ORIGINAL ARTICLE

CONTENTS

Development and validation of a non-invasive risk prediction nomogram for metabolic syndrome in young adults: A cross-sectional study based on NHANES 2011–2018

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ABSTRACT

Aim: To develop and validate non-invasive predictive models for detecting metabolic syndrome in young adults using NHANES 2011–2018 data to enable effective screening without laboratory testing.

Materials and Methods: Using data from the National Health and Nutrition Examination Survey (NHANES 2011–2018), we established a homogeneous cohort of Non-Hispanic White individuals (N=2,911). Gender-specific multivariate logistic regression models were developed to predict MetS risk using strictly non-invasive anthropometric and clinical parameters, including age, waist-to-height ratio (WHtR), and blood pressure.

Results: The resulting algorithms demonstrated robust discriminatory power, achieving an area under the ROC curve (AUC) of 0.87 for males and 0.84 for females. WHtR emerged as the most significant independent predictor across both genders (Adjusted OR 1.10 per 0.01 unit increment; $p < 0.001$). Notably, while chronological age was significantly associated with risk in males (OR 1.07), it lacked statistical significance in the female population ($p = 0.904$). This divergence suggests a dominant role of phenotypic features over chronological aging in shaping MetS risk among young women.

Conclusions: The developed nomograms and risk heatmaps enable precise cardiometabolic risk stratification in primary care without requiring laboratory resources. This non-invasive framework provides a scalable and practical tool for early intervention and personalized health management in young adults.

KEY WORDS: metabolic syndrome, risk prediction, nomogram, young adults, non-invasive diagnostics, NHANES, validation, waist-to-height ratio

Wiad Lek. 2026;79(5):1031-1043. doi: 10.36740/WLek/220835 DOI

INTRODUCTION

Metabolic syndrome (MetS) is a pressing global health challenge characterized by a cluster of interconnected risk factors, including central obesity, elevated blood pressure, hyperglycemia, hypertriglyceridemia, and reduced high-density lipoprotein (HDL) cholesterol. Recent evidence suggests a sharp rise in the prevalence of this condition not only among older populations but also within younger age groups, transforming MetS into a systemic threat to healthcare stability worldwide [1-3]. Epidemiological data underscore the scale of this crisis: Bayesian modeling of 3,236 data points covering 45.5 million adults estimates that global MetS prevalence increased from 14.7% (95% CI: 13.1–16.7) in women and 9.0% (95% CI: 7.5–10.8) in men in 2000 to 31.0% (28.5–33.9) and 25.8% (23.5–28.5), respectively, by 2023 [1]. This more than doubling in prevalence in less than a quarter-century indicates a critical decline in population metabolic health.

The shift towards younger demographics is particularly concerning. Among adolescents with obesity, the prevalence of MetS averages 31.2% (95% CI: 26.5–36.2), with regional rates peaking in South America at 43.1% [4]. In the United States, MetS frequency among adolescents is closely linked to socioeconomic determinants, specifically household food insecurity. Data from NHANES (2001–2020) indicates that adolescents from food-insecure households face a significantly higher risk of developing MetS compared to those with stable nutrition [5]. This highlights MetS as a societal issue rooted in unequal access to healthy nutrition and preventive medical care.

Conventional diagnosis per NCEP ATP III (National Cholesterol Education Program Adult Treatment Panel III) criteria requires the presence of at least three of five components: increased waist circumference, hypertriglyceridemia (≥150 mg/dL), reduced HDL cholesterol (<40 mg/dL in men, <50 mg/dL in women), hypertension (SBP ≥130 mmHg or DBP ≥85 mmHg), and elevated fasting glucose (≥100 mg/dL) [6,7]. While clinically robust, this approach faces major hurdles in mass screening, especially among young adults, due to the requirement for laboratory-based fasting tests. The necessity of an 8–12 hour fast is a significant logistical barrier. Young adults typically lead active lifestyles with irregular eating patterns and low rates of routine medical visits. The fasting requirement necessitates visit planning and potential time loss from work or education, leading to poor screening uptake and an underestimation of the actual MetS burden in this demographic.

Furthermore, traditional health assessment tools for obesity have notable drawbacks in the modern epidemiological context, where «metabolically unhealthy» phenotypes are increasingly common even among individuals with normal or slightly elevated body weight. Many diagnostic instruments fail to account for key pathophysiological mechanisms such as insulin resistance, central obesity, or visceral adipose tissue dysfunction, thus underestimating the risk of cardiovascular disease and type 2 diabetes. Body Mass Index (BMI) remains the most widely used tool, yet it lacks the sensitivity to distinguish between muscle and fat mass or account for fat distribution. Consequently, BMI often misses individuals with the «skinny fat» phenotype—those with a normal body weight but high visceral fat and metabolic abnormalities. Research shows that up to 30% of individuals with a normal BMI may exhibit signs of MetS, particularly in the presence of abdominal obesity [5,8]. Moreover, most clinical scales, including those from NCEP ATP III or the Framingham Heart Study, were derived from middle-aged or elderly cohorts and may lack sensitivity for early-stage metabolic shifts in younger groups [5].

The objective of this study was to develop and validate high-precision, non-invasive predictive models for MetS that do not require blood chemistry analysis, specifically tailored for young adults (aged 18–44 years). Unlike universal screening tools, we constructed gender-specific multivariate models to account for the differential impact of risk factors on MetS development. Utilizing a large, representative sample from NHANES (2011–2018), we developed practical diagnostic instruments—nomograms and risk heatmaps—that enable clinicians to instantly assess individual risk during a primary care consultation. This approach facilitates effective mass screening and early identification of high-risk groups without invasive, costly laboratory tests, thereby promoting timely preventive interventions.

AIM

The objective of this study was to develop and validate high-precision, gender-specific predictive models and practical visual tools (nomograms and heatmaps) for detecting metabolic syndrome in young adults (aged 18–44) using strictly non-invasive anthropometric and clinical parameters from the NHANES 2011–2018 dataset, thereby facilitating mass screening without the need for invasive laboratory testing.

MATERIALS AND METHODS

STUDY DESIGN AND DATA SOURCE

This study is based on a cross-sectional analysis of data from the National Health and Nutrition Examination Survey (NHANES) covering the period from 2011 to 2018. NHANES is a nationally representative survey of the United States population conducted by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC) [9]. The NHANES protocols were approved by the NCHS Research Ethics Review Board, and all participants provided informed written consent prior to examination. To ensure the results are representative at the national level, sample weights (MEC weights, WTMEC2YR) were incorporated into all statistical calculations [10].

STUDY POPULATION CHARACTERISTICS

The target sample was derived from the Non-Hispanic White cohort.

INCLUSION CRITERIA

1. age between 18 and 44 years;
2. male or female gender;
3. availability of complete information regarding metabolic syndrome components.

EXCLUSION CRITERIA

1. current pregnancy;
2. missing anthropometric or laboratory data;
3. age outside the specified range.

Following a Complete Case Analysis for variables with a missing data rate of less than 5%, the final sample comprised 2,911 individuals.

OUTCOME DEFINITION

The primary outcome (Risk_Status) was the presence or absence of metabolic syndrome (MetS), defined according to NCEP ATP III criteria [11]. A diagnosis of MetS was established if at least three of the following five criteria were met:

1. Abdominal obesity: Waist circumference > 102 cm for men and > 88 cm for women.
2. Hypertriglyceridemia: Triglyceride levels ≥ 150 mg/dL (1.7 mmol/L).
3. Reduced HDL cholesterol: < 40 mg/dL (1.03 mmol/L) for men and < 50 mg/dL (1.29 mmol/L) for women.

4. Hypertension: Systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg.
5. Fasting hyperglycemia: Plasma glucose ≥ 100 mg/dL (5.6 mmol/L).

PHYSICAL EXAMINATION AND ANTHROPOMETRY

Anthropometric measurements were performed by trained personnel in a Mobile Examination Center (MEC) following standardized protocols [12].

• Waist Circumference: Measured with a horizontal tape measure immediately above the superior border of the iliac crest at the end of a normal expiration.

• Height and Weight: Determined using a digital stadiometer and Mettler-Toledo scales. These data were used to calculate Body Mass Index (BMI) and the primary predictor—waist-to-height ratio (WHtR), defined as waist circumference (cm) divided by height (cm).

• Blood Pressure: Measured three times using the auscultatory method with a Baumanometer mercury sphygmomanometer after a 5-minute rest. The arithmetic mean of the three readings was used for analysis.

LABORATORY PROCEDURES

Blood samples were collected via venipuncture following an 8–9 hour fast.

• Lipid Profile and Glucose: Total cholesterol was determined using enzymatic methods on Roche Modular P or Cobas 6000 analyzers. HDL-C levels were measured via a direct immunoassay. Triglycerides and glucose were measured using enzymatic methods on Roche analyzers.

• Calculated Indices: The Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) was calculated as follows:

The Lipid Accumulation Product (LAP) was calculated using gender-specific formulas incorporating waist circumference and triglycerides.

STATISTICAL ANALYSIS AND MODEL DEVELOPMENT

Data processing was performed in the RStudio environment using the survey, rms, glm, and gtsummary packages (R version 4.3.1).

• Modeling: Two gender-specific binary logistic regression models were constructed to predict MetS risk. Non-invasive predictors included age, WHtR, smoking status, sleep duration, and blood pressure (SBP, DBP). The logit formula (z) was defined as:

$$z = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_k x_k$$

• Validation: The dataset was split into training (70%) and testing (30%) sets. Discriminatory power was assessed using the Area Under the ROC Curve (AUC-ROC). Model calibration was verified via Calibration Plots, and clinical utility was evaluated using Decision Curve Analysis (DCA).

• Visualization: For practical implementation, nomograms and risk heatmaps were generated based on the regression coefficients. Statistical significance was set at $p < 0.05$.

DATA AVAILABILITY AND ETHICAL CONSIDERATIONS

The datasets utilized in this study are publicly available on the official NHANES CDC repository website [12]. This study adheres to the TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis) statement for reporting the development of predictive models for medical applications [13].

ETHICS

The NHANES study protocols were reviewed and approved by the NCHS Research Ethics Review Board (ERB). All participants provided informed written consent. As this study is a secondary analysis of publicly available, de-identified data, it was exempt from additional institutional review board (IRB) review. The study was conducted in accordance with the Declaration of Helsinki.

The datasets analyzed during the current study are publicly available in the National Health and Nutrition Examination Survey (NHANES) repository, maintained by the Centers for Disease Control and Prevention (CDC). Data can be accessed via the official website: https://www.cdc.gov/nchs/nhanes/index.htm.

FRAMEWORK

This work is a continuation of previous research conducted within the framework of the research program "Informativeness of indicators of the body composition in the diagnosis, treatment and prevention of diseases of internal organs" (state registration number 0122U201421).

RESULTS

POPULATION CHARACTERISTICS

A homogeneous cohort of Non-Hispanic White young adults (aged 18–44 years) was established for model

Table 1. Anthropometric and biochemical characteristics of the study population (M ± SD or n, %)

Parameter	Total Sample (n=2,911)	Men (n=1,477)	Women (n=1,434)	p-value
Age, years	31.4 ± 7.8	31.2 ± 7.9	31.6 ± 7.7	0.165
WC, cm	96.2 ± 16.4	99.8 ± 15.2	92.5 ± 16.8	<0.001
WHtR	0.56 ± 0.09	0.57 ± 0.08	0.56 ± 0.10	0.004
SBP, mmHg	119.4 ± 13.6	123.2 ± 12.4	115.5 ± 13.8	<0.001
DBP, mmHg	72.8 ± 11.2	74.5 ± 10.8	71.1 ± 11.4	<0.001
Glucose, mg/dL	102.3 ± 24.5	104.8 ± 26.1	99.7 ± 22.4	<0.001
Triglycerides, mg/dL	138.4 ± 98.2	152.6 ± 112.4	123.8 ± 78.5	<0.001
HDL-C, mg/dL	52.6 ± 14.8	47.4 ± 12.6	57.9 ± 15.2	<0.001
Smoking (%)	880 (30.2%)	466 (31.6%)	414 (28.9%)	0.029
Sleep, hours	7.3 ± 2.5	7.1 ± 1.4	7.5 ± 3.6	<0.001
MetS (Diagnosis), n (\%)	652 (22.4%)	318 (21.5%)	334 (23.3%)	0.252

Abbreviations: WC, waist circumference; WHtR, waist-to-height ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; MetS, metabolic syndrome.
Source: compiled by the authors of this study

development and validation. After data cleaning and excluding participants with incomplete anthropometric or laboratory records, the final sample comprised 2,911 individuals. The gender distribution was balanced: 1,477 men (50.7%) and 1,434 women (49.3%). National representativeness was ensured by applying MEC sample weights [10].

METABOLIC SYNDROME PREVALENCE

According to NCEP ATP III criteria, MetS prevalence was 22.4% (n=652). Although prevalence was slightly higher in women (23.3%, n=334) than in men (21.5%, n=318), this difference was not statistically significant (p=0.252), indicating a comparable metabolic burden across sexes in this demographic.

DEMOGRAPHIC AND ANTHROPOMETRIC PARAMETERS

The mean age of the cohort was 31.4 ± 7.8 years, with no significant gender difference (p=0.165). Pronounced sexual dimorphism was observed in key anthropometric measures: men had significantly larger waist circumferences (99.8 ± 15.2 cm vs. 92.5 ± 16.8 cm, p<0.001) and higher WHtR (0.57 ± 0.08 vs. 0.56 ± 0.10, p=0.004).

CLINICAL AND LABORATORY PROFILES

Detailed comparisons of MetS components are presented in Table 1:

- **Hemodynamics:** Men had significantly higher systolic (123.2 ± 12.4 mmHg) and diastolic (74.5 ± 10.8 mmHg) blood pressure than women (115.5 ± 13.8 and 71.1 ± 11.4 mmHg, respectively; p<0.001).
- **Metabolism:** Fasting glucose (104.8 ± 26.1 mg/dL) and triglycerides (152.6 ± 112.4 mg/dL) were elevated in men (p<0.001). Conversely, HDL-C levels were higher in women (57.9 ± 15.2 mg/dL vs. 47.4 ± 12.6 mg/dL, p<0.001), consistent with known physiological lipid variations.
- **Behavioral factors:** Women reported longer sleep duration (7.5 ± 3.6 vs. 7.1 ± 1.4 hours, p<0.001), while active smoking was more frequent among men (31.6% vs. 28.9%, p=0.029).

These baseline data reveal a substantial MetS burden in a relatively young population, necessitating precision screening tools that account for these gender-specific clinical profiles.

PREDICTORS OF METABOLIC SYNDROME (MULTIVARIATE ANALYSIS)

Two gender-specific multivariate logistic regression models were constructed to identify independent determinants of metabolic syndrome (MetS) and develop predictive algorithms. The models integrated a comprehensive set of non-invasive parameters: waist-to-height ratio (WHtR), chronological age, hemodynamic indicators (SBP, DBP), and behavioral factors (smoking status and sleep duration).

THE ROLE OF ANTHROPOMETRIC INDICATORS AND SCALING

Waist-to-height ratio (WHtR) emerged as the most potent shared predictor of MetS across both cohorts. To enhance clinical interpretability, coefficients were linearly scaled by 0.01 units. Each 0.01 increase in WHtR (equivalent to a 1% increment) was associated with a

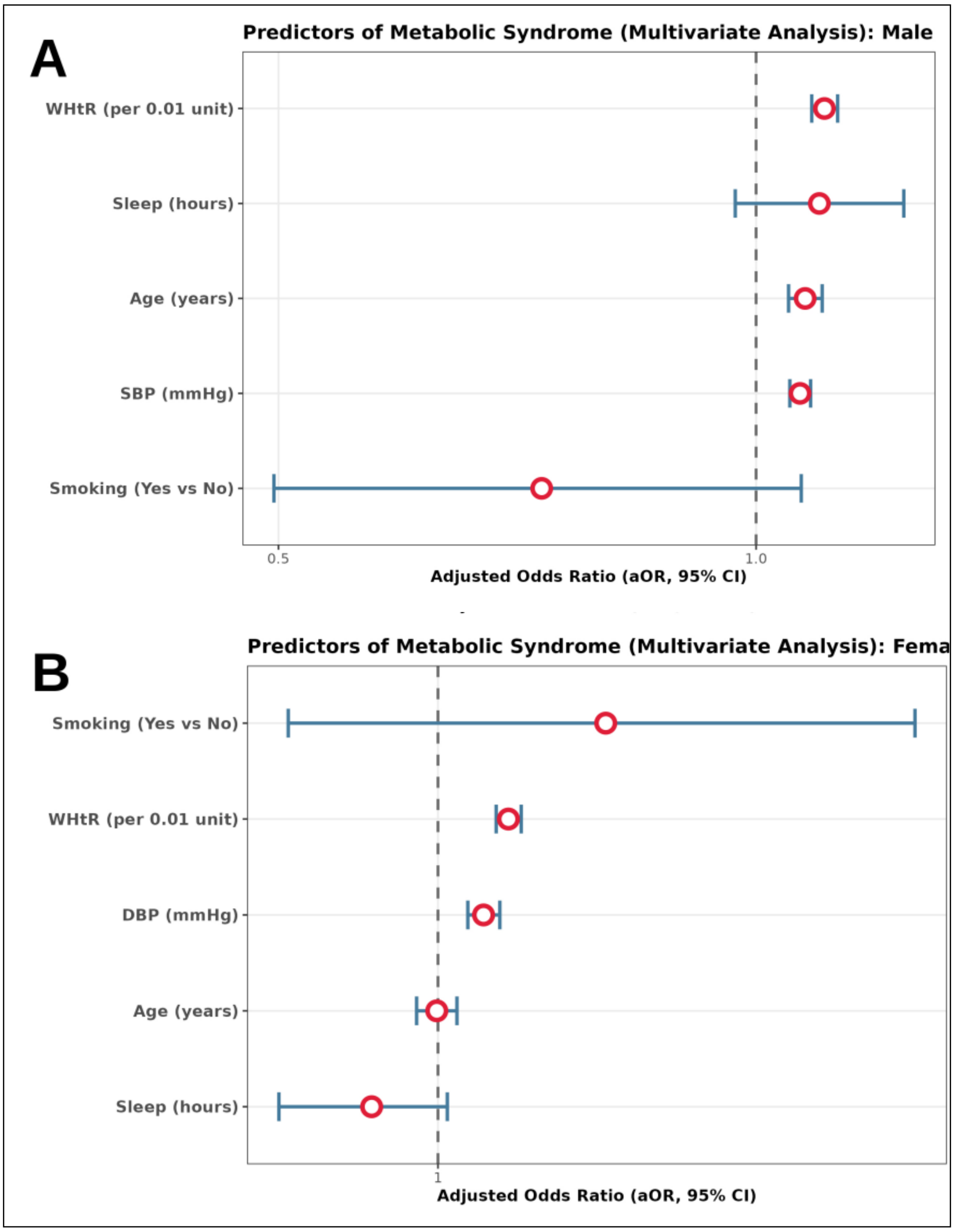

Fig. 1. Multivariate analysis of non-invasive predictors for metabolic syndrome. Forest plots displaying adjusted Odds Ratios (aOR) and 95% confidence intervals (CI) for (A) women and (B) men. Significant predictors ($p < 0.05$) are those with confidence intervals that do not cross the vertical reference line (OR = 1.0). WHtR is calculated per 0.01-unit increment
Picture taken by the authors

10% increase in MetS risk regardless of gender (Adj. OR 1.10; 95% CI: 1.08–1.12; $p < 0.001$).

Multivariate analysis revealed significant sexual dimorphism in the secondary predictor structure (Table 2).

- **Male model (n=1,477):** Beyond WHtR, chronological age (Adj. OR 1.07; 95% CI: 1.05–1.10; $p < 0.001$) and systolic blood pressure (SBP) (Adj. OR 1.06; 95% CI: 1.05–1.08; $p < 0.001$) significantly contributed to the risk profile.
- **Female model (n=1,434):** Age was not a significant predictor (Adj. OR 1.00; $p = 0.904$), suggesting that phenotypic traits dominate over chronological aging in metabolic risk development among women aged 18–45. Diastolic blood pressure (DBP) was identified as the primary hemodynamic predictor for this group (Adj. OR 1.06; 95% CI: 1.04–1.09; $p < 0.001$).

Behavioral factors, including sleep duration and active smoking, demonstrated no independent statistical significance in either model after adjusting for anthropometric and clinical parameters ($p > 0.05$) (Fig. 1).

The derived regression coefficients were used to establish logit (z) equations for calculating individual probability (P):

MODEL PERFORMANCE AND VALIDATION

The predictive reliability of the gender-specific models was evaluated by analyzing their discriminatory power and calibration accuracy in accordance with TRIPOD protocols [13].

Receiver Operating Characteristic (ROC) analysis confirmed the high performance of both non-invasive

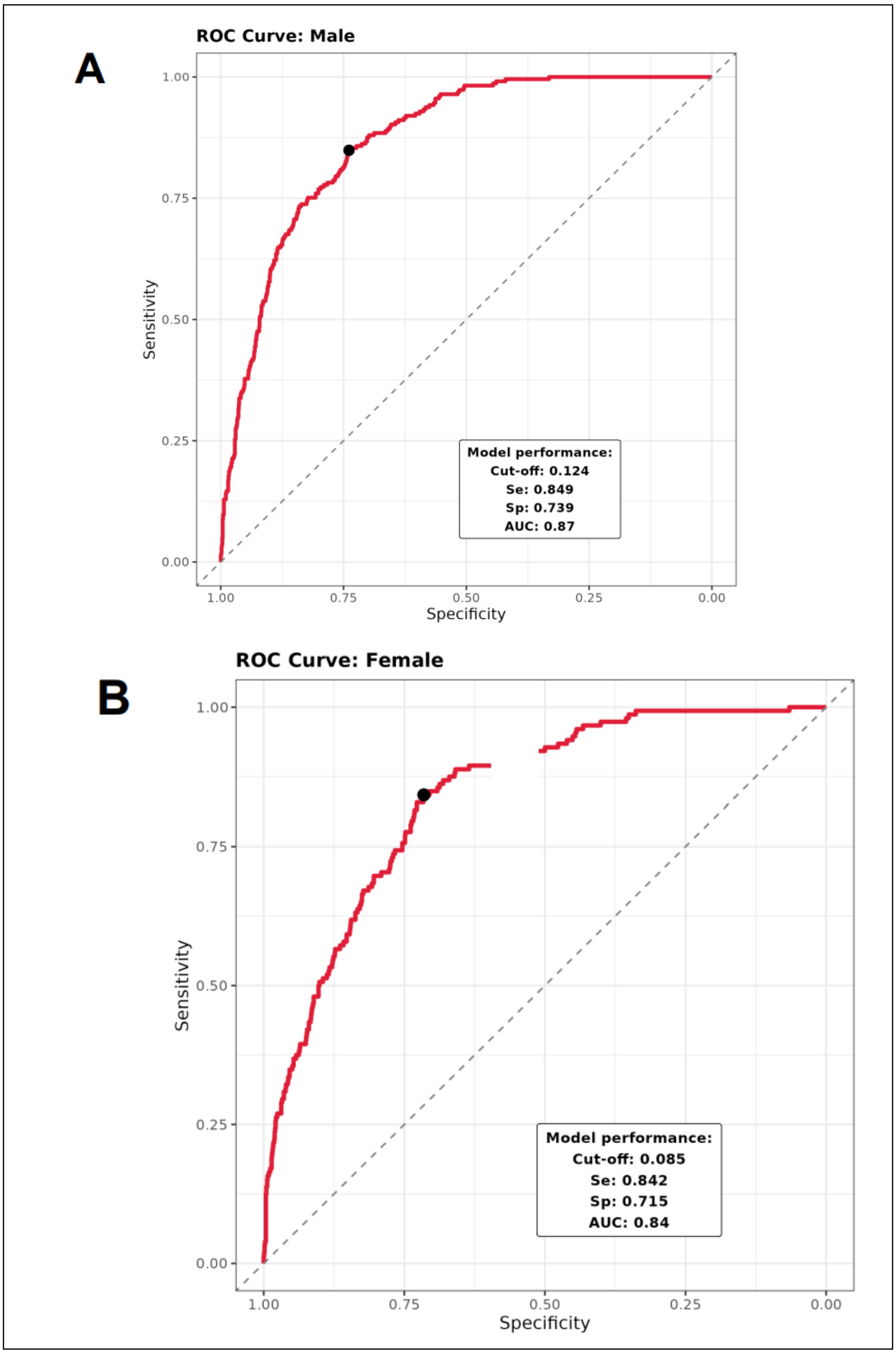

Fig. 2. ROC curves and diagnostic performance of the predictive models. Receiver Operating Characteristic (ROC) analysis for (A) the male cohort and (B) the female cohort. The black dots represent the optimal cut-off points determined by the Youden index. (A) Male model: AUC = 0.87, Cut-off = 0.124. (B) Female model: AUC = 0.84, Cut-off = 0.085
Picture taken by the authors

algorithms in classifying metabolic syndrome (MetS) status among young adults.

• **Male model:** The Area Under the Curve (AUC) was 0.87, indicating «excellent» discriminatory power. The optimal cut-off point, determined by the Youden index, was 0.124, yielding high sensitivity (Se: 0.849) and specificity (Sp: 0.739).

• **Female model:** The AUC was 0.84, representing «very good» predictive accuracy. The optimal cut-off for the female population was 0.085, with a sensitivity of 0.842 and a specificity of 0.715.

High sensitivity values (exceeding 84% for both sexes) justify the use of these models as primary screening tools to minimize false negatives in resource-limited clinical settings (Fig. 2).

Calibration plots were constructed to assess the agreement between predicted probabilities and the actual observed frequency of MetS.

• **Men:** The model trend demonstrates close convergence with the ideal calibration diagonal. Predicted risks show stable agreement with observed data across

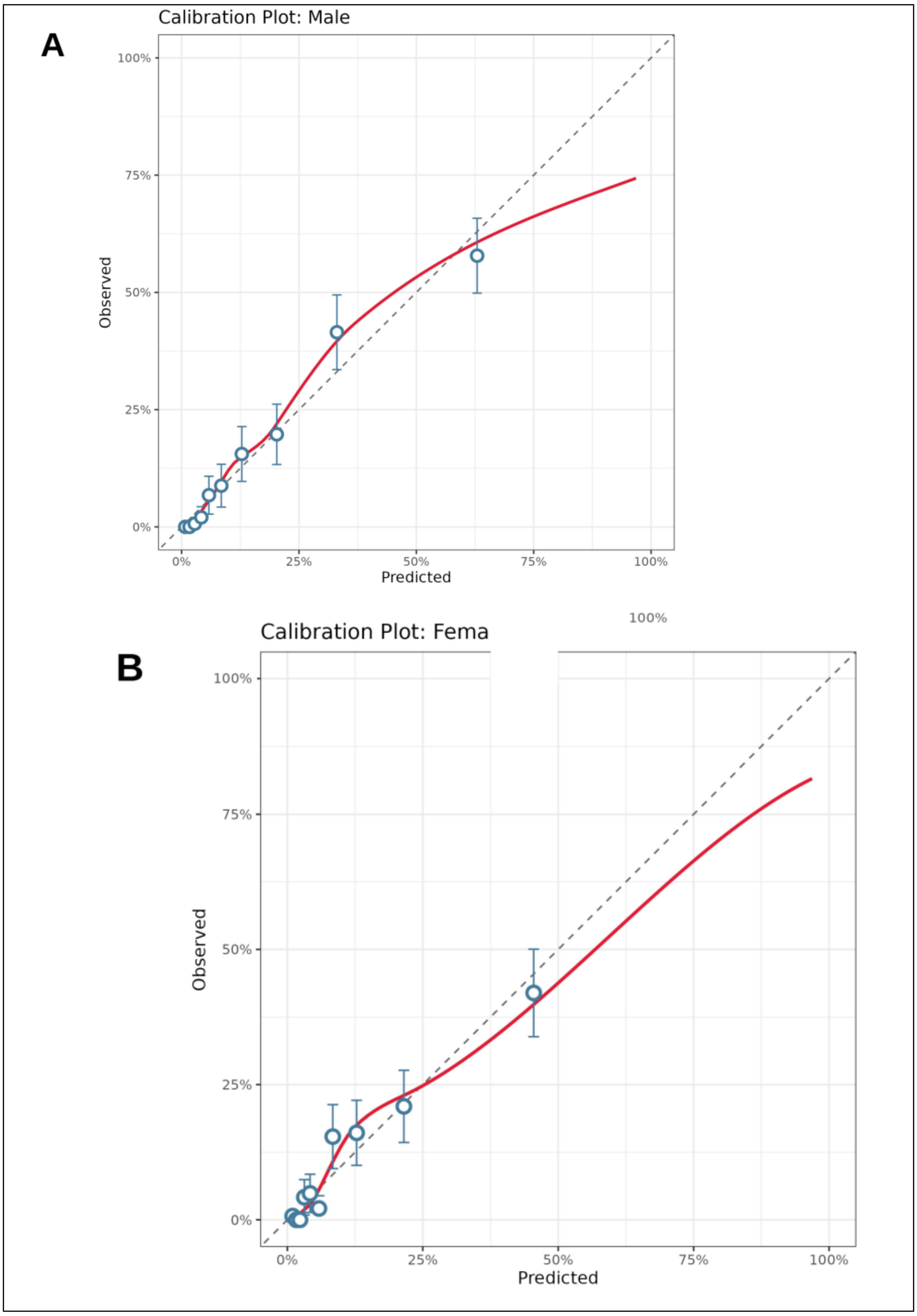

Fig. 3. Calibration plots for the predicted MetS risk. Agreement between the predicted probabilities (X-axis) and the actual observed frequencies (Y-axis) of metabolic syndrome for (A) men and (B) women. The dashed diagonal line represents perfect calibration (Slope = 1, Intercept = 0). The solid line represents the model trend, showing high reliability across the probability range
Picture taken by the authors

the entire probability range, characterized by an intercept near 0 and a slope near 1.

• **Women:** The calibration curve shows high accuracy within the low-to-moderate probability range (up to 0.5). However, at extremely high predicted risks (above 0.6), a slight overestimation occurs. This trend may be attributed to the lower frequency of terminal-stage abdominal obesity observations within this specific age cohort (Fig. 3).

Overall, the validation results indicate that non-invasive models based on WHtR and blood pressure provide clinically acceptable accuracy. These algorithms serve as a reliable alternative to laboratory-based testing for mass screening in young adults.

PREDICTIVE TOOLS AND RISK VISUALIZATION

To implement the statistical analysis into clinical practice, two types of visual tools were developed based on the gender-specific logistic regression models: nomograms and

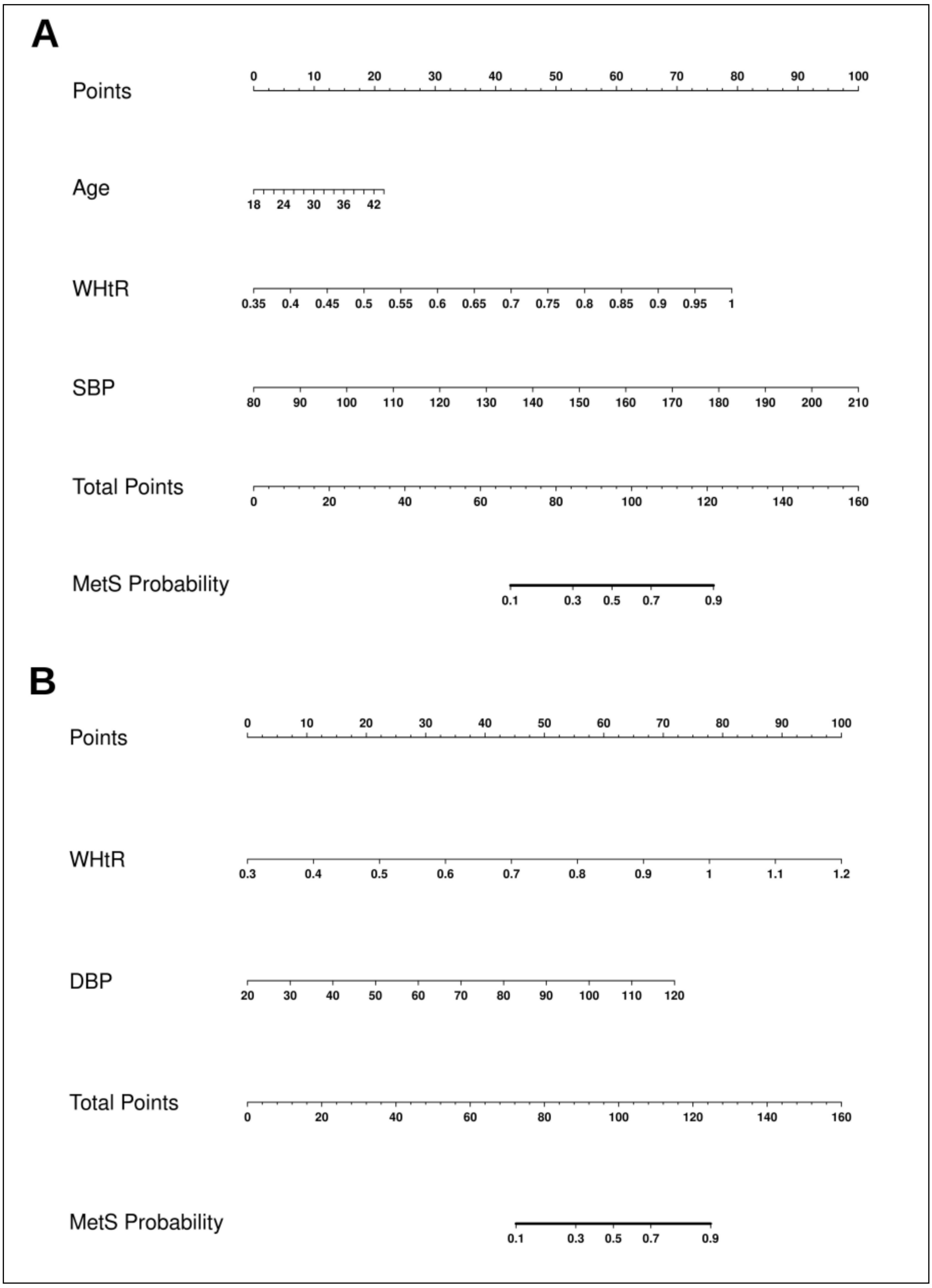

Fig. 4. Clinical nomograms for individual MetS risk assessment. Graphical scoring systems developed for (A) women and (B) men. Points are assigned for age, WHtR, and blood pressure (SBP for men, DBP for women). The «Total Points» sum corresponds to the «Probability of MetS» scale at the bottom of the nomogram
Picture taken by the authors

risk heatmaps. These tools enable clinicians to perform an instantaneous assessment of metabolic syndrome (MetS) probability without requiring complex mathematical logit calculations.

STRATEGIC RISK ZONES AND CLINICAL INTERPRETATION

Based on the Youden threshold analysis and the probability distribution within the young adult sample (N=2,911), three strategic risk zones were identified:

- **Green Zone (Low Risk):** P < 12.4 % for men and P < 8.5 % for women. This range corresponds to the population norm, where the probability of MetS is minimal. Patients in this category require only standard preventive observation.
- **Yellow Zone (Moderate Risk):** Ranging from 12.4 %/8.5 % to 50.0 %. This represents a zone for preventive intervention. Although clinical criteria according to NCEP ATP III may not be fully met, the patient has a high predisposition to their manifestation, necessitating early lifestyle modification.
- **Red Zone (High Risk):** P ≥ 50.0 %. This is a zone of high diagnostic certainty where the probability of MetS pres-

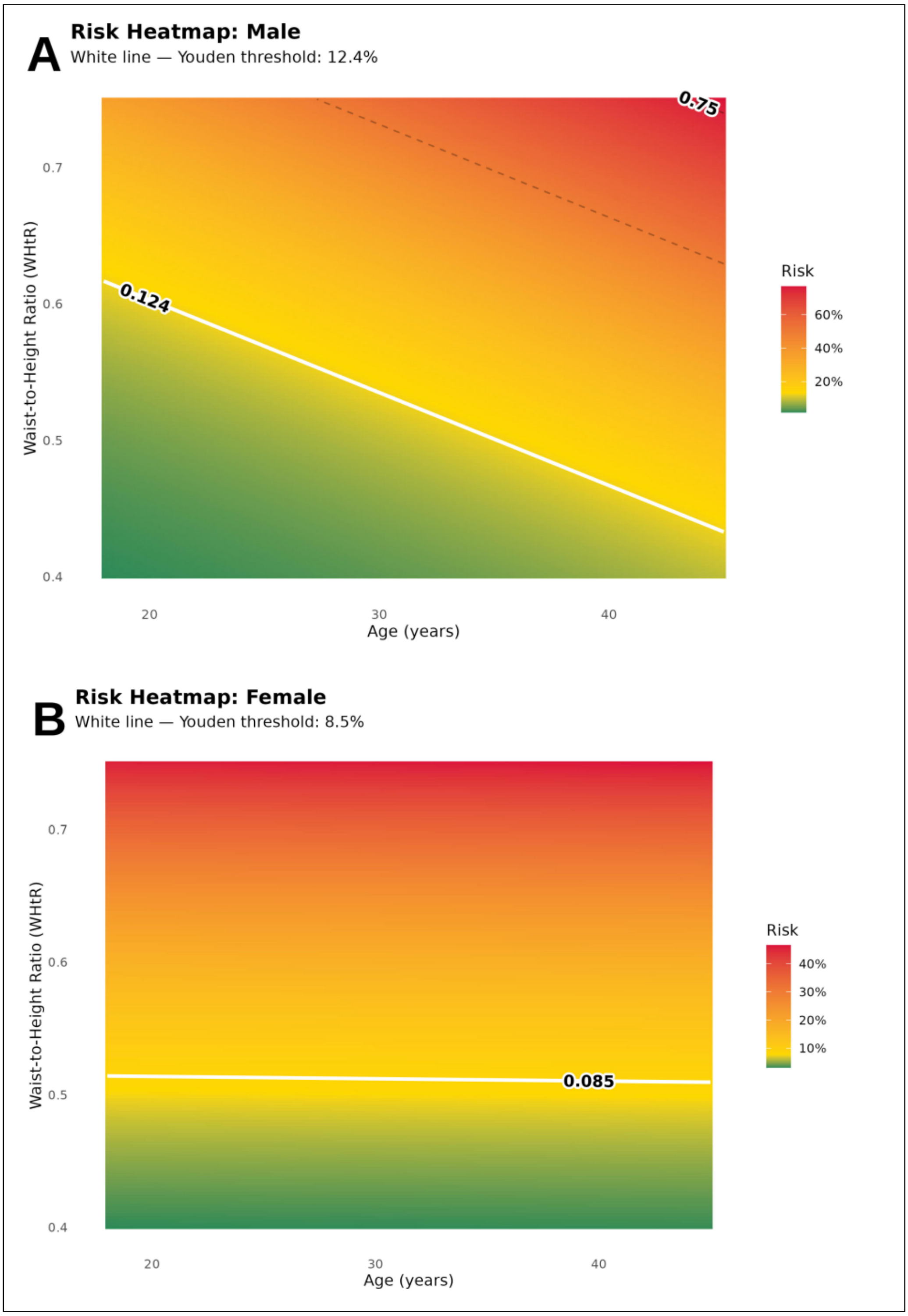

Fig. 5. Risk heatmaps for metabolic syndrome stratification. Visual representation of individual risk based on the interaction between age (X-axis) and WHtR (Y-axis) for (A) women and (B) men. Color-coded zones indicate low (green), moderate (yellow), and high (red) risk levels. The white dashed line represents the Youden index threshold for each gender group
Picture taken by the authors

ence exceeds the probability of its absence. Classification into this zone requires immediate clinical evaluation and invasive laboratory diagnostics (glucose and lipid profiles).

NOMOGRAM CLINICAL WORKFLOW

Nomograms (Fig. 4, Fig. 5) function as graphical calculators where specific values of each predictor correspond to a point score. The clinical workflow includes the following steps:

1. **Identify predictor values:** For each patient parameter (age, WHtR, and SBP for men or DBP for women), the clinician identifies the corresponding point on the predictor scale.
2. **Project to the point scale:** A perpendicular line is drawn upward from the identified value to the «Points» scale (0–100).
3. **Calculate Total Points:** The points for all significant non-invasive parameters are summed.

Table 2. Logistic regression parameters for MetS risk prediction

Predictor	Coefficient (β)	SE	Wald χ2	p-value	Adj. OR (95% CI)
Men (n=1,477)					
Constant	-17.502	1.14	235.6	<0.001	—
Age (years)	0.068	0.012	46233	<0.001	1.07 (1.04–1.10)
WHtR (per 0.01)	0.099	0.009	109.8	<0.001	1.10 (1.08–1.12)
SBP (mmHg)	0.063	0.008	67.7	<0.001	1.06 (1.05–1.08)
Women (n=1,434)					
Constant	-12.304	0.94	171.6	<0.001	—
Age (years)	0.002	0.013	0.02	0.904	1.00 (0.97–1.03)
WHtR (per 0.01)	0.093	0.008	121.0	<0.001	1.10 (1.08–1.12)
DBP (mmHg)	0.060	0.011	46203	<0.001	1.06 (1.04–1.09)

Abbreviations: \beta, regression coefficient; SE, standard error; OR, Odds Ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure.
Source: compiled by the authors of this study

4. **Determine probability:** The total value is located on the «Total Points» scale, from which a line is drawn downward to the «Probability of MetS» scale.

INTERPRETATION OF RISK HEATMAPS

Heatmaps (Fig.5) provide immediate visual risk stratification based on age and WHtR. In the female heatmap, the Youden threshold (represented by a white line at 8.5%) is nearly horizontal. This indicates that for women aged 25 and 40 with the same WHtR (e.g., 0.52), the MetS risk is identical, marking the onset of the moderate risk zone. Conversely, the male Youden threshold (12.4%) exhibits a distinct slope. While a 20-year-old man with a WHtR of 0.60 is situated in the moderate risk zone (~40.0%), by age 45 with the same WHtR, he automatically transitions into the «red» high-risk zone (P > 60.0 %), demonstrating the synergistic effect of age in the male population.

Integrating these tools into primary care facilitates the identification of high-risk patients without invasive procedures, aligning with contemporary principles of personalized medicine.

DISCUSSION

SUMMARY OF MAIN FINDINGS

The primary outcome of this study is the development and internal validation of gender-specific predictive models for metabolic syndrome (MetS) in young adults (aged 18–44 years) using exclusively non-invasive parameters. Leveraging representative data from the NHANES 2011–2018 cycles, we demonstrated that integrating anthropometric, demographic, and clinical indicators achieves high classification accuracy without requiring costly and invasive biochemical blood tests. The models exhibited excellent discriminatory power, with an Area Under the Curve (AUC) of 0.87 for men and 0.84 for women. These results support the hypothesis that, for Non-Hispanic White young adults, a combination of basic physical parameters is sufficient for the precise identification of cardiometabolic risk.

Waist-to-height ratio (WHtR) emerged as the most potent shared predictor of MetS across both cohorts. Every 0.01-unit (1%) increase in WHtR was associated with a 10% elevation in the risk of the pathology, independent of gender (Adj. OR 1.10; 95% CI: 1.08–1.12). This underscores abdominal obesity as a critical marker of metabolic derangement in young individuals, outperforming traditional BMI in predictive value.

Our analysis revealed significant gender-specific differences in MetS predictor structures. For young men, chronological age and systolic blood pressure (SBP) were significant risk-enhancing factors (OR 1.07 and 1.06, respectively). Conversely, in women aged 18–44, chronological age did not significantly influence MetS probability (OR 1.0; $p > 0.05$), shifting the diagnostic focus for this demographic primarily toward anthropometric parameters and blood pressure.

The derived mathematical models were translated into applied visualization tools—nomograms and risk heatmaps. These instruments convert complex logistic regression equations into a simplified scoring system accessible for use during primary care consultations. This approach facilitates rapid screening and identifies patients in the «high-risk» zone who genuinely require further invasive evaluation according to NCEP ATP III criteria. Consequently, these findings not only validate non-invasive MetS diagnostics but also offer a ready-to-implement algorithm capable of reducing the economic burden on healthcare systems by optimizing laboratory testing in low-risk groups.

ETHNIC HOMOGENEITY AND MODEL VALIDITY

Metabolic syndrome and its components exhibit pronounced ethnic specificity, particularly concerning anthropometric indicators like waist circumference (WC) and BMI. These differences are not solely biologically determined but reflect a complex interplay of genetic, epigenetic, cultural, socioeconomic, and behavioral factors [14]. Populations from South and East Asia, as well as the Pacific region, develop metabolic complications at much lower levels of total fat mass compared to European populations [15-17]. For instance, research by Sigit et al. (2020) [18] indicated that Indonesians have significantly higher levels of abdominal obesity and hypertriglyceridemia at the same BMI as Dutch individuals, explaining their higher MetS risk at lower body weights. Similarly, age-standardized MetS prevalence in Chinese ethnic groups varied from 24.6% in Han populations to 13.7% in Miao groups [19], suggesting intra-national variations linked to genetic predisposition and lifestyle.

Waist circumference remains a pivotal indicator of abdominal obesity. Data from two large New Zealand cohorts (Workforce Diabetes Study and the Diabetes, Heart and Health Survey) showed that the Metabolic Syndrome Severity Score (MetSSS) correlates strongly with glucose-regulatory and cardiovascular status, an association clearly linked to ethnicity: the highest MetSSS levels were found in Māori and Pacific participants compared to Europeans [20]. This necessitates ethnicity-specific diagnostic criteria. Furthermore, research in Suriname [21] established optimal WC and BMI thresholds for predicting hypertension and metabolic risk across six distinct ethnic groups, proving that universal criteria are clinically inadequate. Additionally, Rønn et al. (2017) [22] found that traditional anthropometrics (BMI and WC) have varying degrees of informativeness for quantifying visceral adipose tissue (VAT) across ethnic groups. Identical waist measurements may indicate different volumes of metabolically active VAT, directly impacting risk levels, with South Asian populations being particularly vulnerable.

A systematic review and meta-analysis by Adjei et al. (2024) [14] across 23 high-income countries demonstrated that MetS prevalence varies substantially by ethnicity, often significantly exceeding rates in White populations for groups such as African Americans, Hispanics, and Pacific Islanders. This variability is tied to differing distributions of anthropometric risks. Scientific evidence thus argues against universal anthropometric standards, confirming that ethnic specificity is a fundamental principle in MetS diagnosis and treatment.

LIMITATIONS AND GENERALIZATION

The current results, including the nomograms and heatmaps, have limited applicability to Asian, African American, or Indigenous populations, where different correlation coefficients and risk thresholds are required [23,24]. These models cannot be recommended for non-White populations without additional external validation and coefficient recalibration. However, this narrow specialization contributed to the high accuracy (AUC 0.87 for men) observed. Restricting the study to a White cohort is viewed here as a methodological advantage aligned with personalized medicine principles, avoiding the «averaging» of risks and providing clinicians with a tool tailored to the biological characteristics of a specific population group [22].

The cross-sectional nature of the NHANES data is a significant limitation for establishing causality. While the models effectively predict MetS presence at the time of examination, they do not confirm that predictors such as WHtR or blood pressure are primary etiological factors [25]. Furthermore, data regarding lifestyle, sleep duration, and smoking status are self-reported, which may introduce classification errors due to recall bias or social desirability bias [26]. Such errors may slightly underestimate the weight of behavioral factors in the final logit equations.

In large epidemiological cohorts, it is also challenging to fully account for the influence of antihypertensive, hypoglycemic, or lipid-lowering medications already being taken by participants [20]. Since therapy can artificially normalize MetS components (BP, glucose, or lipids), it may mask the actual prevalence of the syndrome and lead to an underestimation of the strength of certain predictors [18].

Consequently, the clinical applicability of the developed nomograms is strictly limited to individuals not currently receiving antihypertensive therapy. Since the models rely heavily on unmodified blood pressure values, medication-induced normalization would artificially lower the calculated risk score, rendering the prediction inaccurate for treated patients.

DIRECTIONS FOR FURTHER RESEARCH

To enhance accuracy and expand the clinical scope of the diagnostic algorithm, prospective studies using independent international cohorts are a priority next step to evaluate the capacity of non-invasive nomograms to predict long-term cardiometabolic risks, such as type 2 diabetes or cardiovascular events. Subsequent stages should involve developing specific nomograms for other populations (Asian, African American, Hispanic), accounting for their unique anthropometric thresholds and visceral fat accumulation patterns.

The creation of automated clinical decision support tools (web-based calculators) based on the derived mathematical formulas is a promising direction [27, 28]. This would provide clinicians with instantaneous risk calculations during outpatient visits. Future research must also incorporate factors such as food security, education levels, and income, as these socioeconomic determinants significantly impact MetS prevalence and may explain substantial risk variability even within the same ethnic group.

CONCLUSIONS

This study establishes gender-specific, non-invasive predictive models for metabolic syndrome (MetS) in young adults, demonstrating robust discriminatory power (AUC ≥ 0.84). The findings identify waist-to-height ratio (WHtR) as the most significant independent determinant of MetS across both sexes. A distinct gender dimorphism was observed: chronological age significantly enhances risk in men but lacks predictive value in women, underscoring the dominance of phenotypic features over chronological aging in female cardiometabolic risk stratification.

The resulting nomograms and heatmaps provide evidence-based tools for immediate risk assessment in primary care settings. These instruments enable the identification of high-risk individuals without the need for invasive laboratory diagnostics, offering a scalable solution for early intervention. By streamlining screening protocols and reducing reliance on fasting biochemical profiles, these tools can improve diagnostic uptake and reduce healthcare costs in young populations.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 17.01.2026
ACCEPTED: 21.04.2026