10-year risk of cardiovascular disease was scored in percentage and respondents were categorised as low risk (< 10%), intermediate risk (10 to 20%), and high risk (> 20%).[21] This questionnaire was pretested at the General Hospital, Ekpoma, a nearby town with subjects of similar characteristics. The pretested questionnaire was thereafter used to collect the data for the study.

Data Analysis:

All data collected with the questionnaires were entered into a computer and analysed using the Excel worksheet (2007) and Stata version 16.

Descriptive Statistics:

The categorical variables were summarized using counts, proportions, frequency tables and charts. Quantitative variables such as Age; were summarized using mean, median, Standard deviation and frequency table. The participants' ages were grouped and the proportion of those who were positive by age group compared to each other. The risk percentage of those on statins/low-dose aspirin and those not on the medications were compared.

Test Statistics: Chi-square test statistics were used to test for an association between the risk of cardiovascular disease and history of use of statins/low-dose aspirin and ascertain the statistical significance of the difference observed; with a 95% Confidence interval computed and level of significance set at P value < 0.05%.

Duration of The Study and Funding:

The study was conducted between May and July 2023. There was no external funding for this study. The cost was borne by the researchers.

RESULTS

A total of 394 patients were recruited for this study (Table 1). The youngest among them was 19 years old, while the eldest was 94 years. The mean age was about 54 years and the age group most affected was more than 60 years old (elderly). More than half of the participants were females (55.3%) and the majority of them were Traders. Almost half of the participants (45.0%) had a tertiary level of education.

Table 1. Sociodemographic characteristics of respondents

Variables	Frequency (N=394)	Percent (%)
Age (years)		
< 20	2	0.51
20-29	16	4.06
30-39	65	16.50
40-49	69	17.51
50-59	88	22.33
≥ 60	154	39.09
Mean ± SD	53.95 ± 15.47	
Sex		
Female	218	55.33
Male	176	44.67
Ethnicity		
Akoko Edo	30	7.62
Bini	21	5.33
Esan	169	42.89
Etsako	82	20.81
Hausa	12	3.05
Ibo	24	6.09
Owan	50	12.69
Yoruba	6	1.52
Occupation		
Artisan	77	19.54
Civil servant	129	32.74
Farmer	59	14.98
Trader	105	26.65
Unemployed	24	6.09
Educational status		
No level of education	53	13.45
Primary	56	14.21
Secondary	109	27.67
Tertiary	176	44.67

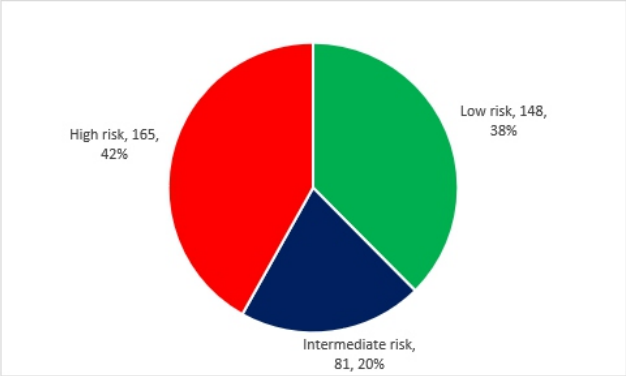

Fig 1. The risk of cardiovascular disease among patients with hypertension and diabetes using the Framingham 10-year Risk of General Cardiovascular Disease.

Figure 1. Showed the risk of developing cardiovascular diseases (CVD) among patients with hypertension and diabetics using FRS categorization. The majority of the patients had a high risk of developing CVD in 10 years.

There was a statistically significant difference between primary preventive medication use (Low dose Aspirin, Statin) in relation to the risk of developing CVD. Table 2. Patients on low-dose aspirin had a lower risk of CVD compared to those who were not and the difference was significant (p=0.01). Also, patients on statins had a significantly lower risk compared to those not on statins (p=0.01).

Table 2. The association between primary preventive medication, obesity, and the risk of developing cardiovascular disease in respondents.

Variable	Low risk (n=148)	Intermediate risk (n=81)	High risk (n=165)	P-Value
Low dose Aspirin				
Yes	44 (69.84)	8 (12.70)	11 (17.46)	0.01
No	104 (31.42)	73 (22.05)	154 (46.53)	
Statin				
Yes	71 (82.56)	9 (10.46)	6 (6.98)	0.01
No	77 (25.00)	72 (23.38)	159 (51.62)	

Table 3 illustrates the predictors of the risk of developing CVD among respondents. For every annual increase in age, the odds of CVD will increase by 46%. The odds of CVD in males will increase by 197 folds as compared to females. Similarly, for every unit increase in systolic blood pressure and fasting blood sugar, the Odds of CVD will increase by 7% and 3% respectively. [1]OR=Odds ratio, AD=Adjusted Odds ratio, BMI= Body mass index, WHR= Waist hip ratio, SBP= Systolic blood pressure, DBP= Diastolic blood pressure, FBS= Fastened blood sugar, FSP= Fastened Lipid profile, Ref= Reference

Table 3. Predictors of risk factors for developing CVD in patients with hypertension and diabetes.

	Univariable regression		logistic	Multivariable regression		logistic
Variables	OR	95% Confidence Interval	P-Value	AOR	95% Confidence Interval	P-Value
Age (years)	1.26	1.20-1.32	< 0.05	1.46	1.27-1.67	0.01
Sex						
Female	1	Ref		1	Ref	
Male	4.84	3.04-7.68	< 0.05	197.87	13.18-29.70	0.01
Occupation						
Artisan	1	Ref		1	Ref	
Farmer	1			1		
Civil servant	1.16	0.66-2.04	0.61	3.82	0.40-36.59	0.24
Trader	0.78	0.44-	0.42	1.84	0.16-20.73	0.62
Unemployed	3.17	1.07-9.37	0.04	49.03	0.01-24.08	0.48
Educational status						
No formal education	1	Ref		1	Ref	
Primary	0.14	0.03-0.68	0.02	2.56	0.01-100.43	0.86
Secondary	0.05	0.01-0.21	0.01	5.52	0.01-198.74	0.75
Tertiary	0.04	0.01-0.17	0.01	4.17	0.01-192.88	0.79
SBP	1.07	1.06-1.09	0.01	1.11	1.05-1.18	0.01
DBP	1.07	1.05-1.08	0.01	1.03	0.97-1.10	0.28
FBS (Mg/dl)	1.03	1.01-1.04	0.01	1.06	1.03-1.14	0.01
FLP (Mg/dl) TC	1.01	0.99-1.01	0.17	1.02	0.99-1.05	0.14
FLP (Mg/dl) TG	1.01	1.00-1.01	0.03	0.99	0.96-1.02	0.70

Diabetic patients are likely to have an 11-fold increase in odds of CVD when compared with non-diabetics. There is also a 16-fold increase in the odds of having CVD among hypertensive patients when compared with non-hypertensive patients. Patients who were not on low dose Aspirin had a 5.9-fold increase in odds of having CVD compared to patients who were on low dose Aspirin. Also, those not on statin had a 14.2 times increase in the odds of developing CVD when compared to those on stations. Table 4.

Table 4. Primary preventive medication uses and the risk of developing CVD in patients with hypertension and diabetes.

	Univariable regression		logistic	Multivariable regression		logistic
Variables	OR	95% Confidence Interval	P-Value	AOR	95% Confidence Interval	P-Value
Diabetics						
No	1	Ref		1	Ref	
Yes	11.01	5.16-23.48	< 0.01	29.68	11.31-77.88	0.01
Hypertensives						
No	1	Ref		1	Ref	
Yes	8.70	5.42-13.97	< 0.01	16.76	7.90-35.56	0.01
Dyslipidaemia						
No	1	Ref		1	Ref	
Yes	2.32	0.95-5.65	0.06	1.20	0.36-3.98	0.76
Dose Aspirin Use						
Yes	1	Ref		1	Ref	
No	5.91	3.31-10.56	0.01	18.98	2.61-137.91	0.01
Statin Use						
Yes	1	Ref		1	Ref	
No	14.2	7.68-26.23	0.01	5.02	0.48-56.00	0.18

OR=Odds ratio, AD=Adjusted Odds ratio, Ref= Reference

DISCUSSIONS

This study was conducted to determine the association between the use of primary preventive medication (low-dose soluble aspirin and statin) on the risk of atherosclerotic cardiovascular diseases among 394 patients with hypertension and diabetes attending Irrua Specialist Teaching Hospital (ISTH), Irrua, Nigeria. The mean age of the participants was 54 years with a female preponderance. The subjects were mostly civil servants who made up 32%. This also reflected their educational status where a majority of them had tertiary education (45%) and as few as 13% did not have any education. This may reflect the semi-urban nature of the study setting with its institutions which include a teaching hospital, universities, polytechnics, colleges of education, banks, ministries of both state and LGs, as well as schools of nursing.

The 10-year Framingham estimated risk of developing CVD among the subjects was high with 42% of respondents having a greater than 20% (high risk) of developing CVD. This buttresses the need for primary medication use for the prevention of CVDs among such subjects. The ACC/AHA in their guidelines on the primary prevention of CVD recommends the use of aspirin, statins and blood pressure-lowering medications as they were shown to reduce the risk of ASCVD events from 10% to 25% among individuals without prevalent ASCVD. Statins were also shown to reduce the risk of all-cause mortality by 14%.[15,19] This is particularly important in environments like ours where civil service occupation predominated and their lifestyle could be sedentary throughout most parts of the days despite not statistically being a significant risk of developing CVD.

The use of primary prevention of CVD with low-dose aspirin/statins was statistically significant for CVD risk reduction. This could be quite encouraging despite having a sample size of 394 in this study as subjects on low-dose aspirin/statins were twice those not on aspirin/statin. Again, subjects not on low-dose aspirin/statin had a 5.9 and 14.2-fold increased risk of developing CVD respectively. This further enforces the need for primary prevention among diabetics and hypertensives in this environment and from the study, subjects who were on low-dose aspirin/statin were twice those not on these medications hence brighter prospects for primary prevention initiatives in this environment. Although subjects not on low-dose aspirin/statins were twice fewer, this number could be large if transposed into the wider community.

Other studies corroborated statin use to be protective against Type 2DM and the effect was reduced beyond the age of 75years and disappeared below 40years.[12,18] The mean age of our subjects was 54 years and the study by Ji Eun Jun et al[7] further gives credence to this fact in our environment. The ASCEND study group found aspirin use reduced the risk of CVD.[12] However, its benefits and hazards (bleeding) for the prevention of first CVD need further studies. The use of low-dose aspirin/statin as primary prevention medications had significant benefits on the risk of developing CVD with significant OR among diabetics and hypertensives.

LIMITATIONS

The study was a cross-sectional study. The findings would not be used to establish a cause-effect relationship between primary preventive medication and the risk of CVD. A randomised control trial would have been more appropriate. However, the study establishes an association between primary preventive medications with low-dose aspirin and statin and the risk of developing CVD.

CONCLUSION

The majority of Diabetic/Hypertensive subjects had a high 10-year Framingham risk of developing CVD in this study. This risk was further related significantly to age and female sex. The use of low-dose aspirin/statin for primary prevention of CVD was associated with risk reduction with those not on low-dose aspirin/statin having a 6 and 14-fold increased risk of developing CVD respectively.

Routine prescription of low-dose aspirin and/or statins is recommended for patients with hypertension and/or diabetes except those in whom the medications are contraindicated. It is also recommended that the risk of developing CVD be routinely assessed for patients with hypertension or diabetes presenting to health facilities using the 10-year Framingham assessment to ascertain their risk levels and institute appropriate interventions.

DECLARATIONS

Ethics approval and consent to participate:

Approval for this study was obtained from the Ethical and Research Committee of ISTH (ISTH/HREC/20221204/280) and informed written consent was obtained from the participants before the commencement of the study and recruitment of subjects respectively. Details of this research (including the procedure, benefits etc) were explained to the participants in a language they could understand and interpreters were engaged where necessary.

Consent for publication

Not Applicable

Author contributions

EPE, OTIA, FNF: Conceived the study, developed the protocol, conducted the study, wrote the manuscript, and edited and approved the final draft.

OI, IA, ABT, and ACC developed the protocol, analysed the data, wrote the manuscript, and edited and approved the final draft.

Acknowledgements

We thank the management and staff of the Department of Family Medicine, ISTH for allowing us to use their facilities and patients for the study. We also thank the patients for their cooperation during the study.

Funding

No funding whatsoever was received for the study. The study was funded by the authors.

Competing interests

The authors declare no conflicting interest whatsoever.

Availability of data and material

Data and other materials are available on request from the corresponding author.

REFERENCES

1. Barquera S, Pelrosa-Tobia A, Medina C, Hernandez-Barrera L, Bibbin-Domingo K, Lozano R et al. Global overview of the epidemiology of atherosclerotic cardiovascular disease. Archives of Medical Research 2015; 46(5): 328-338
2. Imes CC, Lewis MF. Family history of cardiovascular disease, perceived cardiovascular disease risk and health-related behaviour. A review of literature. J cardiovasc Nurs 2014 Mar-Apr; 29(2): 108-129
3. Ike SO, Onyema CT. Cardiovascular Diseases in Nigeria: what has happened in the past 20years?Nig J Cardiol.2020;17:21-26.
4. Amegah AK. Tackling the growing burden of cardiovascular disease in sub-Saharan Africa: Need for dietary guideline. Circulation 2018; 138: 2449-2451
5. Adedapo AD. Rising trends of Cardiovascular disease among SouthWestern Nigerian Female patients. Niger J Cardiol 2017;14: 71-74.
6. Ulasi LL, Ijoma CK, Onwubere BJ, Arodiwe E, OnodugoO, Okafor C. High Prevalence and low awareness of Hypertension in a market population in Enugu Nigeria. Int J Hypert 2011;1-5.
7. Mukhtar IG, Abdullahi AT, Muhammad SM, Sabiu NH, Salisu AI. Prevalence of modifiable cardiovascular risk factors among undergraduate students in Kano Nigeria: A need for action. Journal of Taibah University Medical Sciences. 2022 Aug 1;17(4):578-86.
8. Hansson G, Hermansson A. The immune system in atherosclerosis. Nat Immunol 2012; 12: 204-212
9. Bowman L, Mafham M, Wallendszus K, Stevens W, Buck G, Barton J. Effects of aspirin for primary prevention in persons with diabetes mellitus: the ASCEND Study Collaborative Group. Journal of Vascular Surgery. 2019 Jan 1;69(1):305.
10. Colwell JA. American Diabetes Association. Aspirin therapy in diabetes. *Diabetes Care*. 2003;26:(1) 587-588
11. Mortensen MB, Nordestgaard BG. Statin use in primary prevention of atherosclerotic cardiovascular disease according to 5 major guidelines for sensitivity, specificity, and number needed to treat. JAMA Cardiology. 2019 Nov 1;4(11):1131-8.
12. Guirguis-Blake JM, Evans CV, Senger CA, Rowland MG, Connor EAO, Whitlock EP. Aspirin for the primary prevention of cardiovascular events: a systematic evidence review for the U.S Preventive Service Task Force. Rockville(MD): Agency for Healthcare Research and Quality(U.S);2015 Sep.Report NO:13-05195-EF-1.PMID;26491760.
13. Grundy SM, Stone NJ, Guideline Writing Committee for the 2018 Cholesterol Guidelines†. 2018 Cholesterol clinical practice guidelines: synopsis of the 2018 American Heart Association/American College of Cardiology/Multisociety cholesterol guideline. Annals of internal medicine. 2019 Jun 4;170(11):779-83.
14. Ward NC, Watts GF, Eckel RH. Statin toxicity: mechanistic insights and clinical implications. Circulation research. 2019 Jan 18;124(2):328-50.
15. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019 Sep 10;140(11):e596-646.
16. Qureshi WT, Kaplan RC, Sweet K, Burke G,

Daviglus M, Jung M, et al. American College of Cardiology/American Heart Association (ACC/AHA) Class I Guidelines for the Treatment of Cholesterol to Reduce Atherosclerotic Cardiovascular Risk: Implications for US Hispanics/Latinos Based on Findings From the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). J Am Heart Assoc 2017;6(5):e005045.

17. Karmali KN, Lloyd-Jones DM, Berendsen MA, Sanghavi DM, Brown NC, Korenovska L, et al. Drugs for primary prevention of atherosclerotic Cardiovascular Disease: An overview of systematic reviews. JAMA Cardiol, 1;1(3):341-349.
18. Jun JE, Jeong IK, Ahn KJ, Chung HY, Hwang YC. Statin use for primary prevention in patients with type 2 diabetes: Can it benefit all ages?–A nationwide propensity-matched cohort study. Diabetes Research and Clinical Practice. 2021 Oct 1;180:109044.
19. Coke LA, Himmelfarb CD. Guideline on the primary prevention of cardiovascular disease: let's get it into practice! Journal of Cardiovascular Nursing. 2019 Jul 1;34(4):285-8.
20. Sohn C, Kim J, Bae W. The Framingham risk score, diet, and inflammatory markers in Korean men with metabolic syndrome. Nutrition research and practice. 2012 Jun 1;6(3):246-53.
21. Jahangiry L, Farhangi MA, Rezaei F. Framingham risk score for estimation of 10-years of cardiovascular diseases risk in patients with metabolic syndrome. *J Health Popul Nutr* 2017; 36, 36. https://doi.org/10.1186/s41043-017-0114-0