

Development and Evaluation of the Atherosclerosis and Metabolic Risk Score Using Data from the National Health and Nutrition Examination Survey

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ABSTRACT

Background: Metabolic disorders are major contributors to cardiovascular morbidity and premature mortality worldwide. Conventional clinical assessment approaches typically evaluate individual metabolic parameters separately and may not adequately capture the complex interactions among metabolic pathways.

Objectives: To develop and evaluate the atherosclerosis and metabolic risk score (AMRS), a composite logarithmic index integrating anthropometric, biochemical, and demographic variables to quantify metabolic burden and classify individuals with metabolic abnormalities.

Materials and methods: A cross-sectional design included 8,402 adults aged 18-85 years from the public-use database of the NHANES [National Health and Nutrition Examination Survey] (2016-2017). The AMRS was calculated as a log-linear combination of nine clinical variables including: age, sex, body mass index (BMI), systolic and diastolic blood pressure (SBP, DBP), triglycerides (TG), total cholesterol (TC), fasting blood glucose (FBG), and HbA1c. Model performance was assessed using ROC curve analysis, subgroup analysis, risk stratification using percentiles, and chi-squared tests. To test the discriminative power of the model, sensitivity analyses were conducted by excluding one outcome-defining variable at a time from the AMRS formula. An external validation was also performed using an independent NHANES 2013-2014 cohort.

Results: AMRS demonstrated good discrimination against glycemic abnormalities and moderate discrimination for lipid and blood pressure disorders. Area under curve values were 0.81 for hyperglycemia, 0.81 for elevated HbA1c, 0.73 for hypertriglyceridemia, 0.71 for hypercholesterolemia, and 0.72 for hypertension. Sensitivity analyses demonstrated that the score retained moderate discriminatory ability even after the removal of outcome-defining variables. External validation showed consistent discrimination across outcomes.

Conclusion: The AMRS provides an integrated quantitative measure of cardiometabolic burden by combining multiple metabolic domains into a single composite index. The score demonstrated stable discrimination and robustness across analyses and may support population-level metabolic risk stratification and classification of metabolic burden.

Keywords: Diabetes Mellitus; Hypertension; Dyslipidemias; Cardiometabolic predictor.

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INTRODUCTION

Metabolic disorders, including obesity, type 2 diabetes mellitus, dyslipidemia, and hypertension, represent a major and increasing global health burden and are important contributors

to cardiovascular disease and premature mortality worldwide [1, 2]. These conditions frequently occur together as a cluster of interrelated metabolic abnormalities commonly referred to as metabolic syndrome, which substantially increases the risk of cardiovascular disease, diabetes, and other chronic complications [3].

Several clinical tools have been developed to estimate cardiometabolic risk, including the Framingham Risk Score and the diagnostic criteria for metabolic syndrome [3, 4]. These methods may not fully capture the complex relationships

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among anthropometric, biochemical, and demographic variables that contribute to metabolic disease. This limitation has stimulated increasing interest in composite indices that integrate multiple metabolic parameters into a single quantitative measure reflecting overall metabolic burden [5, 6].

Therefore, the main aim of this study was to develop and evaluate a composite logarithmic scoring system called the Atherosclerosis and Metabolic Risk Score (AMRS) that combines nine anthropometric, biochemical, and demographic risk indicators using data collected through the National Health and Nutrition Examination Survey (NHANES) to quantify metabolic burden and classify individuals with metabolic abnormalities, such as diabetes, hyperlipidemia and hypertension to address limitations of other indices.

MATERIALS AND METHODS

Study design and data source

This study employed a cross-sectional study design using the publicly available data collected during the NHANES 2016-2017 cycle in accordance with the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) guidelines [7]. The analysis for the present study was performed between June 2025 and January 2026.

Study population

The sample study was based on a subset of respondents who had completed the 2016-2017 cycle of the survey. Respondents with outliers (more than 3 standard deviations from the sample mean) were excluded because these respondents may create undue skewing when evaluating the product of multiple predictors. After applying these inclusion/exclusion criteria, 8,402 respondents remained in the sample.

Variables included in the AMRS

The variables that were incorporated into the AMRS were chosen "a priori" using evidence from both physiological and epidemiologic literature to show that the association of these variables with each other and their relationship to an increased risk for cardiometabolic diseases [8]. These variables include triglyceride (TG) levels; total cholesterol levels; fasting glucose levels; glycated hemoglobin (HbA1c); systolic blood pressure (SBP); diastolic blood pressure (DBP); body mass index (BMI); age; and sex.

Prior to developing the scoring system, we assessed multicollinearity between our selected metabolic domain variables by calculating variance inflation factors (VIF).

Derivation of the AMRS

The composite scores were constructed to evaluate the combined effect of dyslipidemia, glycemic control, hypertension, body fat, and demographic factors on cardiovascular disease through a common mathematical structure. Therefore, the AMRS provides a quantifiable score for ranking individuals according to their degree of metabolic burden and does not serve as a predictive model for the likelihood of future disease states. The AMRS was defined using the following logarithmic formulation:

$$AMRS = \ln \left(\frac{TG \times \text{Total Cholesterol} \times \text{Glucose} \times \text{HbA1c} \times \text{SBP} \times \text{Age}}{BMI \times \text{DBP} \times \text{Sex}} \right)$$

The variables were scaled so that TG, total cholesterol, glucose, and HbA1c were all in units of milligrams per deciliter (mg/dL); SBP and DBP were both in millimeters of mercury (mmHg); BMI was in kilograms per square meter (kg/m²); age was in years; and sex was coded as male = 1 and female = 2.

The multiplicative form of the equation was chosen because it is intended to capture the interaction and accumulation of the individual metabolic risk factors for the development of cardiometabolic disease. Each factor influences an interrelated set of physiological processes involved in lipid metabolism, glycemic control, vascular function, adiposity, and ageing. A multiplicative form captures how each domain affects the overall metabolic burden and potentially the interactions of factors that would not be captured by a simple additive model.

Factors included in the numerator are those shown to affect metabolic stress and cardiometabolic dysregulation. They are TG and total cholesterol (factors of lipid metabolism), glucose and HbA1c (factors in glycemic regulation), SBP (a factor of vascular load), and age (a measure of the cumulative effect of exposure to multiple metabolic risk factors over time).

Factors included in the denominator serve to normalize or scale the relative contribution of each physiological component to the composite score and to minimize the contribution of any one physiological component. BMI is used to normalize the metabolic regulatory environment, while DBP serves to provide a baseline level of vascular tone. Sex is included as a binary scaling factor to account for the established sex-based differences in cardiometabolic risk profiles in males and females.

Because multiplicative combinations of physiological variables will often result in highly skewed distributions, the composite score was log-transformed to help minimize skewness, stabilize variance, and improve the statistical characteristics of the index. The use of the natural logarithm allows for the enables non-linear scaling of the metabolic risk factors.

Sensitivity analysis was performed to examine the impact of the choice of score structure on the score's performance. Comparison of additive and multiplicative forms showed a modest improvement in the ability of the multiplicative form to discriminate among the metabolic outcomes examined, with area under the curve (AUC) values increasing by approximately 0.03 to 0.05 compared to the additive form. These results support the use of the selected multiplicative form of the AMRS.

Outcome definition

The diagnosis of diabetes was made when a participant's HbA1c level exceeded 6.5% as per the American Diabetes Association definition [9]. A participant was diagnosed with hypertriglyceridemia if their fasting plasma triglyceride level was ≥ 150 mg/dL. According to the Adult Treatment Panel III (ATP III), a participant was classified as having hypercholesterolemia if their fasting total cholesterol level was ≥ 200 mg/dL. Hypertension was diagnosed if a participant had a resting SBP ≥ 140 mmHg and/or a resting DBP ≥ 90 mmHg as outlined in the Seventh Joint National Committee (JNC 7) [10].

Each metabolic outcome was coded as a binary variable (1 = presence of the condition; 0 = absence of the condition) for use in logistic regression analyses.

Performance assessment

Logistic regression models based on AMRS were developed to evaluate the association of AMRS with each of the metabolic conditions (hypertension, diabetes, hypertriglyceridemia, hypercholesterolemia). The models were evaluated using the AUC, with a 95% confidence interval (CI) derived from 1,000 bootstrap samples. An overall measure of model accuracy was also quantified using the Brier Score. The sensitivity and specificity of the models were estimated at the optimal ROC threshold selected using the Youden Index.

Internal validation

Internal validation of the model was performed using a 10-fold stratified cross-validation method. In addition, model optimism was using 1000 bootstrap iterations of apparent and bias corrected AUCs. There was a mean optimism of 0.012 (CI 95%: 0.009-0.016), there was very little evidence of overfitting.

External validation

Validation of the AMRS was conducted independently in a new dataset from the NHANES 2013-2014 survey cycle. After removing those with missing data, 6500 individuals remained in the validation cohort.

Risk stratification and cutoff determination

To allow clinical interpretation of the AMRS, risk levels were defined using a percentile-based threshold method based on the distribution of the AMRS scores among the population that participated in this study.

Sensitivity analysis

The AMRS was used to assess the possibility of predictor-outcome circularity by removing variables that were directly part of the clinical definition of each outcome. The reduced versions of the AMRS were then used to construct logistic regression equations and to compare their discriminative ability using the ROC curve and AUC.

Furthermore, to establish that excluding extreme data did not affect model performance, a further sensitivity analysis was conducted. A comparison was made between models estimated using all available data and those where all values greater than three standard deviations away from the sample mean were removed; the discrimination, calibration, and total predictive capability of the models were assessed within each data set by comparing the AUC, the calibration slope, and the Brier Score, and the difference in the metric for each model type determined if the removal of extreme values had a material effect on the AMRS's performance.

Subgroup analysis

The AMRS ability to discriminate was analyzed in relation to age, sex, and BMI categories. In each subgroup, the ROC curve and AUC value were determined. The differences in discrimination between the subgroups were formally tested using DeLong's test.

Distributions of outcome across risk categories

The distribution of metabolic abnormalities was measured across the risk categories defined by the AMRS. The distribution of metabolic abnormalities was measured risk categories

using Pearson's Chi-squared statistic to assess higher AMRS categories were associated with greater levels of metabolic burden.

Comparison with established risk indices

ROC analysis was used to compare the performance of the AMRS with several established cardiometabolic indices. Three binary outcomes were evaluated: type 2 diabetes mellitus, hypertension, and hyperlipidemia. For each participant, the following indices were calculated using available clinical and biochemical variables: AMRS, triglyceride-glucose index (TyG) [11], Framingham Risk Score (FRS) [12], cardiometabolic index (CMI) [13], and lipid accumulation product (LAP) [14]. The differences in AUC values were statistically compared to using DeLong's test for correlated ROC curves.

Statistical Analysis

Statistical analysis was completed using Python 3.9.7. The data was cleaned/preprocessed/managed using pandas v1.3.3, NumPy v1.21.2. Regression analysis was completed using statsmodels v0.12.2 and SciPy v1.7.1. Discrimination of AMRS and the comparator indices was evaluated by calculating ROC curves and then determining AUC for each outcome. Confidence intervals for the AUC were determined through bootstrapping (1000 iterations). Additionally, pairwise comparisons of ROC curves were performed using DeLong's Test for correlated ROC curves. Internal validation of the model was completed using 10-Fold Stratified Cross-Validation, and optimism of the model was assessed using bootstrapping. Additionally, a subgroup analysis was conducted using predefined categories of age, sex, and BMI. ROC curves and AUC values were completed for each subgroup, and statistical differences in the ROC curves for each subgroup were evaluated using DeLong's Test. All statistical tests were two-tailed with a significance level of < 0.05 . Visualisation of the data was completed using matplotlib (v3.4.3), seaborn (v0.11.2), and plotly (v5.3.1).

RESULTS

Discrimination performance

A receiver operating characteristic curve analysis revealed that AMRS had good to excellent discrimination across metabolic disease states (Table 1 and Figure 1). The Highest discrimination was shown for glucose abnormalities. DeLong's test of pairwise comparisons of ROC curves indicated that discrimination for glucose abnormalities was significantly greater than that found for lipid-related abnormalities and hypertension (all P-values < 0.05).

Logistic regression models

Logistic Regression Models showed that the AMRS was positively associated with each of the assessed metabolic abnormalities. As such, higher levels of AMRS were consistently associated with higher odds of metabolic abnormalities across the three primary areas of assessment (glucose, lipids, and blood pressure).

External validation

The discrimination properties of the AMRS remained constant across various metabolic conditions in the external data set (Figure 2).

Table 1. Discriminative performance of AMRS for metabolic disorders.

Outcome	AUC (95% CI)	Optimal threshold (Youden index)	Sensitivity	Specificity	P-value
Hypertriglyceridemia	0.729 (0.709–0.748)	0.310	0.660	0.654	0.001
Hypercholesterolemia	0.704 (0.684–0.723)	0.233	0.852	0.474	0.001
Hyperglycemia	0.812 (0.793–0.830)	0.084	0.827	0.658	0.001
Hypertension	0.714 (0.694–0.733)	0.179	0.810	0.527	0.001
High HbA1c	0.808 (0.789–0.826)	0.110	0.840	0.635	0.001

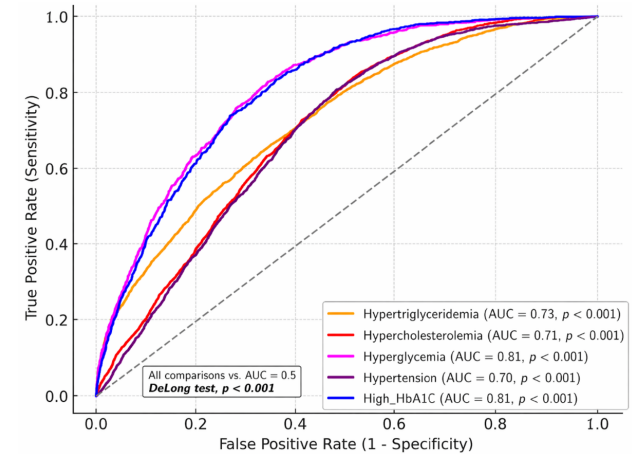


Figure 1. ROC curves illustrating the discriminative performance of the atherosclerosis and metabolic risk score for multiple metabolic abnormalities.

Risk stratification and determination of cut points

The 25th percentile of the AMRS was found to occur at an approximate value of 15.77, while the 75th percentile occurred at an approximate value of 17.56. Using these two values, three categories were established (Figure 3): low-risk category = AMRS < 15.77; moderate-risk category = 15.77–17.56; high-risk category = AMRS > 17.56.

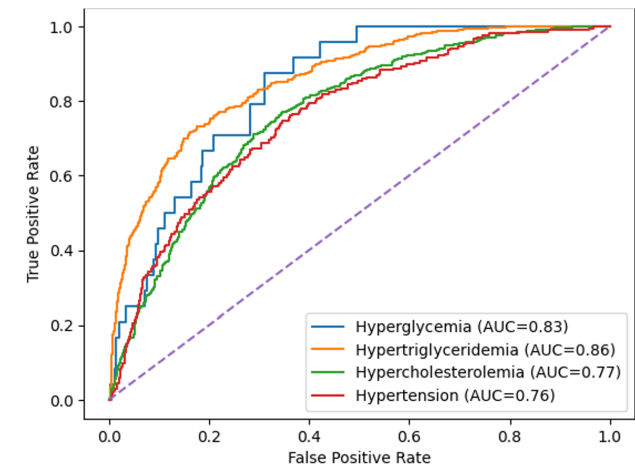


Figure 2. External validation ROC curves of the atherosclerosis and metabolic risk score.

Sensitivity analyses

The sensitivity analyses shown in Figure 4, were conducted across five metabolic outcomes (hyperglycemia, elevated HbA1c, hypertriglyceridemia, hypercholesterolemia, and hypertension) to evaluate the robustness of the AMRS and to assess potential predictor-outcome circularity. Regardless of the exclusion of variables that define the metabolic outcome, the AMRS has sufficient discriminative capability to be useful as a tool for assessing risk. A sensitivity analysis was also done to determine whether removing extreme values ($> \pm 3SD$) would influence how well the model performed. When compared, there was a difference of < 0.003 (AUC) for all evaluated outcomes, and essentially no change in discrimination between models. There was also almost no change (< 0.003) in calibration slope between models, indicating little change in the relationship between predicted and actual outcome. The Brier score, a measure of overall predictive accuracy, changed negligibly (< 0.001).

Subgroup analysis

There was evidence of increasing discriminative capability with decreasing age (Figure 5). When stratified by sex, both men (AUC ≈ 0.80) and women (AUC ≈ 0.77) demonstrated similar discriminative capability. When the data were stratified by BMI category, the AMRS demonstrated AUC values of approximately 0.82 (normal weight), 0.80 (overweight), and 0.78 (obese).

Distribution of metabolic outcomes across AMRS risk categories

Participants classified into higher AMRS categories demonstrated a markedly greater prevalence of metabolic abnormalities. The prevalence of diabetes increased substantially from the low-risk group to the high-risk group, with a similar progressive increase observed for hypertension and hy-

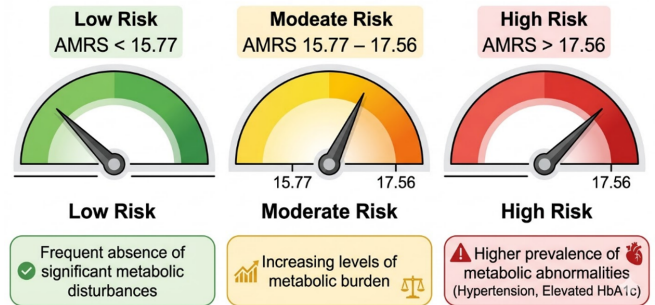


Figure 3. Distribution-based risk stratification of atherosclerosis and metabolic risk score using percentile cutoffs.

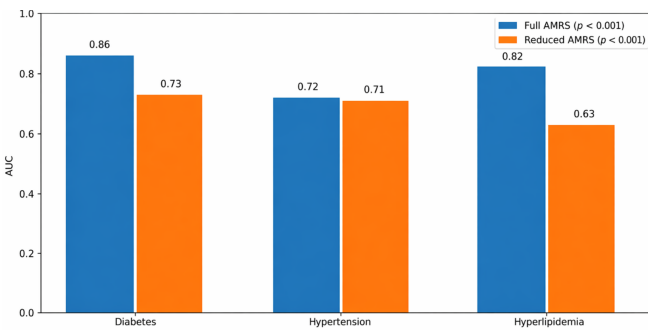


Figure 4. Sensitivity analysis comparing discrimination of the full and reduced AMRS across metabolic outcomes, with all comparisons showing P-value = 0.001 (DeLong test).

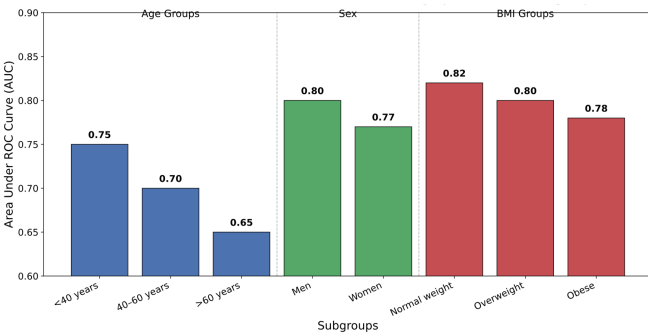


Figure 5. Discriminative performance of AMRS across demographic and body mass index (BMI) subgroups.

perlipidemia. This gradient was most pronounced for hyperlipidemia, which showed the largest increase across AMRS categories (Table 2).

Comparing the discriminative ability of AMRS and other metabolic risk indices

With respect to type 2 diabetes, AMRS had the highest discriminative ability. Pairwise comparisons using DeLong’s test confirmed that the discrimination of AMRS was significantly higher than that of TyG, FRS, CMI, and LAP (all P-values = 0.001). Regarding hypertension, AMRS demonstrated moderate discriminative ability (AUC ≈ 0.72), DeLong’s comparisons indicated that FRS performed significantly better than AMRS for hypertension prediction (P-value < 0.001). However, AMRS remained significantly superior to TyG, CMI, and LAP (all P-values < 0.001). Regarding hyperlipidemia, AMRS shows (AUC ≈ 0.82), DeLong’s test indicated that

Table 2. Distribution of metabolic outcomes across AMRS risk categories.

AMRS Risk Category	Diabetes (%)	Hypertension (%)	Hyperlipidemia (%)
Low	0.2	3.4	7.3
Moderate	6.9	21.2	45.8
High	34.6	34.8	78.7

AMRS demonstrated significantly higher discrimination than FRS and LAP (Figure 6).

DISCUSSION

The AMRS is a composite risk assessment instrument which includes elements of metabolic, anthropometric, and demographic data. As such, it provides a single value (or score) that represents an integrated measure of the risk or burden of cardiovascular disease due to metabolic factors.

The variables included in this score , TGs and total cholesterol, represent an important determinant of cardiovascular risk [15]. Fasting glucose and HbA1c capture short-term and long-term glycemic status, respectively, and are widely used indicators of glucose metabolism and diabetes risk [16]. SBP and DBP represent vascular load and hemodynamic stress and are strongly associated with cardiovascular morbidity [17]. BMI serves as a measure of adiposity and obesity-related metabolic dysfunction [18]. Age was included as a continuous variable to represent cumulative exposure to metabolic risk factors over time [19], while sex was included as a binary variable to account for known physiological differences in metabolic regulation and cardiometabolic risk between men and women [20].

Findings from this study clearly indicated that each participant’s AMRS score was directly correlated to the number of metabolic abnormality criteria that he/she met. Furthermore, the AMRS had the highest discriminative power for identifying participants with abnormal glucose metabolism compared with those without such abnormalities. Discriminative power for detecting lipid disorders and blood pressure-related disorders was also found to be moderate to high when utilizing the AMRS.

These findings are consistent with previous studies suggesting that combining physiological domains of interest into a single composite index can provide a better representation of the overall burden of metabolic disorder than using single clinical markers alone so a composite metabolic indices which have attempted to quantify the interactions of metabolic components related to cardiometabolic disease has been developed such as the TyG index, which is often used as a surrogate marker for insulin resistance and metabolic dysfunction [11].

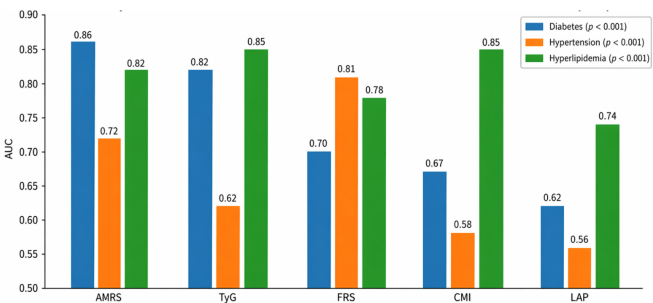


Figure 6. Comparative discriminative performance of cardiometabolic risk indices across metabolic outcomes. (AUC) is shown for the Atherosclerosis and Metabolic Risk Score (AMRS), triglyceride–glucose index (TyG), Framingham Risk Score (FRS), cardiometabolic index (CMI), and lipid accumulation product (LAP) across diabetes, hypertension, and hyperlipidemia. All comparisons were statistically significant (P-value = 0.001, DeLong test).

Similarly, the LAP was developed to reflect lipid overaccumulation and has demonstrated improved performance compared with BMI in identifying cardiovascular risk [14]. The current cardiometabolic risk assessment tools (such as Framingham Risk Score; Metabolic Syndrome Criteria) were developed to assess specific disease outcomes (not to measure an individual's total metabolic burden). The current indices such as CMI provide a single composite risk factor that can be used to integrate anthropometric and lipid related variables. In contrast, the AMRS incorporates all the lipid, glycaemic, hemodynamic, anthropometric, and demographic variables to generate a single risk factor that reflects the various interacting physiological processes involved in metabolic dysfunctions. In addition, the AMRS demonstrated a very high level of discriminant power relative to established indices for the assessment of glycemic disorders [3, 12]. Consequently, these approaches may not fully capture the complex relationships among adiposity, lipid metabolism, glucose regulation, and vascular stress that collectively contribute to the development of cardiometabolic disease. Previous studies have shown that combining multiple metabolic markers can improve the identification of individuals with metabolic abnormalities compared with single-parameter approaches [21].

An important implication of this approach is that the AMRS provides a continuous measure of metabolic burden, which may facilitate earlier identification of individuals with elevated cardiometabolic risk profiles.

In addition, advances in computational modeling and multi-parameter clinical algorithms have increasingly emphasized the importance of integrating multiple physiological variables when assessing metabolic risk [22, 23].

The stability of the AMRS is further demonstrated by external validation in an independent cohort, in which the AMRS exhibited consistent discriminative ability across multiple metabolic endpoints. Additionally, sensitivity analyses were conducted to determine whether the removal of variables directly involved in the definition of outcomes impacted the predictive ability of the AMRS. Overall, removal of these variables resulted in a reduction in the discriminative ability of the AMRS; sensitivity analyses demonstrated that exclusion of extreme observations had negligible effects on discrimination.

This study has certain limitations; first, because it uses cross-sectional survey data, it is impossible to establish a temporal relationship between the variables analyzed. Therefore, the AMRS should be viewed as a classification or metabolic burden stratification index that represents the current metabolic status of an individual, rather than as a predictor of future disease incidence. Second, some inflammatory markers and sex-related metabolic differences may influence cardiometabolic risk profiles and contribute to heterogeneity in metabolic syndrome expression [24, 25]. Finally, although the score demonstrated stable performance across datasets, further validation in independent populations and diverse geographic settings would strengthen evidence supporting its generalizability. Future research should evaluate the AMRS in prospective cohort studies to determine whether the score can capture longitudinal changes in metabolic health and predict incidents of cardiometabolic disease. Integration of AMRS calculation into electronic health record systems may also facilitate automated metabolic risk assessment and support preventive clinical decision-making in routine clinical practice.

CONCLUSION

AMRS was developed as a composite index that integrates metabolic, anthropometric, and demographic variables to quantify overall cardiometabolic burden. In this NHANES-based analysis, the score demonstrated consistent discrimination across several metabolic abnormalities and remained stable following internal and external validation.

ETHICAL DECLARATIONS

Acknowledgments

The authors acknowledge the National Center for Health Statistics and the Centers for Disease Control and Prevention for providing the publicly available NHANES database used in this research.

Ethics Approval and Consent to Participate

This study utilized publicly available data from the National Health and Nutrition Examination Survey conducted by the National Center for Health Statistics, Centers for Disease Control and Prevention. NHANES protocols were reviewed and approved by the NCHS Research Ethics Review Board, and written informed consent was obtained from all participants prior to participation. Because the data analyzed in this study are publicly available and fully de-identified, the present secondary analysis was exempt from additional institutional ethical review.

Consent for Publication

Not applicable. The manuscript does not contain any individual-level identifiable data.

Availability of Data and Material

The datasets analyzed during the current study are publicly available in the NHANES repository: <https://www.cdc.gov/nchs/nhanes>. All data used in this study are open-access and can be freely downloaded without restriction.

Competing Interests

The authors declare that there is no conflict of interest.

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Use of Artificial Intelligence

The authors confirm that no artificial intelligence tools were used for data analysis, statistical modeling, study design, or generation of scientific results. Large language models or generative AI tools may have been used only for limited language editing and manuscript clarity. The authors fully reviewed and verified all content and take complete responsibility for the accuracy, originality, and integrity of the manuscript.

Authors' Contributions

Conceptualization: Ahmed Naseer Kaftan. Methodology: Ahmed Naseer Kaftan. Data curation: Hasanat Aljabery. Statistical analysis: Ahmed Naseer Kaftan. Model development (AMRS): Ahmed Naseer Kaftan. Writing-original draft: Hasanat Aljabery. Writing-review and editing: Ahmed Naseer Kaftan. Supervision: Ahmed Naseer Kaftan. All authors read and approved of the final manuscript.

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