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ORIGINAL ARTICLE

A Comparison of Statin Treatment Algorithms Based on the ACC/AHA and Philippine Guidelines for Primary Prevention of Dyslipidemia in Statin-Naive Filipino Patients

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Abstract

Objectives. This cross-sectional study evaluates the degree of agreement between the 2018 American College of Cardiology/American Heart Association (ACC/AHA2018) and 2020 Philippine Guideline (PG2020) treatment algorithms for the primary prevention of dyslipidemia among Filipinos.

Methodology. This review included 159 charts of statin-naive Filipinos who are 45-79 years old. Using risk profile and lipid measurements, statin treatment recommendation was determined through the PG2020 algorithm and ACC/AHA-ASCVD Risk Estimator Plus web application. The degree of agreement was measured by Cohen's kappa statistic with the two algorithms as independent raters.

Results. A total of 159 patients were included in the final analysis. There was a slight agreement with a kappa coefficient of 0.209 or 4.4% (95% CI 0.078-0.340, p=0.003). Statin treatment was recommended in 69 out of 159 patients (43.4%) by the PG2020 overlapping with ACC/AHA2018 in 56 cases (81.2%). On the other hand, 109 cases (68.6%) were recommended for statin treatment by ACC/AHA2018 overlapping with PG2020 in only 51.4%.

Conclusions. The low degree of agreement between the two treatment algorithms highlights the key demographic and ethnic variations in dyslipidemia management necessitating outcome-based studies to translate these differences. Overestimation of ASCVD risk calculation in the ACC/AHA2018 and consideration of important, unique risk factors among Filipinos favors the applicability of the Philippine guideline.

Key words: dyslipidemia, hypercholesterolemia, algorithms, statins, primary prevention

INTRODUCTION

The Asia-Pacific region is afflicted with approximately half of the burden of cardiovascular disease worldwide.[1] Among its Asian neighbors, the Philippines is leading with 46.9% in terms of total cholesterolemia greater than 200 mg/dL. With regards to low high-density lipoprotein cholesterol (HDL-C), the Philippines is also among those with the highest prevalence, with 71.8% having HDL-C of less than 40 mg/dL. The Philippines similarly has the highest prevalence of high low-density lipoprotein cholesterol (LDL-C) at 47.2%. Hypertriglyceridemia is likewise notable with 38.6% among those surveyed having levels above 150 mg/dL.[2]

Since the majority of events leading to the development of atherosclerotic cardiovascular disease (ASCVD) are clinically silent, much of the early phase of the disease process remains undetected until the development of end-point events. This highlights the pivotal role of risk assessment in the management of dyslipidemia.[3,4]

Despite the availability of local guidelines and equivocal evidence for the use of other risk estimators based on international guidelines, practitioners in the Philippines still predominantly use the ASCVD risk calculator.[3] No head-to-head comparisons have been made between the Philippine Guidelines for the Management of Dyslipidemia in the Philippines (PG2020) and the American College of Cardiology/American Heart Association (ACC/AHA) Guidelines on the Management of Blood Cholesterol (ACC/AHA2018) notwithstanding the prevalence of use. Therefore, the applicability of these guidelines in the selection of appropriate treatment groups in the local setting remains unclear.

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This study was aimed at determining the degree of agreement between PG2020[4] and the ACC/AHA2018[5] based on the eligibility for statin therapy of Filipino patients.

METHODOLOGY

Design and Population

In this cross-sectional chart review study, we screened and reviewed a total of 297 charts of individual patients from the outpatient department of Cebu Velez General Hospital and Velez Medical Arts clinic from January 25 to March 18, 2022. The protocol was subjected to technical review and approved by the Research Committee of the Department of Internal Medicine of Cebu Velez General Hospital. The protocol was also approved by the Institutional Review Board of the same institution.

Personal information was not collected and each chart was identified by a coded chart number. Included patients were Filipinos between 45 to 79 years of age. All participants were either statin naive or have been off statins for at least 6 months before blood collection. The parameters taken for the chart review are all disclosed in the chart including the following details: gender, menstrual status, history of diabetes mellitus and medications, history of hypertension and medications, weight, height and BMI, family history of coronary heart disease, urinalysis and either a 2D-echocardiogram and/or a 12-lead electrocardiogram. All individuals that have the following characteristics were excluded from the study: patients younger than 45 or older than 79 years old, non-Filipino patients, patients with documented chronic kidney disease (CKD), and those who have had documented primary ASCVD. Charts with missing data essential for proper risk stratification as mentioned above were excluded from the final analysis.

Comparison

Eligibility for starting statin therapy was determined through algorithms derived from the PG2020 and ACC/AHA2018 algorithms, respectively. Details for risk profiling and lipid panel were taken solely from each chart review form.

The algorithm in Figure 1 is based on the recommendations and algorithm of the 2020 Philippine Guidelines for the Management of Dyslipidemia in the Philippines. Note however that in the absence of complete clinical data to rule familial hypercholesterolemia by the Dutch lipid network criteria, the algorithm cannot be followed to the letter. Meanwhile, ACC/AHA algorithm was applied using

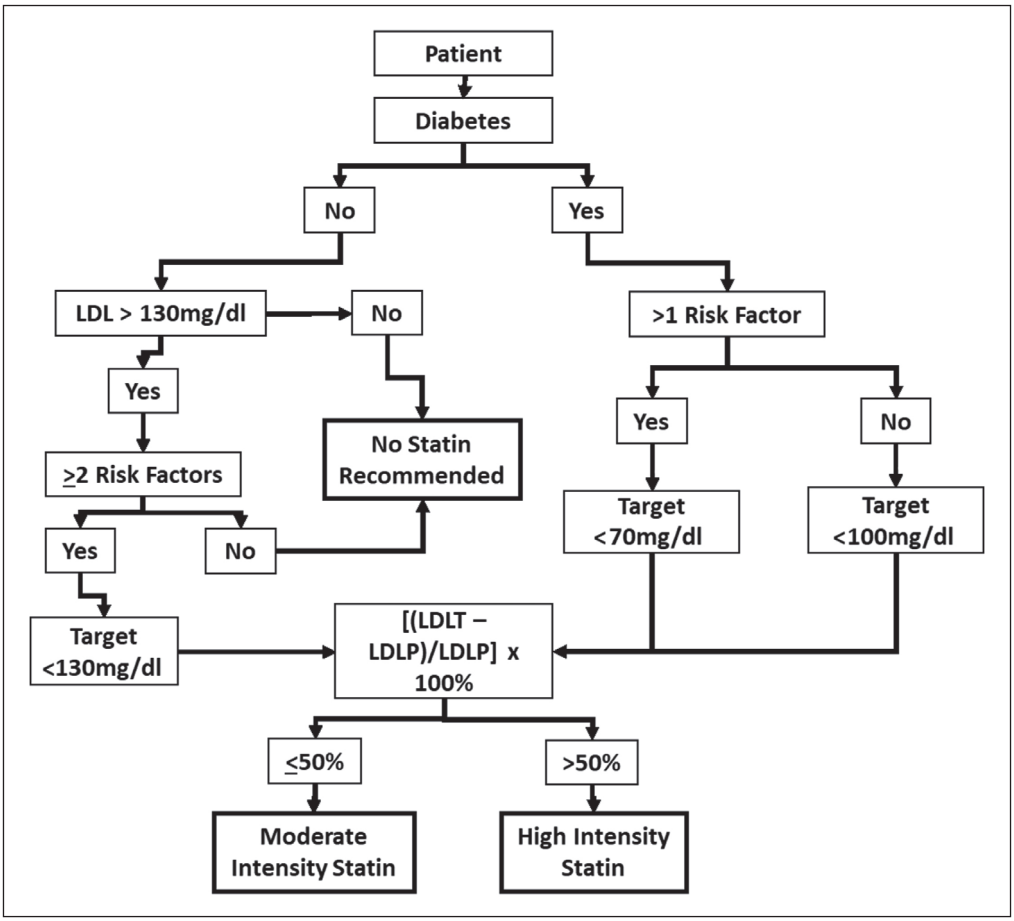

Figure 1. Algorithm based on the 2020 Clinical Practice Guidelines for the management of dyslipidemia in the Philippines.[4] LDLT is the LDL target as recommended by the guideline; LDLP is the patient's LDL level on assessment of lipid profile.

the ASCVD risk calculator plus webapp (accessed thru ASCVD Risk Estimator + (acc.org)) following the 2018 ACC/AHA/AACVPR/AAPA/ABC/ACP Guideline for the management of blood cholesterol.[5] The PG2020 algorithm and ACC/AHA2018 were applied to each case using logic function in Microsoft Excel and the webapp respectively. The application of both algorithms was automated and standardized to avoid operator bias.

Statistical Analysis

The two guideline algorithms were applied to facilitate decision-making on whether to start statin therapy for each of the included patients. The degree of agreement between the two guidelines was analyzed using Cohen's kappa statistic. A minimum of 133 charts was needed to achieve a power of 80% at 0.05 margin of error for a 2x2 cross-tabulation. The study by Bujang et al.,[6] was used as the basis for sample size calculation as well epidemiologic data from the 8th FNRI National Nutrition Survey.[7] Descriptive statistics were measured to summarize demographic characteristics. T-test for independent samples and Chi-Square analyses were used to compare diabetic and non-diabetic subsets for parametric and categorical data, respectively. All statistical analyses were performed using IBM SPSS version 26.0 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armok, NY: IBM Corp).

RESULTS

A total of 297 charts were screened. To reconcile the age restrictions of both guidelines (>45 years old for PG2020 and <80 for ACC/AHA2018), patients outside these age groups were excluded. Patients on statin therapy, those with lacking risk data and those with chronic kidney disease were all excluded. One hundred fifty-nine (159) patients were included in the final analysis.

The mean age was 58.4 years old (SD=8.7 years) with a slight female predominance at 51.6%. The risk characteristics are detailed below in Table 1. Majority of the patients were hypertensive (62.3%) but most of them were already on treatment (67.7%). Diabetes was seen in only 19.5% of included patients. Of the 82 female patients included, most (63.4%) were post-menopausal. Only 17.6% of patients were smokers. Only 1 of the 159 patients screened disclosed a family history of premature ASCVD. Laboratory risk parameters such as left ventricular hypertrophy on electrocardiography and/or echocardiography and proteinuria on urinalysis were seen in a minority of patients, in 6.9% and 8.2% respectively. The average systolic BP on the first consult was 141.9 mmHg (SD=20.8) and the mean BMI was 27.4 kg/m^2 (SD=4.2) among included patients.

Also summarized in Table 1 is a comparison of demographic and risk profiles between patients with and without diabetes. There was no significant difference between the two subsets across parameters except for 10-year ASCVD risk score and systolic blood pressure. Patients without diabetes had significantly higher systolic blood pressure than those with diabetes (142.5 SD=19.4 mmHg vs 139.4 SD=26.1 mmHg; p=0.038). On the other hand, patients with diabetes had significantly higher computed 10-year ASCVD risk (21.1% vs 10.9%; p=0.002).

The lipid parameters of patients included are further summarized in Table 2. The average total cholesterol of study participants was 203.1 (SD=42.4) mg/dL. The mean LDL-C and HDL-C were 122.6 (SD=36.6) mg/dL and 51.4 (SD=20.2) mg/dL, respectively. The lipid profiles of

Table 1. Patient demographics and risk characteristics (n=193)

Variable	Overall (n=159)	With diabetes (n=31)	Without diabetes (n=128)	*p*
Age (years) Mean (SD)	58.4 (8.7)	59.8 (8.4)	58.1 (8.8)	0.595
Sex, Male, N (%)	77 (48.4)	16 (51.6)	61 (47.7)	0.692
Hypertension, N (%)	99 (62.3)	18 (58.1)	81 (63.3)	0.591
Treated	67 (67.7)	13 (72.2)	54 (66.7)	
Untreated	32 (32.3)	5 (27.8)	27 (33.3)	
Diabetes, N (%)	31 (19.5)	-	-	-
Smoking, N (%)	28 (17.6)	5 (16.1)	23 (18.0)	0.809
Post-menopausal, N (%)	52 (63.4% of 100 Female)	9 (29.0)	44 (34.4)	0.571
Proteinuria on UA, N (%)	13 (8.2)	3 (9.7)	10 (7.8)	0.734
LVH, N (%)	11 (6.9)	2 (6.5)	9 (7.0)	0.909
Family history of premature ASCVD, N (%)	1 (0.6)	0 (0.0)	1 (0.8)	0.622
SBP, mmHg, Mean (SD)	141.9 (20.8)	139.4 (26.1)	142.5 (19.4)	0.038
BMI, kg/m^2 Mean (SD)	27.4 (4.2)	27.6 (3.4)	27.4 (4.4)	0.054
10-Year ASCVD Risk, %, Mean (SD)	12.9 (12.2)	21.1 (17.3)	10.9 (9.6)	0.002

UA urinalysis, LVH left ventricular hypertrophy, ASCVD atherosclerotic cardiovascular disease, SBP systolic blood pressure, BMI body mass index

Table 2. Patient lipid profile (n=159)

Parameter	Overall (n=193)	With diabetes (n=35)	Without diabetes (n=163)	*p*
Total cholesterol (mg/dL) Mean (SD)	203.1 (42.4)	207.6 (43.4)	202.0 (40.2)	0.033
LDL cholesterol (mg/dL) Mean (SD)	121.4 (36.9)	125.0 (51.2)	120.5 (35.2)	0.027
HDL cholesterol (mg/dL) Mean (SD)	51.0 (17.1)	50.8 (13.0)	51.0 (18.0)	0.508
Triglycerides (mg/dL) Mean (SD)	150.3 (77.8)	154.4 (69.2)	149.3 (79.9)	0.989

LDL low density lipoprotein, HDL high density lipoprotein

Table 3A. Cross tabulation of best recommended statin from Philippine Guideline Algorithm vs ACC/AHA Guideline Algorithm

		Philippine Guidelines 2020			
		No Statin Recommended	Moderate Intensity Statin	High Intensity Statin	Total
ACC/AHA 2018	No statin recommended	37	13	0	50
	Moderate intensity statin	50	28	1	79
	High intensity statin	3	21	6	30
	Total	90	62	7	159

Table 3B. Correlation of treatment recommendation and best recommended statin from Philippine Guideline Algorithm vs ACC/AHA Guideline Algorithm

	Kappa	CI	V^2	*p*
Treatment recommendation	0.209	0.078 – 0.340	4.4%	0.003
Specific statin recommendation – PG2020 vs ACC/AHA2018	0.107	-0.0.011 – 0.225	1.1%	0.057

Table 3C. Cross tabulation of treatment recommendation between the Philippine Guideline Algorithm vs ACC/AHA Guideline Algorithm

		Philippine Guidelines 2020		
		Statin not recommended	Statin recommended	Total
ACC/AHA2018	Statin not recommended	37	13	50
	Statin recommended	53	56	109
	Total	90	69	159

patients with and without diabetes were also compared in Table 2. Patients with diabetes mellitus had significantly higher total cholesterol (207.6 vs 202.0 mg/dL, *p*=0.033) and LDL-cholesterol (125.0 vs 120.5 mg/dL, *p*=0.027).

The Kappa agreement coefficient is tabulated in Table 3A. Cohen's κ statistic was run to determine if there was agreement between the two guidelines as to whether or not to start statin therapy. There was slight agreement between the two algorithms, κ = 0.209 or 4.4% (95% CI, 0.078 to 0.340), *p*=0.003. Agreement on the specific type of statin recommended was likewise attempted but the correlation did not reach statistical significance.

The per-patient recommendations of each algorithm are crosstabulated in Table 3B and 3C. Statin treatment was recommended in 69 cases (43.4%) by the PG2020 algorithm. This overlapped with the ACC/AHA2018 by 81.2% with 13 discrepant cases. On the other hand, the ACC/AHA2018 recommended treatment in 109 cases, overlapping with the PG2020 by only 51.4%, with 53 discrepant cases (Table 4). The clinical and laboratory profile of these discrepant cases are tabulated in Table 5. In the subset of 13 patients recommended for treatment by PG2020 but not by ACC/AHA2018, the median age was 55 years, all were females and mostly post-menopausal, 5 (38.5%) were hypertensive, and none were smokers. The median SBP in this subgroup was lower (140 vs 150 mmHg), higher median lipid panel values (TG 236.9 mg/dL, LDL-C 145.1 mg/dL). The computed median 10-year ASCVD risk was significantly lower in this subset with 2.8%.

For the 53 patients recommended for statin therapy by the ACC/AHA2018 but not by the PG2020, the median age was higher at 62 years, and the majority were male (62.3%) and hypertensive (75.5%). Smoking was noted in 30.2%. The lipid panel values were comparatively lower in this subset with median total cholesterol of 179.1 mg/dL and LDL-C of 95.3 mg/dL.

Three patients noted to have an extreme discrepancy in terms of statin recommendation, i.e., high intensity statin is recommended by ACC/AHA 2018 but no statin was recommended by PG2020, are detailed in Table 5. Of note, none of these patients had an LDL-C of 130 mg/dL or more, none had diabetes, all had hypertension and were smokers.

DISCUSSION

The benefit of lowering LDL-C for the primary prevention of ASCVD is largely established. However, there is still much debate as to what levels in a patient's profile constitute dyslipidemia and the threshold levels for treatment. Population-based analysis has largely been inconsistent and determinations of treatment thresholds and targets are mostly individualized.[8–10]

Risk assessment is the cornerstone for the primary prevention of cardiovascular diseases.[11] Several recently published guidelines for the management of dyslipidemia are available. Large studies in the United States and Europe have yielded the creation of risk estimators, such as the ASCVD risk calculator based on pooled cohort equations or PCE used in the ACC/AHA guideline. Similarly, other guidelines make use of other risk calculators such as the Framingham risk calculator (FRC) and the systemic coronary risk evaluation (SCORE) in the Canadian Cardiovascular Society (CCS) and the European Society of Cardiology/

Table 4. Cross tabulation and clinical characteristics of discrepancies in statin treatment recommendations by the Philippine Guidelines vs ACC/AHA Guidelines

	Discrepancies, No. (%), PG2020 and ACC/AHA2018	
	PG2020 Recommended but not by ACC/AHA2018	ACC/AHA2018 recommended but not by PG2020
Overall, No. (%)	13 (18.8)	53 (48.6)
Clinical Characteristics		
Age (years) Median (Min-Max)	55.0 (51-62)	62.0 (45-77)
Sex, Male, N (%)	0 (0.0)	33 (62.3)
Hypertension, N (%)	5 (38.5)	40 (75.5)
Diabetes, N (%)	0 (0.0)	0 (0.0)
Smoking, N (%)	0 (0.0)	16 (30.2)
Post-menopausal, N (%)	12 (92.3)	15 (28.3)
Proteinuria on UA, N (%)	0 (0.0)	6 (11.3)
LVH, N (%)	0 (0.0)	5 (9.4)
Family history of premature ASCVD, N (%)	0 (0.0)	1 (1.9)
SBP (mmHg) Median (Min-Max)	140 (110-160)	150 (100-200)
BMI (kg/m^2) Median (Min-Max)	28.9 (26.7-36.4)	24.9 (16.8-37.6)
Total cholesterol (mg/dL) Median (Min-Max)	236.9 (204.7-282.0)	179.1 (109.5-303.9)
LDL cholesterol (mg/dL) Median (Min-Max)	145.1 (130.7-189.4)	95.3 (76.5-181.0)
HDL cholesterol (mg/dL) Median (Min-Max)	54.4 (45.0-60.0)	46.3 (19.5-73.3)
Triglycerides (mg/dL) Median (Min-Max)	131.2 (37.9-223.5)	135.7 (96.8-482.9)
10-year ASCVD risk	2.8 (1.4-4.8)	12.4 (10.7-43.3)

Table 5. Demographic and risk profile of three patients with extreme discrepancy in statin recommendation (n=3)

Variable	Case 11	Case 138	Case 175
Age, years	57	69	55
Sex	Female	Female	Male
Hypertension	Yes	Yes	Yes
Treated	Yes	Yes	Yes
Diabetes	No	No	No
Smoking	Yes	Yes	Yes
Post-menopausal	Yes	Yes	-
Proteinuria on UA	Yes	Yes	No
LVH	Yes	No	No
Family history of premature ASCVD	No	No	No
SBP (mmHg)	180	150	140
BMI (kg/m^2)	27.1	26.7	24.4
Total cholesterol (mg/dL)	189.2	200.5	242.0
LDL cholesterol (mg/dL)	106.6	117.8	129.1
HDL cholesterol (mg/dL)	21.6	39.3	41.3
Triglycerides (mg/dL)	180.0	217.0	135.7
10-year ASCVD risk (%)	20.7	26.2	20.3

UA urinalysis, LVH left ventricular hypertrophy, ASCVD atherosclerotic cardiovascular disease, SBP systolic blood pressure, BMI body mass index, LDL low density lipoprotein, HDL high density lipoprotein

Table 6. Comparison of ACC/AHA Guideline and Philippine Guideline Algorithms for the primary prevention of dyslipidemia

Parameters	ACC/AHA Guidelines	Philippine Guidelines
Modality of risk estimation	ACC/AHA pooled cohort risk equations	Risk factor counting
Risk parameters	Age, sex, race, SBP, Total cholesterol, HDL cholesterol, LDL cholesterol, diabetes mellitus, smoking, hypertension treatment	Sex, post-menopausal status, smoking, hypertension, BMI, family history, proteinuria, left ventricular hypertrophy
Threshold for treatment	Diabetes without diabetes: • LDL-C ≥70 - <190 mg/dL and • ASCVD risk 5 - <7.5% + risk enhancers or • ASCVD risk > 7.5 - ≤20% or • ASCVD risk >20%	Diabetes without diabetes: • LDL-C ≥130 mg/dL AND • 2 risk factors

European Atherosclerosis Society (ESC/EAS), respectively. These risk estimators facilitated the use of step-by-step algorithms in guiding therapeutic decision-making with, of course, the risk estimators as the pivot point.[12]

The paucity of local data among Asians has limited the availability of risk estimators based on this ethnic population. An extensive literature review of these risk calculators showed that only 2 out of 25 tools were developed for an Asian population.[13] It is for this reason that different countries in Asia utilize different risk estimators. Indonesia, Malaysia, and United Arab Emirates use the ESC/EAS SCORE. Thailand is by far, the only country that uses its very own Thai CV risk score which can estimate risk in the absence of cholesterol measurements. Taiwan and the Philippines employ the use of risk factor counting— duly considering the quantity of risk factors without regard for the relative contribution and interactions between these risk factors. Unlike Thailand, there are no risk estimators available or developed for the Filipino population to date.[3] Additionally, the ASCVD risk score is still used by the majority of Filipino care providers despite the availability of a local guideline since 2015 and an update in 2020.

Several studies have already raised issues as to the applicability of the 10-year ASCVD risk score, particularly the use of these PCEs in populations where they are not based on.[10,14-17] Similar studies have assessed their applicability to other ethnicities. For instance, a study among Malaysians showed that the FRS and SCORE are more suitable alternative risk estimators than the World Health Organization/International Society of Hypertension calculator.[18] Another study among a multi-ethnic Asian cohort showed an overestimation of risk using the FRS.[19]

The ACC/AHA guidelines and the Philippine guidelines are compared in detail in Table 6. The ASCVD risk score

PCE is based on a US-derived pool to estimate a 10-year risk of adverse cardiovascular outcomes. As such, this tool is by design and evidence, specific to race, i.e., for whites and blacks.[20]

In a study involving the use of the ASCVD risk calculator among Asians and Hispanic Americans, 17.6% of whom are Filipinos, the comparison of the predicted incidence of ASCVD by way of PCE and observed major adverse cardiovascular events during a follow-up period showed that the PCE overestimated the risk for Asians. Despite having a disproportionately higher observed event rate than whites and blacks, the Filipino-American predicted event rate was still higher than observed by 0.5%.[10] Additionally, a study on Filipino-American women showed that the ASCVD risk score in its current state tends to overestimate the risk and results in overtreatment of patients unnecessarily. Moreover, it was shown that the addition of measures of central obesity improved clinical discrimination in this cohort of patients.[15]

Several factors play an important role in the estimation of ASCVD risk,[20] especially in a diverse racial population. A systematic review of studies among different minority ethnic groups in Canada including Arabs, Chinese, Hispanic, and Filipinos have shown significant variability of CVD risk factors. Filipinos were found to have higher LDL-C and triglycerides than white cohorts. Moreover, hypertension and diabetes were more prevalent in the Filipino cohort.

When combined, these non-minority factors tend to mask unique CVD risk factors of minority groups such as relatively higher triglycerides and central obesity. Additionally, this would minimize the contribution of these risk factors prevalent in minority groups but are uncommon in the majority group. This can skew the outcomes of risk estimators in favor of the majority.[16,21]

Overall, this study has shown only a slight correlation between the two algorithms compared considering that both algorithms overlapped in only 56 cases to concordantly recommend statin treatment and in only 37 cases to concordantly recommend against statin therapy in our sample of 159 patients. This finding is corroborated by another comparison of dyslipidemia algorithms where in the ESC and ACC/AHA did not align in terms of primary prevention on an individual patient basis.[23] A closer examination of the clinical and laboratory characteristics of the discrepant cases may shed light on this discordance.

The results of this study have shown that among 109 patients recommended for statin therapy by the ACC/AHA2018, 53 (48.6%) were recommended not to start statin by the PG2020. In the analysis of this subset proposed to be started on statin therapy by the ACC/AHA2018 guideline, of note was a significantly lower median total cholesterol (179.1 mg/dL) and LDL-C (95.3 mg/dL) when compared to the PG2020 discrepant subset with 236.9 mg/dL and 145.1 mg/dL, respectively. None of these cases had diabetes.

If we compare the individual algorithms, it is important to consider that for the primary prevention in the non-diabetic subset, the Philippine guidelines will consider treatment if the LDL-C is at least 130 mg/dL with the presence of at least 2 risk factors. In contrast, the ACC/AHA algorithm recommends initiating statins in patients between 40-75 years old and with LDL-C between 70 to 190 mg/dL depending on the percentage of ASCVD risk.[5] The discrepancy is most likely explained by this difference in treatment threshold. It must be acknowledged that, overall, the mean total cholesterol and LDL-C for this study appear to be lower than those seen in national surveys[2,7] which may limit generalizations. Nonetheless, analysis of the discrepant subset of ACC/AHA2018 showed a median 10-year ASCVD risk of 12.4% with a maximum of 43.3%, compared to the PG2020 discrepant subset with a risk score of only 2.8%, hence considered low risk. This is consistent with similar literature previously cited showing overestimation of risk using PCE.[10,14] Although overtreatment would prompt additional cost and unnecessary exposure to potential side effects such as statin-associated muscle symptoms and elevated transaminases,[23] it is also important to recognize the consequences of undertreatment.

A limitation is that this study does not reflect outcomes, and thus may be interpreted in favor of the ACC/AHA guideline. The implications of undertreatment may be more consequential, such as a missed opportunity to start statins amidst the potential risk of future adverse cardiovascular outcomes. This effect may be reflected in the three cases presented in Table 5, showing an extreme discrepancy where high-intensity statin was recommended by the ACC/AHA2018 and otherwise not recommended by the PG2020.

On the other hand, of the 69 patients considered for statin therapy by the PG2020, a discrepant subset of 13 patients (18.8%) is noted. The Philippine guidelines and that of the ACC/AHA differ in terms of parameters included in risk estimation. Unique to the Philippine guidelines are consideration of BMI, postmenopausal status, proteinuria, and left ventricular hypertrophy as additional risk factors. The 2018 update of the ACC/AHA guideline did add the ASCVD risk enhancers such as ethnicity, gender-specific risk factors, and inflammatory conditions. The inclusion of BMI in the assessment of risk is important, considering population-based studies on Filipino-American women have identified that an increased BMI even as low as >23-24.9 kg/m^2 is associated with adverse cardiovascular outcomes.[16,19] In our study, the PG2020 discrepant subset showed a higher proportion of post-menopausal women at 92.3% and a significantly higher median BMI of 28.9 kg/m^2. This strongly supports the iteration that unique peculiarities of population groups contribute significantly to the applicability of the guideline to its target population.

Analysis of both discrepant subsets revealed that the difference in treatment threshold reflected in the two guidelines augments the discordance. Note again that among non-diabetics, the threshold for statin treatment

recommended by the Philippine guideline is 130 mg/dL versus that of 70 mg/dL by the ACC/AHA. The combination of a relatively higher treatment threshold (Philippine guideline) and overestimation of risk (ACC/AHA) skewed the treatment recommendations in opposite directions, portending a lack of overall concordance between the two treatment algorithms.

Both guidelines are concordant on the role of diabetes mellitus, hypertension and smoking in the development of atherogenesis and adverse cardiovascular outcomes as elucidated in the Framingham heart study.[24,25] This is corroborated by the findings of the Five Risks Algorithm study showing diabetes, hypertension, and smoking as independent risk factors in addition to male gender and hypertriglyceridemia.[26]

The results of this study should be interpreted in light of the several limitations which conjointly diminish its generalizability. First, the cross-sectional design limits the detection of differences between the two treatment algorithms in terms of measurable outcomes, particularly, actual cardiovascular events. This limitation highlights the need for longitudinal studies to determine how these differences affect the occurrence of adverse cardiovascular outcomes. Second, the best recommended statin was determined by an algorithm devised from the guideline as released and as interpreted by the authors. Third, it should be reiterated that the mean lipid panel results in this study were lower compared to those found in national surveys. The use of larger research data and standardization of laboratory measurements may improve correlation. Lastly, this study was based on patient and laboratory data taken for clinical purposes and not originally intended for research and as such present inherent limitations. Data concerning the screening for familial hypercholesterolemia (FH) using criteria such as the Dutch lipid network criteria could not be obtained in full and as such could not be included. This study was done in a resource-limited setting, thus may introduce selection bias of included patients. The study, in terms of an analysis of specific statin recommendations, is likewise limited by the sample size.

CONCLUSION

We found that despite the prevalent use of the ACC/AHA guideline in the Filipino population, its agreement with the local guideline was poor overall, highlighting the impact of demographic and ethnic differences in dyslipidemia management. Overestimation of the PCE in this population and the consideration of unique risk factors by the Philippine guidelines favor the applicability of the local guideline. Because of the lack of longitudinal outcome-based studies, whether or not the application of the guideline results to overtreatment or undertreatment, has yet to be elucidated.

Statement of Authorship
All authors certified fulfillment of ICMJE authorship criteria.

Author Contribution Statement
BPM, AJ and JR conceived the study, designed the methodology;, conducted the research, verified research outputs, and reviewed and edited the manuscript. BPM synthesized, curated and presented the study data and prepared the original draft. AJ and JR provided the study materials and supervised the research activity planning. AJ coordinated the research activity planning.

Author Disclosure
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References
1. Lee ZV, Llanes EJ, Sukmawan R, et al. Prevalence of plasma lipid disorders with an emphasis on LDL cholesterol in selected countries in the Asia-Pacific region. Lipids Health Dis. 2021;20(1):33. PMID: 33858442. PMCID: PMC8051043. https://doi.org/10.1186/s12944-021-01450-8.
2. Lin CF, Chang YH, Chien SC, Lin YH, Yeh HY. Epidemiology of Dyslipidemia in the Asia Pacific Region. Int J Gerontol. 2018;12(1):2-6. doi:10.1016/j.ijge.2018.02.010
3. Alshamiri M, Ghanaim MMA, Barter P, et al. Expert opinion on the applicability of dyslipidemia guidelines in Asia and the Middle East. Int J Gen Med. 2018;11:313-22. PMID: 30050317. PMCID: PMC6055898. https://doi.org/10.2147/IJGM.S160555.
4. Gonzalez-Santos LE, Oliva R, Jimeno C, et al. Executive summary of the 2020 Clinical Practice Guidelines for the management of dyslipidemia in the Philippines. J ASEAN Fed Endocr Soc. 2021;36(1):5-11. PMID: 34177082. PMCID: PMC8214350. https://doi.org/10.15605/jafes.036.01.01.
5. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019;73(24):3168-209. PMID: 30423391. https://doi.org/10.1016/J.JACC.2018.11.002.
6. Bujang MA, Baharum N. Guidelines of the minimum sample size requirements for Cohen's Kappa. Epidemiol Biostat Public Health. 2017;14(2):e12267-1.
7. FNRI. Philippine Nutrition Facts and Figures 2013: 8th National Nutrition Survey Overview. Taguig City, Manila: FNRI Institute; 2015. Available from http://enutrition.fnri.dost.gov.ph/assets/uploads/publications/Overview_8thNNS_050416.pdf. Accessed May 27, 2022.
8. Barter PJ, Yamashita S, Laufs U, et al. Gaps in beliefs and practice in dyslipidaemia management in Japan, Germany, Colombia and the Philippines: Insights from a web-based physician survey. Lipids Health Dis. 2020;19(1):131. PMID: 32522192. PMCID: PMC7285462. https://doi.org/10.1186/s12944-020-01265-z.
9. LaRosa JC, Grundy SM, Waters DD, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. N Engl J Med. 2005;352(14):1425-35.
10. Rodriguez F, Chung S, Blum MR, Coulet A, Basu S, Palaniappan LP. Atherosclerotic cardiovascular disease risk prediction in disaggregated Asian and Hispanic subgroups using electronic health records. J Am Heart Assoc. 2019;8(14):e011874. PMID: 31291803. PMCID: PMC6662141. https://doi.org/10.1161/JAHA.118.011874.
11. Wilson PWF, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation. 1998;97(18):1837-47. PMID: 9603539. https://doi.org/10.1161/01.cir.97.18.1837.
12. Tibrewala A, Jivan A, Oetgen WJ, Stone NJ. A comparative analysis of current lipid treatment guidelines: Nothing stands still. J Am Coll Cardiol. 2018;71(7):794-9. PMID: 29447742. https://doi.org/10.1016/j.jacc.2017.12.025.
13. Liau SY, Mohamed Izham MI, Hassali MA, Shafie AA. A literature review of the cardiovascular risk-assessment tools: Applicability among Asian population. Heart Asia. 2010;2(1):15-8. PMID: 27325935. PMCID: PMC4898587. https://doi.org/10.1136/ha.2009.001115.
14. Ancheta IB, Battie CA, Volgman AS, Ancheta CV, Palaniappan L. Cardiovascular disease risk score: Results from the Filipino–American women cardiovascular study. J Racial Ethn Health Disparities. 2017;4(1):25-34. PMID: 27294770. https://doi.org/10.1007/s40615-015-0196-6.
15. Ancheta IB, Battie CA, Tuason MT, Borja-Hart N, Ancheta CV. The prevalence of cardiovascular risk factors and diabetes increases with a body mass index of ≥23 kg/m2 in Filipino American women. Ethn Dis. 2014;24(1):48-54. PMID: 24620448.

16. Gasevic D, Ross ES, Lear SA. Ethnic differences in cardiovascular disease risk factors: A systematic review of North American evidence. Can J Cardiol. 2015;31(9):1169-79. PMID: 26239006. https://doi.org/10.1016/j.cjca.2015.06.017.
17. Goh LGH, Dhaliwal SS, Welborn TA, Lee AH, Della PR. Ethnicity and the association between anthropometric indices of obesity and cardiovascular risk in women: A cross-sectional study. BMJ Open. 2014;4(5):e004702. PMID: 24852299. PMCID: PMC4039846. https://doi.org/10.1136/bmjopen-2013-004702
18. Selvarajah S, Kaur G, Haniff J, et al. Comparison of the Framingham Risk Score, SCORE and WHO/ISH cardiovascular risk prediction models in an Asian population. Int J Cardiol. 2014;176(1):211-8. PMID: 25070380. https://doi.org/10.1016/J.IJCARD.2014.07.066.
19. Chia YC, Gray SYW, Ching SM, Lim HM, Chinna K. Validation of the Framingham general cardiovascular risk score in a multiethnic Asian population: A retrospective cohort study. BMJ Open. 2015;5(5):e007324. PMID: 25991451. PMCID: PMC4442208. https://doi.org/10.1136/BMJOPEN-2014-007324
20. Lloyd-Jones DM, Braun LT, Ndumele CE, et al. Use of risk assessment tools to guide decision-making in the primary prevention of atherosclerotic cardiovascular disease circulation: Special report from the American Heart Association and American College of Cardiology. Circulation. 2019;139:1162-77. PMID: 30586766. https://doi.org/10.1161/CIR.0000000000000638
21. Ancheta IB, Carlson JM, Battie CA, Borja-Hart N, Cobb S, Ancheta CV. One size does not fit all: Cardiovascular health disparities as a function of ethnicity in Asian-American women. Appl Nurs Res. 2015;28(2):99-105. PMID: 25069635. https://doi.org/10.1016/J.APNR.2014.06.001
22. Pavlović J, Greenland P, Deckers JW, et al. Comparison of ACC/AHA and ESC guideline recommendations following trial evidence for statin use in primary prevention of cardiovascular disease: Results from the population-based rotterdam study. JAMA Cardiol. 2016;1(6):708-13. PMID: 27439175. https://doi.org/10.1001/JAMACARDIO.2016.1577
23. Ridker PM, Cook NR. Statins: New American guidelines for prevention of cardiovascular disease. Lancet. 2013;382(9907):1762-5. PMID: 24268611. https://doi.org/10.1016/S0140-6736(13)62388-0
24. Fox CS, Coady S, Sorlie PD, et al. Increasing cardiovascular disease burden due to diabetes mellitus: The Framingham Heart Study. Circulation. 2007;115(12):1544-50. PMID: 17353438. https://doi.org/10.1161/CIRCULATIONAHA.106.658948
25. Torp-Pedersen C, Jeppesen J. Diabetes and hypertension and atherosclerotic cardiovascular disease: Related or separate entities often found together. Hypertension. 2011;57(5):887-8. PMID: 21403088. https://doi.org/10.1161/HYPERTENSIONAHA.110.168583.
26. Devroey D, Vandevoorde J. The "five risks algorithm": An easy tool for cardiovascular risk estimation. Cent Eur J Public Health. 2009;17(3):133-8. PMID: 20020602. https://doi.org/10.21101/cejph.b0016.