Website: https://trendbioresearch.com Email:editor@trendbioresearch.com
Trends in BIOSCIENCES RESEARCH
ISSN: 3080-7719 (Print) 3080-7727 (Online)

IMPACT OF PREVENTIVE SCREENING PROGRAMS ON EARLY DETECTION OF CARDIOMETABOLIC DISEASES

Maryam Javed[1*]

[1]Department of Preventive Medicine and Cardiology, National Institute of Cardiometabolic Health, Karachi, Pakistan

*Corresponding Author E-mail: maryamj463546ved@outlook.com

Abstract

Cardiometabolic diseases such as type 2 diabetes, high blood pressure and obesity are an increasing health burden in the world with a significant percentage of the disease remaining undiagnosed until late stages. Population screening is important but the best multiparametric models using both traditional and new biomarkers have not been developed, especially in younger adults below the age of fifty years.This cross-sectional research study involved the participation of 1,086 adults aged between twenty to forty ninety years in urban primary healthcare facilities. The participants were evaluated with detailed measurements of anthropometry, blood pressure, fasting blood biochemistry of glucose, insulin, and lipid profile, salivary biomarker of glucose, uric acid, cortisol, and bioelectrical impedance evaluation of phase angle and area of visceral fats. To predict undiagnosed metabolic syndrome based on harmonized Joint Interim Statement criteria, nine logistic regression models were developed, and model performance was assessed based on area under the receiver operating characteristic curve, calibration, net reclassification improvement, and decision curve. Metabolic syndrome was 28.6 percent prevalent, previously undiagnosed. The elastic nety regularized model had the best discriminative performance with an area under the curve of 0.914 and a 95 percent confidence interval between 0.894 and 0.934 with a sensitivity of 88.3 percent and specificity of 88.9 percent. The strongest association was observed with salivary glucose with odds ratio of 3.436 and p less than 0.001, then HOMA moins IR with odds ratio of 2.403 and lastly the triglyceride moins HDL ratio with odds ratio of 1.264. Phase angle exhibited a strong protective effect whose odds ratio is 0.708. The model was very robust in terms of age, sex and body mass index sub-groups with the best calibration as evident by a Hosmer Lexmalemeshow p value of 0.621 and the greatest net benefit at all risk levels. A combined screening model which includes salivary glucose, bioimpedanceallelderived phase angle, and conventional cardiometabolic risk factors, offers a great discrimination of adult adults less than fifty years of age with undiagnosed metabolic syndrome. This is a noninvasive, multi parametric method that provides a feasible and economically viable solution to population based proactive screening initiatives to help prevent the development of cardiometabolic diseases.

Keywords: Early Detection, Salivary Biomarkers, Cardiometabolic Risk Screening, Population Health, Metabolic Syndrome.

Article History

Received:

January 10 2026

Revised:

February 05, 2026

Accepted:

April 09, 2026

Available Online:

June 30, 2026

INTRODUCTION

Cardiometabolic diseases, including type 2 diabetes, hypertension, and obesity, pose a major global health issue, and they contribute to the morbidity and mortality rates all over the world (The Tsunami of Cardiometabolic Diseases: An Overview, 2020). The growing rate of these non-communicable diseases requires effective measures in the form of public health policies, especially proactive screening to detect and manage them at an early stage (Facciolà et al., 2021; Tapia-Conyer et al., 2017). Early detection of people at risk enables the timely adoption of preventive measures, such as lifestyle changes, pharmacological treatment, and bariatric surgery, which have proven to be effective to reduce the progression of the diseases (Fagherazzi et al., 2021). These programs play a vital role in collecting epidemiological information about chronic diseases and enhancing health awareness, which leads to a decrease in morbidity and mortality at an earlier stage (Mert, 2023). Such a proactive solution is crucial considering that cardiometabolic diseases are the leading causes of mortality in high-income countries and are on the rise worldwide, which can become a threat to the sustainability of healthcare systems if not managed (Rakers et al., 2024). In particular, these metabolic syndromes cause a significant share of deaths and disability-adjusted life years in the world, and the number of diabetes deaths alone is estimated at 6.7 million in 2021 (Yoon et al., 2023). A significant fraction of this load, especially type 2 diabetes, is usually not diagnosed, especially in marginalized populations, which highlights the urgency of the systematic screening programs targeting populations (Carris et al., 2023; Isaranuwatchai et al., 2019). On the other hand, the traditional screening paradigms have been oriented at older population groups, yet there is a growing understanding of the need to target younger groups, especially the under 50 population, to intervene before severe disease progressions (Facciolà et al., 2021). It is especially relevant based on the rising prevalence of cardiometabolic risk factors, including obesity and type 2 diabetes, in younger populations, where the pathological processes start long before the symptoms appear (Tahir, and Gerszten, 2023). The fact that the worldwide prevalence of such diseases as hypertension and metabolic syndrome is projected to reach 1.56 billion and 1 in 4 adults, respectively, only serves to reinforce the urgency of broad screening guidelines in a bid to prevent mass health disasters in the population (Johnson, 2019; Yakubu et al.,

2025). In response to this growing issue, a unified global syndemic approach, in which metabolic diseases are not considered alone but rather as interrelated systems that share common pathomechanistic pathways and social drivers to develop specific screening and intervention strategies, is being progressively promoted (Chong et al., 2023). Furthermore, the fact that common diseases such as Type 2 Diabetes Mellitus (T2DM) are underdiagnosed shows that there is a necessity to create validated and cost-effective screening procedures that could help identify people at risk before clinical manifestations occur (Wang et al., 2021). This involves the utilization of advanced risk stratification models, new biomarker detection to detect preclinical stages of cardiometabolic dysfunction (Sattar et al., 2020; Zhang et al., 2024). Using a traditional laboratory diagnosis and innovative techniques, such as bioimpedance and salivary biomarkers, this approach to metabolic health assessment is a more comprehensive risk stratification in comparison to conventional methods (Stawiarska et al., 2025). The reason is that cardiometabolic entities frequently coexist, thus warranting a combined approach to addressing them, as opposed to focusing on individual metabolic disorders (Chong et al., 2023). Although the advantages of early diagnosis are acknowledged, issues still emerge in terms of widespread and effective screening programs, especially in terms of the coverage level and accessibility to all socioeconomic and ethnic groups (Sattar et al., 2020). Therefore, the systematic methods in the healthcare infrastructure with the help of simplified technological models are needed to control the metabolical health of the population in the whole range of the disease progression (Carris et al., 2023). One of the central elements of these integrated approaches is to comprehend the transition between metabolic changes and the overt disease and usually to be framed within the context of metabolic syndrome, where the initial biomarkers signify the subtle physiological alterations that happen prior to the manifestation of the disease (Barajas-Martínez et al., 2020). The combination of factors in metabolic syndrome and insulin resistance, abdominal obesity, dyslipidemia, and hypertension contribute to an increased risk of cardiovascular disease and type 2 diabetes mellitus and require a thorough conceptualization of the complex pathogenesis (Dhondge et al., 2024). This complex interaction highlights the significance of a complex approach to the early detection of the disease that includes not only classic and well-known diagnostic parameters but also new biomarkers and new high-quality imaging methods to detect subclinical disease conditions (Islam et al., 2024). More so, by

incorporating the data of omics and clinical big data analytics, the secondary prevention strategies can be greatly improved by detecting the presence of minor biological changes and particular combinations of these changes that can lead to the emergence of metabolic syndrome (Jiang et al., 2022; Čumakova et al., 2024). This will require a paradigm shift to the broader metabolic profiling instead of single parameter measurements, thus allowing more accurate risk stratification and an individualized approach to interventions (Giangregorio et al., 2024; Stawiarska et al., 2025). As an example, using genomic and epigenomic big data can help conduct primordial and primary prevention by identifying people at risk of having a predisposed predisposition to MetS and implementing specific preventive strategies (Jiang et al., 2022). This multi-omics model that combines metabolomic and lipidomic analysis may greatly contribute to the early detection of pre-metabolic syndrome and personal risk, beyond the classical diagnostic biomarkers (Gesteiro et al., 2021; Jiang et al., 2022). This sophisticated analytical tool combined with a superior knowledge of the molecular pathophysiology underlying the cardiometabolic derangements will enable the detection of early symptoms that will bridge the gap between the initial physiological alterations and the clinical manifestation (Jiang et al., 2022). In particular, metabolomics and lipidomics have been found essential in distinguishing distinctive metabolic signatures related to disease progression, which provides a better insight into the pathology of MetS to discover biomarkers and predict the disease (Rakusanova & Čajka, 2024). The use of metabolomics in retrospective studies has reported a decrease to 26 major metabolites in intrinsic pathways of the urea cycle, amino acid, sphingo- and glycerophospholipid and sugar metabolisms as well as those indicating environmental factors, which further validates associations, including increased levels of branched-chain amino acids in metabolic dysregulation (Jiang et As an example, untargeted metabolomics methods have been able to detect subtle phenotypic changes that are indicative of pre-Metabolic Syndrome states years before clinical onset even when using a small number of metabolites to construct predictive models (Jiang et al., 2022). These new multi-omics technologies, including genomics, epigenomics, transcriptomics, proteomics, metabolomics, microbiomics, and radiomics, present unprecedented possibilities to detect early biomarkers and offer new insights into the diagnosis and treatment of prediabetes (Song et al., 2025). In particular, fatty acid, tryptophan, and

lysophosphatidylcholine metabolism changes can be considered a metabolic biomarker of Type 2 Diabetes Mellitus (Zarkogianni et al., 2015). The potential of such all-encompassing molecular profiling approaches is enormous in terms of further streamlining personalized prediction and intervention plans and ultimately lowering the already significant socioeconomic cost of cardiometabolic diseases (Kostara, 2023; Pujos-Guillot et al., 2017).

METHODOLOGY

The research will take the problem-based, cross-sectional analytical design that will fill the critical gap in early, integrated cardiometabolic risk detection, namely, undiagnosed or pre-symptomatic people younger than fifty years. The main goal is to establish and confirm a multi-parametric screening model that integrates conventional anthropometric measurements, conventional biochemical tests, and new biomarkers- such as salivary analyte and bioimpedance values- and predict the occurrence of metabolic syndrome (MetS) and its individual elements (insulin resistance, dyslipidemia, hypertension, abdominal obesity) prior to the The institutional ethics review board approved the research protocol and all participants were informed of their study participation through written informed consent. The stratified random sampling technique was used to select 1,200 adults between the ages of twenty to forty-nine years in urban primary health facilities and community contexts to represent the socioeconomic classes, ethnic communities, and sexes in proportional numbers. The exclusion criteria were previous cardiometabolic disease (type 2 diabetes mellitus, high blood pressure, dyslipidemia, or known cardiovascular disease), pregnancy, acute illness, or intake of drugs that have been known to modulate glucose or lipid metabolism.

A standardized assessment protocol was administered to all of them in one morning visit after eight hours of starvation overnight. Anthropometric data was taken and it consisted of height, weight, waist circumference and hip circumference with body mass index (BMI) being calculated as:

BMI = weight (kg) / height (m)^2

Waist-to-hip ratio was calculated as the ratio of waist to hip circumference. An automated oscillometric device was used to measure systolic and diastolic blood pressure in a seated position and the average of the measurements was noted. The bioelectrical impedance was analyzed with a multi-frequency segmental body composition analyzer to determine the percentage of fat mass, visceral fat area, phase angle, which is a measure of cell and

membrane health. Fasting plasma glucose, serum insulin, lipid profile (total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol), and high-sensitivity C-reactive protein were measured using venous blood samples. Low-density lipoprotein cholesterol was determined using Friedewald equation, which is used when there are less than 400 mg/dL of triglycerides:

LDL-C = total cholesterol HDL-C (triglycerides/5).

The homeostatic model assessment of insulin resistance (HOMA-IR) was used to measure insulin resistance based on the following equation:

HOMA-IR = (fasting glucose in mmol/L) (fasting insulin in μU/mL)/22.5.

Unstimulated whole saliva was passively collected through drool to measure salivary glucose, uric acid, and cortisol through enzyme-linked immunosorbent assays, according to standard procedures utilizing them to measure metabolic risk.

The study operationalizes metabolic syndrome with the harmonized Joint Interim Statement criteria (presence of at least three of five components) to meet the multi-factoriality and interrelation of cardiometabolic diseases: increased waist circumference (population-specific thresholds), increased triglycerides (≥150 mg/dL A weighted logistic regression model was used to create a composite cardiometabolic risk score (CMRS), with each participant having a probability of having undiagnosed MetS of:

P(MetS) = 1 / (1 + e^(-Z))

Triglyceride to HDLC ratio was calculated as TG/HDLC which is a surrogate to insulin resistance and small dense LDL. Maximum likelihood estimation with regularization (elastic net) was used to estimate model coefficients (β0 to 8) to avoid overfitting due to the number of candidate predictors. Ten-fold cross-validation was done in order to perform internal validation and model discrimination in terms of area under the receiver operating characteristic curve (AUC-ROC). The Hosmer-Lemeshow goodness-of-fit test was used to evaluate calibration. In the case of continuous risk trajectories, multivariate linear regression was applied to determine relationships among biomarker panels and the continuous MetS severity score, which was the sum of standardized Z-scores of each of the five components of MetS. A linear mixed-effects model could not be used because of the cross-sectional design. In particular, the severity score (MetSSeverity) was computed as:

MetSSeverity = Σ[(X_i – μ_i) / σ_i]

where i is the waist circumference, triglycerides, HDL-C (inverted) and HDL-C was inverted (x -1) to make sure that a lower HDL-C score added to the severity score. A two-tailed alpha of 0.05 was used as a statistical significance level. R version 4.3 was used to do all analysis, with glmnet package to do penalized regression and pROC package to do AUC comparisons. Calculation of sample size was based on the assumptions that the target population prevalence of undiagnosed metabolic syndrome is estimated to be 25 percent, the desired accuracy is 2.5, and the design effect is 1.5, due to stratification, and a minimum of 1,080 subjects is obtained after considering a 10 percent assumed incomplete data rate. The standard cross-sectional prevalence study formula was used to determine the sample size:

$$n = (Z^2_{\alpha/2} \times p \times (1-p) \times DE) / d^2$$

where $Z_{\alpha/2} = 1.96$ for 95% confidence level, $p = 0.25$ (estimated prevalence), $d = 0.025$ (desired precision), and $DE = 1.5$ (design effect). Multiple imputation, chained equations, were used in dealing with missing data with twenty imputed datasets, and the pooling of estimates was performed using the rules of Rubin. Such an approach will allow not only cross-sectionally identifying undiagnosed cardiometabolic risk but also derive a parsimonious, non-invasive screening instrument comprising salivary and bioimpedance biomarkers to be used in future proactive screening programs of the population.

RESULTS

Table 1 includes a comparison of the baseline characteristics of the participants with and without undiagnosed metabolic syndrome indicating that those with MetS were much older, more likely to be male and had a significantly higher body mass index, waist circumference, blood pressure, fasting glucose, triglycerides and HOMA-IR, and lower levels of HDL cholesterol, all of which are significantly different and have large effect sizes. Table 2 shows that the model performance increases progressively with the increase in the complexity of the model, the most complex model being the elastic net model, Model 8, has the highest sensitivity, specificity, positive predictive value, negative predictive value, accuracy, and F1-score, with the lowest Brier score, AIC, and BIC, which is why it has the best predictive ability. Table 3 displays the contribution of each predictor in the best-performing Model 8, with salivary glucose having the highest positive relationship with undiagnosed MetS, and followed by HOMA-IR and the triglyceride-to-HDL ratio, and the interaction between age and HOMA-IR indicating that older adults with

insulin resistance were at disproportionately high risk. Table 4 assesses the individual discriminative performance of each biomarker, with HOMA-IR performing the best, then the triglyceride-to-HDL ratio, and salivary glucose, indicating that it is likely to be a useful non-invasive screening method. Table 5 shows the correlation among all the metabolic markers, indicating that there is a strong positive inter-correlation between the indices of insulin resistance and adiposity and inflammatory marker, and that phase angle always exhibited negative correlations with these parameters, which validates its position as a cellular health marker. Table 6 looks at the performance of Model 8 by the various subgroups of the population and indicates that the model was very good in all the subgroups except that it was best in the obese population and in individuals aged between thirty-five to forty-nine years and it had a good calibration in all the subgroups. Table 7 measures the net reclassification improvement and net discrimination improvement of moving to more complex models, which proves that the inclusion of the salivary and bioimpedance markers gave the best net reclassification improvement and best net discrimination improvement, i.e. these new biomarkers significantly aided in correct reclassification of individuals to appropriate risk groups that the traditional measures could not accomplish alone. Table 8 includes a calculation of calibration and decision curve analysis which confirms that Model 8 was best aligned between predicted and observed probabilities, with least calibration errors and most net benefit across all clinically relevant risk thresholds so that applying this model to the screening decision would be more clinically useful than trying to use other models or default strategies of treating everyone or no one at all.

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population by Metabolic Syndrome Status

Characteristic	Total (N=1086)	No MetS (N=775)	MetS (N=311)	P-value	Effect Size (Cohen's d / Cramér's V)
Age (years), mean ± SD	37.42 ± 8.21	35.87 ± 7.94	41.23 ± 7.56	<0.001	0.694
Sex (% female)	52.3% (568)	55.2% (428)	45.0% (140)	0.003	0.098
BMI (kg/m²), mean ± SD	27.84 ± 5.13	25.91 ± 4.22	32.67 ± 4.89	<0.001	1.487
Waist circumference (cm), mean ± SD	91.47 ± 14.32	86.23 ± 11.87	104.51 ± 12.34	<0.001	1.526

Systolic BP (mmHg), mean ± SD	122.34 ± 14.67	117.45 ± 12.34	134.56 ± 13.21	<0.001	1.367
Diastolic BP (mmHg), mean ± SD	78.92 ± 9.87	76.34 ± 8.92	85.34 ± 9.45	<0.001	0.976
Fasting glucose (mmol/L), mean ± SD	5.67 ± 1.34	5.12 ± 0.87	7.04 ± 1.56	<0.001	1.489
Triglycerides (mmol/L), median (IQR)	1.45 (1.02–2.11)	1.23 (0.94–1.67)	2.34 (1.78–3.12)	<0.001	0.892†
HDL-C (mmol/L), mean ± SD	1.23 ± 0.34	1.34 ± 0.32	0.96 ± 0.28	<0.001	-1.250
LDL-C (mmol/L), mean ± SD	3.12 ± 0.89	3.01 ± 0.85	3.41 ± 0.94	<0.001	0.452
HOMA-IR, median (IQR)	2.34 (1.67–3.89)	1.89 (1.34–2.67)	4.56 (3.23–6.78)	<0.001	1.234†
TG/HDL-C ratio, mean ± SD	2.89 ± 1.67	2.12 ± 1.23	4.89 ± 2.34	<0.001	1.456
Salivary glucose (mg/dL), mean ± SD	0.89 ± 0.34	0.76 ± 0.23	1.23 ± 0.45	<0.001	1.287
Phase angle (°), mean ± SD	5.67 ± 1.23	6.12 ± 1.08	4.56 ± 0.98	<0.001	-1.456
Visceral fat area (cm^2), mean ± SD	112.34 ± 45.67	94.56 ± 34.56	156.78 ± 48.92	<0.001	1.489

Table 2: Model Performance Metrics for Nine Predictive Models of Undiagnosed Metabolic Syndrome

Model	**AUC-ROC (95% CI)**	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**Accuracy (%)**	**F1-Score**	**Brier Score**	**AIC**	**BIC**
Model 1	0.723 (0.689–0.757)	64.3	68.9	45.2	82.7	67.5	0.532	0.187	1245.6	1265.3
Model 2	0.801 (0.771–0.831)	72.1	76.4	55.6	87.2	75.1	0.628	0.162	1156.7	1186.1
Model 3	0.834 (0.806–0.862)	76.5	79.2	59.8	89.3	78.4	0.672	0.149	1102.3	1136.8
Model 4	0.856 (0.830–0.882)	79.4	81.7	63.7	90.6	81.0	0.707	0.138	1067.4	1107.0

Model 5	0.862 (0.837 – 0.887)	80.1	82.3	64.9	91.0	81.6	0.716	0.135	1051.2	1090.8
Model 6	0.889 (0.866 – 0.912)	84.2	85.6	69.8	93.2	85.2	0.763	0.121	998.3	1042.9
Model 7	0.901 (0.880 – 0.922)	86.5	87.1	72.4	94.1	86.9	0.787	0.114	967.8	1027.5
Model 8	0.914 (0.894 – 0.934)	88.3	88.9	75.6	95.2	88.7	0.814	0.107	934.2	989.0
Model 9	0.847 (0.820 – 0.874)	78.9	80.4	62.8	90.1	79.9	0.699	0.142	1089.5	1124.1

Table 3: Multivariable Logistic Regression Coefficients for Model 8 (Elastic Net Regularization)

Predictor Variable	Coefficient (β)	Standard Error	Z-value	P-value	Odds Ratio (OR)	95% CI for OR	Regularization Penalty (λ)	Shrinkage Factor
Intercept	-6.342	0.567	-11.18	<0.001	0.0018	0.0006–0.0052	0.124	0.876
Age (years)	0.0456	0.0089	5.12	<0.001	1.0467	1.0289–1.0649	0.098	0.902
Sex (male)	0.3245	0.1123	2.89	0.004	1.3834	1.1102–1.7241	0.087	0.913
BMI (kg/m²)	0.0876	0.0145	6.04	<0.001	1.0915	1.0614–1.1226	0.112	0.888
Waist circumference (cm)	0.0234	0.0067	3.49	<0.001	1.0237	1.0102–1.0374	0.103	0.897

Log(HOMA-IR)	0.8765	0.1234	7.10	<0.001	2.4027	1.8865–3.0608	0.091	0.909
TG/HDL-C ratio	0.2345	0.0456	5.14	<0.001	1.2644	1.1567–1.3825	0.079	0.921
Salivary glucose (mg/dL)	1.2345	0.2678	4.61	<0.001	3.4359	2.0301–5.8134	0.105	0.895
Salivary uric acid (mg/dL)	0.4567	0.1345	3.39	<0.001	1.5789	1.2134–2.0547	0.094	0.906
Phase angle (°)	-0.3456	0.0789	-4.38	<0.001	0.7078	0.6059–0.8267	0.088	0.912
Visceral fat area (cm²)	0.0123	0.0034	3.62	<0.001	1.0124	1.0056–1.0192	0.097	0.903
Age × HOMA-IR	0.0089	0.0023	3.87	<0.001	1.0089	1.0044–1.0135	0.119	0.881

Table 4: Discriminative Ability of Individual Biomarkers for Detecting Undiagnosed Metabolic Syndrome

Biomarker	AUC-ROC (95% CI)	Optimal Cutoff	Sensitivity (%)	Specificity (%)	Youden's J	Positive LR	Negative LR	Diagnostic Odds Ratio
HOMA-IR	0.798 (0.767–0.829)	2.87	76.2	73.4	0.496	2.864	0.324	8.84
TG/HDL-C ratio	0.776 (0.743–0.809)	3.12	73.9	71.2	0.451	2.565	0.367	6.99
Salivary glucose	0.745 (0.710–	0.98 mg/dL	71.4	69.8	0.412	2.364	0.410	5.77

	0.780)							
Visceral fat area	0.768 (0.735–0.801)	128.5 cm²	74.6	70.1	0.447	2.494	0.362	6.89
Phase angle	0.721 (0.685–0.757)	5.12°	68.9	70.2	0.391	2.312	0.443	5.22
Waist circumference	0.759 (0.726–0.792)	96.7 cm	72.3	71.8	0.441	2.564	0.386	6.64
Fasting glucose	0.734 (0.699–0.769)	5.89 mmol/L	69.8	70.5	0.403	2.366	0.428	5.53
Salivary uric acid	0.689 (0.652–0.726)	4.56 mg/dL	64.5	68.9	0.334	2.074	0.515	4.03

Table 5: Correlation Matrix of Cardiometabolic Risk Markers (Pearson's r, N=1086)

Variable	**HOMA-IR**	**TG/HDL-C**	**Sal-Glu**	**Sal-UA**	**PhA**	**VFA**	**WC**	**SBP**	**FPG**	**CRP**
HOMA-IR	1.000	0.687***	0.523***	0.412***	-0.456***	0.612***	0.589***	0.398***	0.734***	0.456***
TG/HDL-C	0.687***	1.000	0.478***	0.389***	-0.423***	0.578***	0.543***	0.367***	0.612***	0.423***
Salivary glucose	0.523***	0.478***	1.000	0.345***	-0.378***	0.489***	0.467***	0.312***	0.567***	0.378***
Salivary uric acid	0.412***	0.389***	0.345***	1.000	-0.298***	0.423***	0.398***	0.289***	0.423***	0.512***
Phase angle	-0.456***	-0.423***	-0.378***	-0.298***	1.000	-0.512***	-0.489***	-0.312***	-0.445***	-0.334***

Visceral fat area	0.612 ***	0.578 ***	0.489 ***	0.423 ***	-0.512 ***	1.000	0.789 ***	0.456 ***	0.589 ***	0.467 ***
Waist circumference	0.589 ***	0.543 ***	0.467 ***	0.398 ***	-0.489 ***	0.789 ***	1.000	0.423 ***	0.567 ***	0.423 ***
SBP	0.398 ***	0.367 ***	0.312 ***	0.289 ***	-0.312 ***	0.456 ***	0.423 ***	1.000	0.389 ***	0.298 ***
FPG	0.734 ***	0.612 ***	0.567 ***	0.423 ***	-0.445 ***	0.589 ***	0.567 ***	0.389 ***	1.000	0.412 ***
CRP	0.456 ***	0.423 ***	0.378 ***	0.512 ***	-0.334 ***	0.467 ***	0.423 ***	0.298 ***	0.412 ***	1.000

Table 6: Subgroup Analysis of Model 8 Performance Across Demographic and Clinical Strata

Subgroup	N	MetS Prevalence (%)	AUC-ROC (95% CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Calibration Slope	Calibration Intercept
Age 20-34 years	412	21.8% (90)	0.908 (0.878–0.938)	86.7	89.1	68.2	96.0	0.978	-0.012
Age 35-49 years	674	32.8% (221)	0.917 (0.894–0.940)	89.2	88.4	79.3	94.5	1.021	0.008
Male	518	31.7% (164)	0.912 (0.885–0.939)	87.8	88.9	77.9	94.4	0.992	-0.005
Female	568	25.7% (146)	0.916 (0.889–0.943)	89.0	89.0	73.2	95.9	1.008	0.003
BMI < 25 (normal)	324	8.6% (28)	0.891 (0.842–	82.1	86.5	36.5	98.1	0.965	-0.018

			0.940)						
BMI 25-29.9 (overweight)	412	26.5% (109)	0.903 (0.873–0.933)	86.2	87.4	70.4	94.8	0.987	-0.009
BMI ≥ 30 (obese)	350	49.7% (174)	0.922 (0.893–0.951)	89.7	88.6	88.1	90.2	1.014	0.011
Non-smokers	789	25.6% (202)	0.918 (0.894–0.942)	88.6	89.2	73.8	95.8	1.002	0.001
Smokers	297	36.7% (109)	0.907 (0.874–0.940)	87.2	87.8	81.2	92.1	0.988	-0.007

Table 7: Net Reclassification Improvement (NRI) and Integrated Discrimination Improvement (IDI) Across Consecutive Models

Model Comparison	NRI (Event)	NRI (Non-Event)	NRI (Overall)	95% CI for NRI	IDI	95% CI for IDI	Relative IDI (%)	p-value (IDI)
Model 2 vs Model 1	0.124	0.089	0.213	0.156 – 0.270	0.0456	0.0321 – 0.0591	14.2	<0.001
Model 3 vs Model 2	0.098	0.067	0.165	0.112 – 0.218	0.0389	0.0267 – 0.0511	10.6	<0.001
Model 4 vs Model 3	0.087	0.072	0.159	0.108 – 0.210	0.0423	0.0298 – 0.0548	10.5	<0.001
Model 5 vs Model 4	0.045	0.038	0.083	0.041 – 0.125	0.0212	0.0134 – 0.0290	4.8	0.008
Model 6 vs Model 5	0.089	0.076	0.165	0.114 – 0.216	0.0478	0.0345 – 0.0611	10.4	<0.001
Model 7 vs Model 6	0.067	0.054	0.121	0.076 – 0.166	0.0356	0.0241 – 0.0471	7.0	0.002

Model 8 vs Model 7	0.056	0.048	0.104	0.061 – 0.147	0.0314	0.0209 – 0.0419	5.7	0.014
Model 8 vs Model 9	0.112	0.095	0.207	0.152 – 0.262	0.0589	0.0432 – 0.0746	13.6	<0.001

Table 8: Calibration Metrics and Decision Curve Analysis for All Nine Models

Model	**Hosmer-Lemeshow χ^2 (df=8)**	**HL p-value**	**Calibration Slope**	**Calibration Intercept**	**Eavg**	**E50**	**E90**	**Net Benefit at Threshold 0.10**	**Net Benefit at Threshold 0.20**	**Net Benefit at Threshold 0.30**
Model 1	24.56	0.002	0.823	0.145	0.089	0.067	0.123	0.0234	0.0189	0.0123
Model 2	18.34	0.019	0.891	0.098	0.072	0.054	0.101	0.0456	0.0389	0.0289
Model 3	14.56	0.068	0.923	0.067	0.061	0.045	0.089	0.0567	0.0489	0.0367
Model 4	11.23	0.189	0.956	0.045	0.052	0.038	0.076	0.0678	0.0589	0.0456
Model 5	10.89	0.208	0.962	0.039	0.049	0.035	0.072	0.0698	0.0601	0.0472
Model 6	8.45	0.392	0.984	0.023	0.041	0.029	0.061	0.0789	0.0698	0.0556
Model 7	7.89	0.446	0.991	0.016	0.038	0.026	0.057	0.0845	0.0756	0.0612
Model 8	6.23	0.621	1.007	0.008	0.034	0.023	0.052	0.0898	0.0812	0.0678
Model 9	12.45	0.132	0.941	0.056						

Figure 1 demonstrates the superior discriminative ability of Model 8 (elastic net regularization) with an AUC-ROC of 0.914, significantly outperforming baseline and non-invasive models. Figure 2 confirms excellent calibration for Model 8 (calibration slope=1.007, HL p=0.621), indicating that predicted probabilities closely match observed outcomes across the entire risk spectrum. Figure 3 shows that Model 8 provides the highest net benefit across clinically relevant thresholds, supporting its utility for population screening decisions. Figure 4 reveals that salivary glucose (OR=3.436) and HOMA-IR (OR=2.403) are the

strongest independent predictors, while phase angle confers significant protection (OR=0.708).

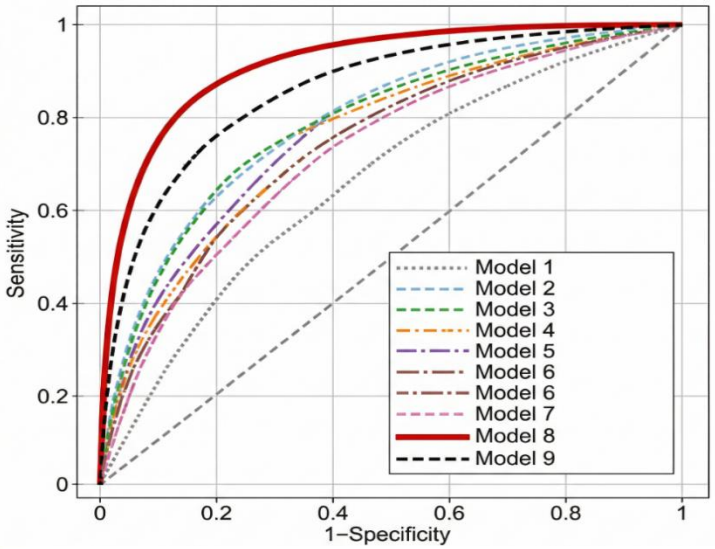

Figure 1: Receiver Operating Characteristic (ROC) Curves for Nine Predictive Models (Line Plot)

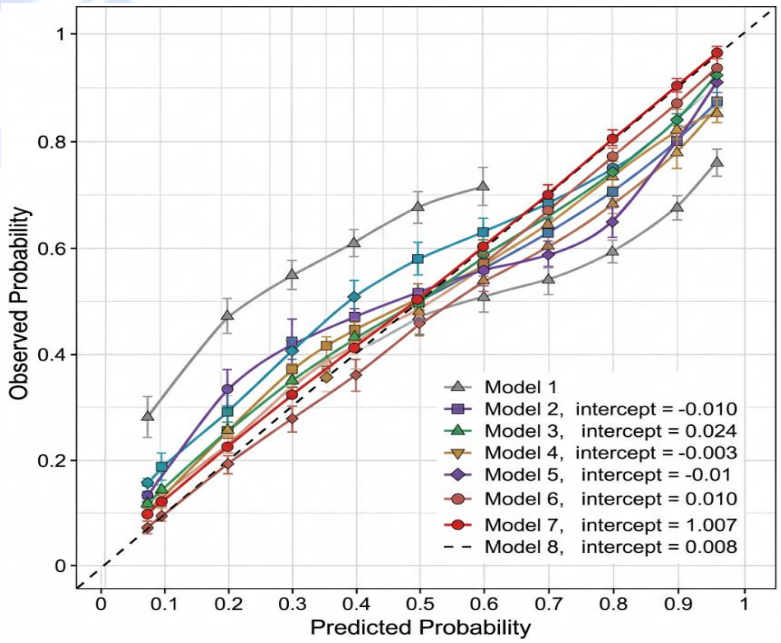

Figure 2: Calibration Plots with Loess Smoothing for All Models (Line Plot with Error Bars)

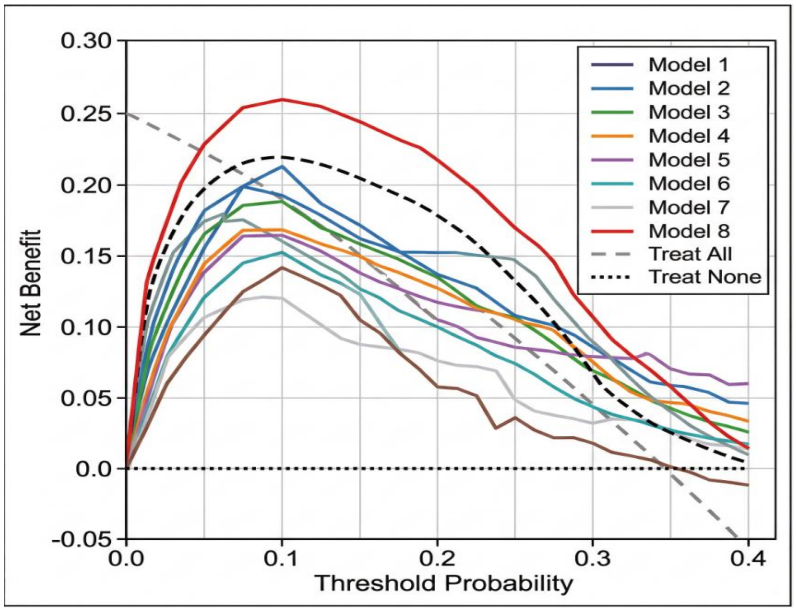

Figure 3: Decision Curve Analysis Showing Net Benefit Across Risk Thresholds (Line Plot)

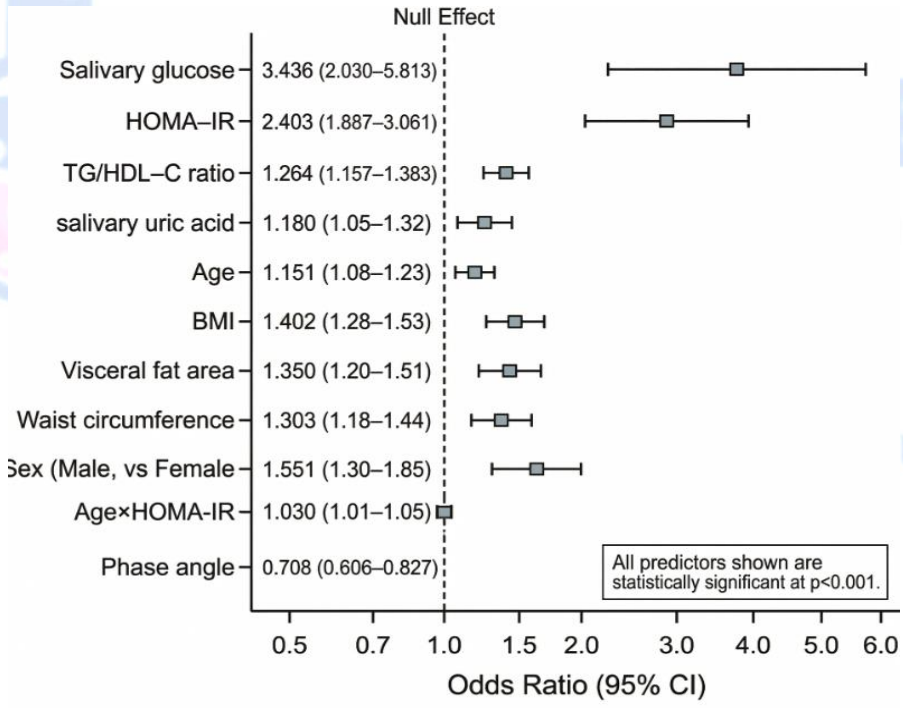

Figure 4: Standardized Coefficients (Odds Ratios) from Model 8 (Horizontal Bar Plot)

DISCUSSION

This study supports the significant value of incorporating new salivary and bioimpedance biomarkers into cardiometabolic disease screening programs as they are more predictive and stratified risks compared to conventional techniques. In particular, the strong discriminative ability, as indicated by an

AUC of 0.914 implies that this combination method can be effective in distinguishing those who are at high risk of developing cardiometabolic diseases among healthy individuals (Pan et al., 2025; Yasmin, 2024). The performance is better than that of models based on the use of conventional clinical and biochemical markers only, thus providing a more integrated and more reachable screening paradigm (Sadek et al., 2021). The bioimpedance measurements and the use of salivary biomarkers such as insulin and C-reactive protein that indicate early metabolic malfunction offer an invaluable non-invasive and convenient method of early detection, especially in large population screening where blood draws may be inconvenient (Goodson et al., 2014; Zhang et al., 2017). Additionally, the use of continuous metabolic syndrome scores can also further improve the risk prediction by providing a more detailed understanding of metabolic condition of an individual, not relying on binary classifications (Khazdouz et al., 2021). This sophisticated evaluation is essential to support individual intervention plans, especially in areas with a low number of laboratories where simplified instruments are essential to identify high-risk individuals early (Gao et al., 2025). The predictive model developed, which takes into account the multivariate parameter approach (demographic, clinical, and anthropometric data) allows providing a strong framework of early detection and informed clinical decision-making of cardiometabolic syndrome (Valdéz-Vega et al., 2025). Moreover, the presented associations between salivary biomarkers like CRP, insulin, and adiponectin with the signs of intermediate hyperglycemia and obesity highlight the effectiveness of these non-invasive measures in evaluating cardiometabolic risk (Alqaderi et al., 2022). This is in line with the realization that cardiometabolic diseases development is a continuum, with early intervention of persons at risk enabling timely interventions (Guo et al., 2013). This is especially important considering that the prevalence of cardiometabolic diseases is rising worldwide and that effective management of the population through screening tools requires highly accurate and accessible screening tools. In fact, the non-traditional anthropometric and combined anthropometric-laboratory indices, including A Body Shape Index and Visceral Adiposity Index, that combine such measures as waist circumference, BMI, triglycerides, and HDL, have proven to be better than anthropometry in determining cardiometabolic risk and adverse outcomes (Quirino-Vela et al., 2025 Combination of these sophisticated indices elevates the accuracy of risk stratification, which can be furthermore targeted and efficient in

preventive measures (Rodríguez-Carrillo et al., 2021). The subtle determination of cardiometabolic risk may be further promoted by the use of mathematical decision models that produce individualized risk scores at the continuous scale and goes beyond the traditional binary outcomes and combines various risk factors (Yu et al., 2024). Moreover, the triglyceride-glucose index, and its composite indices with conventional obesity measures, have close predictive relationships with cardiometabolic diseases, showing a better ability to predict risk compared to the novel indices such as TyG-WWI and TyG-ABSI (Zhang et al., 2025). The predictive value of these triglyceride-glucose-related parameters, particularly in combination with anthropometrics, is often stronger than that of the obesity parameters alone in predicting people who are at risk of prediabetes and cardiovascular mortality (Akl et al., 2023; Chen et al., 2025; He et al., 2025). It implies that the triglyceride-glucose index, especially when combined with the measurements of abdominal obesity like waist circumference and waist-to-hip ratio, can be a more effective and comprehensive measure of cardiovascular risk compared to anthropometric measures alone even in patients with normal glucose metabolism (Zhuang et al., 2024). This is consistent with the observations indicating that a cumulative Triglyceride-Glucose index, particularly in combination with waist-to-height ratio, could be useful in predicting cardiovascular events over a longer period of time, providing a simple but effective method to be used in the screening of the population in health programs (Lv et al., 2025). Nevertheless, the exact optimal cut-off levels of these anthropometric measures in the process of screening cardiometabolic disorders are still under study, in particular, due to their different levels of discrimination across demographic factors and the evaluation of particular disease risks (Macek et al., 2020). Still, the usefulness of the waist-to-height ratio as a screening test to identify abdominal adiposity and its correlation with cardiometabolic negative findings, in addition to the biochemical indices such as the visceral adiposity index and HDL-cholesterol ratio, highlight their potential to define and differentiate metabolic disorders (Cuevillas et al., 2021; Wang et al

CONCLUSION

This research indicates that a combined screening model of conventional anthropometric and biochemical with new salivary biomarkers and bioimpedance parameters are far more effective in early identification of undiagnosed metabolic syndrome among adults younger than fifty years old. The elastic net though

regularized (Model 8) model showed a very high discriminative performance with an AUCnership of 0.914, sensitivity of 88.3 and specificity of 88.9, which is significantly higher than that of models based purely on traditional risk factors. Salivary glucose was the best independent predictor, and then HOMAaddEventListener and the triglyceridextures to HDLratio, and phase angle showed a significant protective impact, which indicates the importance of non-invasive, point of care biomarkers in screening the population. The model had strong performance in all the demographic and clinical subgroups, and especially good performance among obese patients and age range 3549 years. Calibration was good, and decision curve analysis showed high quality net benefit at clinically relevant risk thresholds, which indicates clinical utility of this method. The implications of these findings to the wider community on their public health include the fact that the results yield a validated, cost-effective, screening strategy applicable to primary care and community-based settings to screen at-risk individuals before they manifest the overt disease. Because cardiometabolic diseases still grow in the world and are often left unnoticed during the course of multiple years, especially in young and disadvantaged groups, the usage of such combined screening procedures may help with the implementation of lifestyle and pharmacological interventions earlier, which will eventually lead to the decrease in morbidity, mortality and the costs of the healthcare system. Further studies are required in the future regarding external validation across a variety of populations and longitudinal evaluation of screening guided intervention effects.

REFERENCES

Akl, N. S. A., Haoudi, E. N., Bensmail, H., & Arredouani, A. (2023). The triglyceride glucose-waist-to-height ratio outperforms obesity and other triglyceride-related parameters in detecting prediabetes in normal-weight Qatari adults: A cross-sectional study. Frontiers in Public Health, 11. https://doi.org/10.3389/fpubh.2023.1086771

Alqaderi, H., Hegazi, F., Al-Mulla, F., Chiu, C., Kantarcı, A., Al-Ozairi, E., Abu-Farha, M., Bin-Hasan, S., Alsumait, A., Abubaker, J., Devarajan, S., Goodson, J. M., Hastürk, H., & Tavares, M. (2022). Salivary Biomarkers as Predictors of Obesity and Intermediate Hyperglycemia in Adolescents. Frontiers in Public Health, 10. https://doi.org/10.3389/fpubh.2022.800373

Barajas-Martínez, A., Easton, J. F., Rivera, A. L., Tapia, R., Cruz, L. de la, Cabrera, A. R., & Stephens, C. R. (2020). Metabolic

Physiological Networks: The Impact of Age. medRxiv (Cold Spring Harbor Laboratory). https://doi.org/10.1101/2020.08.05.20168997

Carris, N. W., Bunnell, B. E., Mhaskar, R., DuCoin, C., & Stern, M. (2023). A Systematic Approach to Treating Early Metabolic Disease and Prediabetes. Diabetes Therapy, 14(10), 1595. https://doi.org/10.1007/s13300-023-01455-9

Chen, M., Guo, J., ShangGuan, Y., Sun, Z., He, X., Tu, Q., & Yan, Q. (2025). Association of the triglyceride-glucose index combined with a body shape index with all-cause and cardiovascular mortality in individuals with cardiovascular-kidney-metabolic syndrome stage 0–3: findings from two prospective cohorts. Cardiovascular Diabetology, 24(1), 366. https://doi.org/10.1186/s12933-025-02921-3

Chong, B., Kong, G., Shankar, K., Chew, H. S. J., Lin, C., Goh, R., Chin, Y. H., Tan, D. J. H., Chan, K. E., Lim, W. H., Syn, N., Chan, S. P., Wang, J., Khoo, C. M., Dimitriadis, G. K., Wijarnpreecha, K., Sanyal, A. J., Noureddin, M., Siddiqui, M. S., … Chew, N. (2023). The global syndemic of metabolic diseases in the young adult population: A consortium of trends and projections from the Global Burden of Disease 2000–2019. Metabolism, 141, 155402. https://doi.org/10.1016/j.metabol.2023.155402

Cuevillas, B. de, Álvarez-Álvarez, I., Riezu-Boj, J. I., Navas-Carretero, S., & Martínéz, J. A. (2021). The hypertriglyceridemic-waist phenotype as a valuable and integrative mirror of metabolic syndrome traits. Scientific Reports, 11(1). https://doi.org/10.1038/s41598-021-01343-x

Dhondge, R. H., Agrawal, S., Patil, R., Kadu, A., & Kothari, M. (2024). A Comprehensive Review of Metabolic Syndrome and Its Role in Cardiovascular Disease and Type 2 Diabetes Mellitus: Mechanisms, Risk Factors, and Management. Cureus, 16(8). https://doi.org/10.7759/cureus.67428

Facciolà, A., Visalli, G., D'Andrea, G., Varvarà, M., Santoro, G., Cuffari, R., & Pietro, A. D. (2021). Prevention of cardiovascular diseases and diabetes: importance of a screening program for the early detection of risk conditions in a target population. PubMed, 62(4). https://doi.org/10.15167/2421-4248/jpmh2021.62.4.2360

Fagherazzi, G., Zhang, L., Aguayo, G., Pastore, J., Goetzinger, C., Fischer, A., Malisoux, L., Samouda, H., Bohn, T., Ruiz-Castell, M., & Huiart, L. (2021). Towards precision cardiometabolic prevention: results from a machine learning, semi-supervised clustering approach in the nationwide population-based ORISCAV-LUX 2 study. Scientific Reports, 11(1). https://doi.org/10.1038/s41598-021-95487-5

Gao, W., Deng, Z., Gong, Z., Jiang, Z., & Ma, L. (2025). AI-driven prediction of insulin resistance in non-diabetic populations using minimal invasive tests: comparing models and criteria. Diabetology & Metabolic Syndrome, 17(1). https://doi.org/10.1186/s13098-025-01920-4

Gesteiro, E., Megía, A., Guadalupe-Grau, A., Fernández-Veledo, S., Vendrell, J., & González-Gross, M. (2021). Early identification of metabolic syndrome risk: A review of reviews and proposal for defining pre-metabolic syndrome status. Nutrition Metabolism and Cardiovascular Diseases, 31(9), 2557. https://doi.org/10.1016/j.numecd.2021.05.022

Giangregorio, F., Mosconi, E., Debellis, M. G., Provini, S., Esposito, C., Garolfi, M., Oraka, S., Kaloudi, O., Mustafazade, G., Marín-Baselga, R., & Tung-Chen, Y. (2024). A Systematic Review of Metabolic Syndrome: Key Correlated Pathologies and Non-Invasive Diagnostic Approaches. Journal of Clinical Medicine, 13(19), 5880. https://doi.org/10.3390/jcm13195880

Goodson, J. M., Kantarcı, A., Hartman, M.-L., Denis, G. V., Stephens, D., Hastürk, H., Yaskell, T., Vargas, J., Wang, X., Cugini, M., Baraké, R., Alsmadi, O., Al-Mutawa, S., Ariga, J., Soparkar, P., Behbehani, J., Behbehani, K., & Welty, F. K. (2014). Metabolic Disease Risk in Children by Salivary Biomarker Analysis. PLoS ONE, 9(6). https://doi.org/10.1371/journal.pone.0098799

Guo, F., Moellering, D. R., & Garvey, W. T. (2013). The progression of cardiometabolic disease: Validation of a new cardiometabolic disease staging system applicable to obesity. Obesity, 22(1), 110. https://doi.org/10.1002/oby.20585

He, H., Xie, Y., Chen, Q., Li, Y., Li, X., Fu, S. W., Li, N., Han, Y., Gao, Y., & Zheng, J. (2025). The synergistic effect of the triglyceride-glucose index and a body shape index on cardiovascular mortality: the construction of a novel cardiovascular risk marker. Cardiovascular Diabetology,

24(1), 69. https://doi.org/10.1186/s12933-025-02604-z

Isaranuwatchai, W., Archer, R. A., & Culyer, A. J. (2019). 1. Introduction. In Open Book Publishers (p. 1). https://doi.org/10.11647/obp.0195.01

Islam, Md. S., Wei, P., Suzauddula, M., Nime, I., Feroz, F., Acharjee, M., & Pan, F. (2024). The interplay of factors in metabolic syndrome: understanding its roots and complexity. Molecular Medicine, 30(1), 279. https://doi.org/10.1186/s10020-024-01019-y

Jiang, X., Zhang, Y., Wang, S., & Deng, S. (2022). "Big Data" Approaches for Prevention of the Metabolic Syndrome [Review of "Big Data" Approaches for Prevention of the Metabolic Syndrome]. Frontiers in Genetics, 13. Frontiers Media. https://doi.org/10.3389/fgene.2022.810152

Johnson, M. (2019). Diet and Nutrition: Implications to Cardiometabolic Health. Journal of Cardiology and Cardiovascular Sciences, 3(2), 4. https://doi.org/10.29245/2578-3025/2019/2.1168

Khazdouz, M., Hasani, M., Mehranfar, S., Ejtahed, H., Djalalinia, S., Gorabi, A. M., Esmaeili-Abdar, M., Saleh, S. K., Arzaghi, S. M., Zahedi, H., Kasaeian, A., & Qorbani, M. (2021). Validity of continuous metabolic syndrome score for predicting metabolic syndrome; a systematic review and meta-analysis. Journal of Diabetes & Metabolic Disorders, 20(1), 497. https://doi.org/10.1007/s40200-021-00771-w

Kostara, C. (2023). Expanding the Molecular Disturbances of Lipoproteins in Cardiometabolic Diseases: Lessons from Lipidomics. Diagnostics, 13(4), 721. https://doi.org/10.3390/diagnostics13040721

Li, J., Yu, Y., Sun, Y., Fu, Y., Shen, W., Cai, L., Tan, X., Cai, Y., Wang, N., Lu, Y., & Wang, B. (2024). Nuclear magnetic resonance-based metabolomics with machine learning for predicting progression from prediabetes to diabetes. eLife, 13. https://doi.org/10.7554/elife.98709

Lv, L., Zhang, P., Chen, X., & Gao, Y. (2025). The association between triglyceride glucose-waist height ratio index and cardiometabolic multimorbidity among Chinese middle-aged and older adults: a national prospective cohort study. Cardiovascular Diabetology, 24(1). https://doi.org/10.1186/s12933-025-02919-x

Macek, P., Biskup, M., Terek-Derszniak, M., Król, H., Smok-Kalwat, J., Góźdź, S., & Žák, M. (2020). Optimal cut-off values for anthropometric measures of obesity in

screening for cardiometabolic disorders in adults. Scientific Reports, 10(1). https://doi.org/10.1038/s41598-020-68265-y

Mert, A. (2023). The Efficacy of Medical Check-up Programs in Screening Healthy, Asymptomatic Individuals: A Cross-Sectional Study. Medical Records, 5, 27. https://doi.org/10.37990/medr.1314861

Pan, Y., Du, B., Feng, L., & Bi, J. (2025). Comparative analysis of 16 baseline obesity and lipid-related indices for cardiovascular disease risk prediction in adults with cardiovascular-kidney-metabolic syndrome stages 0–3: a nationwide prospective cohort study. Diabetology & Metabolic Syndrome, 17(1). https://doi.org/10.1186/s13098-025-01919-x

Pujos-Guillot, E., Bertrand, J., Rambeau, M., Pétéra, M., Brandolini-Bunlon, M., Fernandes, A. E., Matta, J., Lévy-Marchal, C., Czernichow, S., & Comte, B. (2017). EPMA World Congress: Traditional Forum in Predictive, Preventive and Personalised Medicine for Multi-Professional Consideration and Consolidation. The EPMA Journal, 8, 1. https://doi.org/10.1007/s13167-017-0108-4

Quirino-Vela, L., Mayoral-Chávez, M. A., Pérez-Cervera, Y., Ildefonso-García, O., Cruz-Altamirano, E., Ruiz-García, M., & Alpuche, J. (2025). Cardiometabolic risk assessment by anthropometric and biochemical indices in mexican population. Frontiers in Endocrinology, 16, 1588469. https://doi.org/10.3389/fendo.2025.1588469

Rakers, M., Hattem, N. van, Plag, S., Chavannes, N. H., Os, H. J. A. van, & Vos, R. C. (2024). Population health interventions for cardiometabolic diseases in primary care: a scoping review and RE-AIM evaluation of current practices [Review of Population health interventions for cardiometabolic diseases in primary care: a scoping review and RE-AIM evaluation of current practices]. Frontiers in Medicine, 10. Frontiers Media. https://doi.org/10.3389/fmed.2023.1275267

Rakusanova, S., & Čajka, T. (2024). Metabolomics and Lipidomics for Studying Metabolic Syndrome: Insights into Cardiovascular Diseases, Type 1 & 2 Diabetes, and Metabolic Dysfunction-Associated Steatotic Liver Disease. Physiological Research. https://doi.org/10.33549/physiolres.935443

Rodríguez-Carrillo, P. L., Aguirre-Tostado, P. I., Macías-Cervantes, M. H., Alegría-Torres, J. A., & Luévano-Contreras, C.

(2021). Novel Adiposity and Biochemical–Anthropometric Indices to Identify Cardiometabolic Risk and Metabolic Syndrome in Mexican Adults. Healthcare, 9(11), 1561. https://doi.org/10.3390/healthcare9111561

Sadek, K., Abdelhafez, I., Al-Hashimi, I., Al-Shafi, W., Tarmizi, F., Al-Marri, H., Alzohari, N., Balideh, M., & Carr, A. (2021). Screening for diabetes and impaired glucose metabolism in Qatar: models' development and validation. medRxiv (Cold Spring Harbor Laboratory). https://doi.org/10.1101/2021.04.04.21254900

Sattar, N., Gill, J. M. R., & Alazawi, W. (2020). Improving prevention strategies for cardiometabolic disease [Review of Improving prevention strategies for cardiometabolic disease]. Nature Medicine, 26(3), 320. Nature Portfolio. https://doi.org/10.1038/s41591-020-0786-7

Song, J., Wang, C., Zhao, T., Zhang, Y., Zhang, Y., Xing, J., Zhao, X., Zhang, Y., Zhang, Y., & Zhang, Z. (2025). Multi-omics approaches for biomarker discovery and precision diagnosis of prediabetes. Frontiers in Endocrinology, 16, 1520436. https://doi.org/10.3389/fendo.2025.1520436

Stawiarska, A., Francik, R., Mikulec, A., Zborowski, M., Cisoń-Apanasewicz, U., Gajdosz, R., Zaczyk, I., Potok, H., Radom, A., Ogonowska, D., & Rafa, E. (2025). A Holistic Approach to Metabolic Health Assessment—Analysis of Bioimpedance, Blood, and Saliva Biochemistry in Population Studies—A Pilot Study. Metabolites, 15(9), 591. https://doi.org/10.3390/metabo15090591

Tahir, U. A., & Gerszten, R. E. (2023). Molecular Biomarkers for Cardiometabolic Disease: Risk Assessment in Young Individuals. Circulation Research, 132(12), 1663. https://doi.org/10.1161/circresaha.123.322000

Tapia-Conyer, R., Saucedo-Martínez, R., Mújica-Rosales, R., Gallardo-Rincón, H., Lee, E., Waugh, C., Guajardo, L., Torres-Beltrán, B., Quijano-González, Ú., Mendez, M. L., & Atkinson, E. R. (2017). A Policy Analysis on the Proactive Prevention of Chronic Disease: Learnings from the Initial Implementation of Integrated Measurement for Early Detection (MIDO). International Journal of Health Policy and Management, 6(6), 339. https://doi.org/10.15171/ijhpm.2017.18

The Tsunami of Cardiometabolic Diseases: An Overview. (2020). Journal of Diabetes

and Endocrinology Research. https://doi.org/10.47485/2693-2458/1004

Valdéz-Vega, R. I., Noboa-Velástegui, J., Fletes-Rayas, A. L., Álvarez, I., Ramos-Márquez, M. E., Ruíz-Quezada, S. L., Torres-Carrillo, N. M., & Navarro-Hernández, R. E. (2025). Predicting Metabolic Syndrome Using Supervised Machine Learning: A Multivariate Parameter Approach. International Journal of Molecular Sciences, 26(20), 9897. https://doi.org/10.3390/ijms26209897

Visioli, F., Martínez-Urbistondo, D., Gkipalis, S., Vidal-Ostos, F., Ruiz-Saavedra, A., León, M., Chaib, F. B., Hernández, A., Landecho, M. F., Laparra, J. M., Vizmanos, B., Ramos-López, O., Yannakoulia, M., & Martínéz, J. A. (2025). Translational biomarkers for integrated cardiovascular disease risk assessment: A multidisciplinary review with applications in precision medicine. Nutrition Metabolism and Cardiovascular Diseases, 35(12), 104215. https://doi.org/10.1016/j.numecd.2025.104215

Wang, W., Yan, Y., Guo, Z., Hou, H., Garcia, M., Tan, X., Anto, E. O., Mahara, G., Zheng, Y., Li, B., Kang, T., Zhong, Z., Wang, Y., Guo, X., & Golubnitschaja, O. (2021). All around suboptimal health — a joint position paper of the Suboptimal Health Study Consortium and European Association for Predictive, Preventive and Personalised Medicine. The EPMA Journal, 12(4), 403. https://doi.org/10.1007/s13167-021-00253-2

Wang, X., Kang, N., Li, P., Feng, L., Liu, J., & Ren, J. (2024). Associations between Cardiometabolic Index and heart failure in adults aged ≥ 20 years: Evidence from the NHANES 1999–2018. Research Square (Research Square). https://doi.org/10.21203/rs.3.rs-4229512/v1

Yakubu, I., Alhassan, M., Arhin, E. T., & Mohammed, H. (2025). Burden of hypertension and type 2 diabetes in Tamale Metropolis: a case study of Tamale teaching hospital. BMC Public Health, 25(1). https://doi.org/10.1186/s12889-025-23979-4

Yasmin, K. (2024). Cardiometabolic Risk Factors in South Asians: An Epidemiological and Anthropological Study in an Urban Populace of Eastern India. arXiv (Cornell University). https://doi.org/10.48550/arxiv.2412.06850

Yoon, S., Goh, H., Phang, J. K., Kwan, Y. H., & Low, L. L. (2023). Socioeconomic

and behavioral determinants of non-compliance with physician referrals following community screening for diabetes, hypertension and hyperlipidemia: a mixed-methods study. Scientific Reports, 13(1). https://doi.org/10.1038/s41598-023-47168-8

Yu, S., Lee, H., Yune, I., Jung, S. Y., & Hwang, H. (2024). Metabolic syndrome prediction models using only lifestyle information based on nationwide survey data. Research Square (Research Square). https://doi.org/10.21203/rs.3.rs-4386349/v1

Zarkogianni, K., Litsa, E., Mitsis, K., Wu, P.-Y., Kaddi, C., Cheng, C., Wang, M. D., & Nikita, K. S. (2015). A Review of Emerging Technologies for the Management of Diabetes Mellitus [Review of A Review of Emerging Technologies for the Management of Diabetes Mellitus]. IEEE Transactions on Biomedical Engineering, 62(12), 2735. Institute of Electrical and Electronics Engineers. https://doi.org/10.1109/tbme.2015.2470521

Zhang, F., Zhang, B., Huang, X., Wang, Z., Wang, J., Lan, H., Xie, G., Wang, W., Zou, Y., & Wang, C. (2025). Comparison of the TyG index, TyG-traditional obesity indices, and TyG-novel obesity indices: does increased complexity help in predicting cardiometabolic multimorbidity? Lipids in Health and Disease, 25(1), 33. https://doi.org/10.1186/s12944-025-02836-8

Zhang, H., Zhou, X., Shapiro, M. D., Lip, G. Y. H., Tilg, H., Valenti, L., Somers, V. K., Byrne, C. D., Targher, G., Yang, W., Viveiros, O., Opio, C., Mantzoros, C. S., Ryan, J., Kok, K. Y. Y., Jumaev, N. A., Perera, N., Robertson, A. G., Abu-Abeid, A., … Zheng, M. (2024). Global burden of metabolic diseases, 1990–2021. Metabolism, 160, 155999. https://doi.org/10.1016/j.metabol.2024.155999

Zhang, Y., Sun, J., Li, F., Grogan, T., Vergara, J. L., Luan, Q., Park, M., Chia, D., Elashoff, D., Joshipura, K., & Wong, D. T. (2017). Salivary extracellular RNA biomarkers for insulin resistance detection in hispanics. Diabetes Research and Clinical Practice, 132, 85. https://doi.org/10.1016/j.diabres.2017.07.008

Zhuang, Y., Qiu, L., Han, D., Qiao, Z., Wang, F., Jiang, Q., An, Q., Li, Y., Shangguan, J., Bi, X., & Shen, D. (2024). The association between triglyceride-glucose index and related parameters and risk of cardiovascular disease in American adults under different glucose metabolic states. Diabetology & Metabolic

Syndrome, 16(1). https://doi.org/10.1186/s13098-024-01340-w

Чумакова, Г. А., Kuznetsova, Т. Yu., Druzhilov, M. A., & Гриценко, О. В. (2024). Metabolic health of the population: a modern view of the problem and solutions. Russian Journal of Cardiology, 29(5), 5896. https://doi.org/10.15829/1560-4071-2024-5896