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Untangling the role of diet quality and other risk factors in the severity of metabolic syndrome: Insights from the Hoveyzeh Cohort study using structural equation modeling

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ABSTRACT

Aims: In this study, we aim to employ structural equation modeling (SEM) to assess the relationships between adherence to diet quality scores, such as the Dietary Diversity Score (DDS), Paleolithic Diet Score (PDS), and EAT-Lancet Diet Score, and other risk factors, including, demographic, socio-economic, behavioral, and clinical characteristics, with MetS severity.

Methods: This cross-sectional study involved 8,086 participants from the Hoveyzeh Cohort Study (3,486 males and 4,600 females). Dietary intake was assessed using a validated semi-quantitative food frequency questionnaire, which was also used to calculate energy-adjusted diet scores. Anthropometric, biochemical, and blood pressure measurements were evaluated following standardized protocols. The interrelationships between risk factors and MetS severity were analyzed using SEM.

Results: The models indicated that the DDS had a statistically significant association with MetS severity through direct effects ($\beta_{Females}$ = -0.04; β_{Males} = -0.04) and indirect effects ($\beta_{Females}$ = -0.06; β_{Males} = -0.09). Similarly, the PDS showed a statistically significant inverse relationship with MetS severity, including direct effects ($\beta_{Females}$ = -0.03; β_{Males} = -0.02) and indirect effects ($\beta_{Females}$ = -0.05; β_{Males} = -0.07). In contrast, the EAT-Lancet Diet Score demonstrated a statistically significant inverse association with MetS severity only through indirect effects ($\beta_{Females}$ = -0.04; β_{Males} = -0.03).

Conclusion: The findings emphasize that improving diet quality as a means of managing modifiable risk factors may reduce MetS severity.

Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; BMI, Body mass index; CFI, Comparative fit index; cMetS-S, Continuous metabolic syndrome severity score; CVD, Cardiovascular disease; FFQ, Food frequency questionnaire; DBP, Diastolic blood pressure; FPG, Fasting plasma glucose; HDL-c, High-density lipoprotein cholesterol; HCS, Hoveyzeh Cohort Study; HSI, Hepatic steatosis index; MET, Metabolic equivalent of the task; MetS, Metabolic syndrome; PDS, Paleolithic Diet Score; RMSEA, Root mean square error of approximation; SBP, Systolic blood pressure; SEM, Structural equation modeling; SRMR, Standardized root mean square residual; TC, Total cholesterol; T2DM, Type 2 diabetes mellitus; TG, Triglycerides; TLI, Tucker-lewis index; WC, Waist circumference; VAI, Visceral adipose index.

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1. Introduction

Metabolic syndrome (MetS) is a cluster of interconnected non-communicable conditions characterized by a combination of cardiometabolic risk factors, including abdominal obesity, dyslipidemia, hypertension, and insulin resistance [1]. MetS increases the risk of developing both cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM). Patients with MetS have about twice the risk of developing CVD and about 3.5 times the risk of developing T2DM [2,3]. The global prevalence of MetS varies widely, ranging from 12.5 % to 31.4 %, and is influenced by geographic and demographic factors, with a noticeable upward trend [4]. In Iran, epidemiological studies report a MetS prevalence of 30.8 % in 2020, highlighting it as a significant public health concern [5]. Previous studies suggested that environmental and lifestyle factors such as socio-economic status, obesity, smoking, poor sleep quality, physical inactivity, and unhealthy dietary habits are contributors to the development of MetS [6,7].

Recent studies have explored various a *priori* dietary patterns that showed an inverse relationship with metabolic disorders. Among these, the Paleolithic Diet Score (PDS) has garnered increasing attention in nutritional epidemiology due to its potential benefits in managing metabolic disorders [8]. The PDS is based on the dietary patterns of Paleolithic hunter-gatherers, emphasizing foods that were available during that era. Specifically, it prioritizes plant-based foods, including calcium-rich wild plants and a diverse range of fruits and vegetables [9]. The US Dietary Guidelines have long advocated for consuming a variety of foods, initially focusing on major food groups and later emphasizing nutrient-dense options within recommended limits [10]. Epidemiological evidence suggests that higher adherence to diverse diets, as measured by the Dietary Diversity Score (DDS), is associated with healthier dietary patterns and adequate intake of essential macro- and micronutrients. The DDS evaluates overall diet quality by assessing the consumption of major food groups, offering a more holistic approach than focusing on individual foods or nutrients [11]. When examining dietary patterns about non-communicable diseases, it is crucial to consider declining adherence to healthy diets and the environmental sustainability of food systems. There is growing advocacy for adopting healthy, environmentally sustainable diets, as they offer dual benefits for both human health and the planet. The 2019 EAT-Lancet Commission report provided global dietary recommendations aimed at promoting both human and planetary health, emphasizing the consumption of plant-based foods, reducing the intake of animal products, and minimizing food waste [12].

Several studies have reported a positive correlation between adherence to dietary quality indices such as DDS, PDS, and the EAT-Lancet dietary pattern and improvements in metabolic syndrome components [8,13,14]. However, potential confounders, such as lifestyle behaviors and socio-demographic variables, make it challenging to study the association between the mentioned dietary quality indices and metabolic disorders. Thus, a more comprehensive understanding of these associations can be achieved by examining complex pathways involving interrelated factors rather than focusing solely on direct relationships. Structural equation modeling (SEM) is a statistical method that allows for the analysis of conceptual models by quantifying relationships and interactions within a network of variables. A key strength of SEM is its ability to simultaneously evaluate all relevant pathways, accounting for the roles of both independent and dependent variables in determining outcomes [15]. To our knowledge, no previous study has simultaneously examined the direct and indirect relationships between the severity of MetS as a continuous variable and modifiable risk factors. Therefore, the current study aimed to explore the relationships between dietary quality scores, specifically the PDS, DDS, and EAT-Lancet Diet Score, lifestyle behaviors, clinical and biochemical factors, socio-demographic variables, and newly developed MetS severity scores in adults, utilizing SEM.

2. Materials and Methods

2.1. Study population

This cross-sectional study utilized data from the baseline phase of the Hoveyzeh Cohort Study (HCS), a population-based prospective cohort initiated in May 2016 as part of the national Prospective Epidemiological Research Study in Iran (Persian Cohort) [16,17]. The HCS aims to investigate the prevalence of non-communicable diseases and associated risk factors among the ethnic Arab population in Khuzestan, southwestern Iran. A detailed overview of the HCS design, including participant selection, data collection, and study objectives, has been published as a Cohort Profile Study [18]. Initially, 10,009 adults (aged 35–70, of Iranian descent, and residing in Hoveyzeh for $\geq$ 9 months/year) were enrolled after providing informed consent. For the present analysis, we included only participants with complete data on demographic, food frequency questioner, anthropometric, biochemical, and clinical variables, excluding those with myocardial infarction (n = 185), stroke (n = 159), renal disease (n = 123), thyroid disease (n = 540), gallstones (n = 297), rheumatic disease (n = 437), cancer (n = 37), type 1 diabetes (n = 5), pregnancy (n = 163), or implausible daily energy intake (<700 or > 5400 kcal/day; n = 199). After exclusions, 8,086 individuals were retained for the final analysis **(Supplementary Fig. 1)**. All study procedures were conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. The research protocol was reviewed and approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences (IR.AJUMS.REC.1402.686).

2.2. Demographics, socio-economic, and lifestyle characteristics

Age, gender, residential status, marital status, educational level (based on the years of education completed), occupation, sleep duration, and medical history were collected through face-to-face interviews using pre-tested questionnaires. A wealth index based on household wealth was used to calculate each participant's socioeconomic status. The methodology for calculating the wealth index is detailed in the **Supplementary Methods**. Smoking was defined as having smoked at least 100 cigarettes for a lifetime. Never-smokers were described as having never smoked. Physical activity was measured using a modifiable activity questionnaire previously validated in the Iranian population [19]. Participants were asked to report the frequency and duration of light, moderate, heavy, and vigorous activities over the past year. Activities consisted of daily routine tasks, and the results were converted into metabolic equivalent hours per week (MET-h/wk). Positive family history for T2DM, hypertension, or ischemic heart disease was defined by self-reported interview data indicating at least one affected first-degree relative. The health status of individuals was determined based on the total number of self-reported diseases, excluding those that met the exclusion criteria (**Supplementary Methods**).

2.3. Anthropometric and blood pressure measurements

The anthropometric data collection was conducted in the morning, following the collection of blood samples to reduce measurement error or bias. Standardized procedures and consistent lighting were used to improve the accuracy of measurements. Participants' weights (kg) were measured using a Seca 755 standing scale, and their heights (cm) were measured using a Seca 206 stadiometer. Additionally, the waist circumference (WC) was measured in centimeters using a Seca tape measure with a locking mechanism. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m^2). The systolic and diastolic blood pressures (SBP and DBP) of participants were measured twice from each arm in a seated position, utilizing standard mercury sphygmomanometers, with a 10-minute rest period between readings. The mean value of the two measurements was calculated and recorded for analysis.

2.4. Biochemical assessment

Blood samples were collected by trained staff from participants after a 10–12-hour fast. Serum was separated from blood by centrifugation at 1000 rpm for 15 min, and samples were stored at −80 °C until analysis. The glucose oxidase technique was used to determine fasting plasma glucose (FPG). Enzymatic kits (Pars Azmoon, Iran) were used to determine lipid and lipoprotein markers, including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG), as well as liver enzymes such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Further details regarding the procedure are outlined in the study protocol [18]. We also calculated the visceral adipose index (VAI) [20] and the hepatic steatosis index (HSI) [21] using the formulas in this study (**Supplementary Methods**).

2.5. Metabolic syndrome severity score

MetS severity scores were calculated for each individual using gender-specific formulas developed and validated in the Iranian population [22] (**Supplementary Methods**, **Table S1**). Confirmatory factor analysis was used to derive the formula for the five components of MetS, including SBP, WC, FPG, TG, and HDL-C. Gender was used as a stratifying variable in this analysis, and the weighted contribution of each element to the latent MetS components was evaluated. The MetS severity scores were subsequently standardized to a mean of 0 and a standard deviation of 1, producing z-scores for each participant [22]. Higher scores indicated greater MetS severity.

2.6. Dietary intake assessment

A 130-item Food Frequency Questionnaire (FFQ) validated for the Persian Cohort Study was used to assess dietary intake over the previous year [18]. FFQ was semi-quantitative and divided into 29 food groups. The participants were asked to report the frequency with which they consumed each food item, ranging from daily to once a year. Dietary intakes were measured in households and converted to grams per day. Nutritionist IV software was used to determine total energy and nutrient intakes.

2.7. Diet quality scores calculation

The residual method was used to energy-adjust all food items and nutrients contributing to the dietary score [23]. The scoring criteria used to calculate the diet quality scores are detailed in the **Supplementary Methods**, **Table S2**.

2.7.1. Dietary diversity score

The Dietary Diversity Score (DDS) calculation encompasses the five main food groups outlined in the USDA Food Guide Pyramid: grains, vegetables, fruits, meat, and dairy products. The primary groups were classified into 23 categories according to the methodology Kant et al. developed [11]. Every leading group reached a diversity score of up to two points on a ten-point scale. The percentage of possible maximum points is given by the score points calculated within each group. The scores of the five main groups, ranging from zero to ten, were summed to provide the DDS.

2.7.2. Paleolithic diet score

The Paleolithic diet score (PDS) was calculated using the method described by Whalen et al. [24] method, which considers 14 dietary factors, such as food groups, nutrient content, and dietary diversity. According to their positive or negative effects on health, 14 food items were classified. Seven food items were considered to have positive effects, including vegetables, fruits, fruit and vegetable diversity, lean meat, nuts, fish, and non-dairy calcium sources. Harmful foods include seven food groups and nutrients, such as red and processed meat, dairy products, sugar-sweetened drinks, baked goods, dietary sodium, grains and starches, and alcohol. Lastly, daily consumption of all food items was categorized into quintiles (1 to 5), with quintile 1 representing the lowest and quintile 5 the highest intake within each food group.

2.7.3. Eat-lancet diet score

For the calculation of the EAT-Lancet diet score, foods were classified into 14 dietary components, including whole grains; tubers and starchy vegetables; vegetables; fruits; dairy foods; beef, lamb, and pork; poultry; eggs; fish and seafood; dry beans, lentils, peas; soy foods; nuts; added fats; and added sugars. The EAT-Lancet Diet Score was then constructed based on the guidelines and reference standards provided by the EAT-Lancet Commission. One score was assigned to participants who followed the diet; otherwise, no score was assigned. The EAT-Lancet Diet Score, ranging from zero (non-adherence) to 14 (perfect adherence), was calculated by summing the scores for each component [12].

The DDS, PDS, and EAT-Lancet Diet Score were selected to assess diet quality from distinct perspectives comprehensively. The DDS evaluates variety across major food groups, reflecting adherence to traditional dietary guidelines [11]. The PDS emphasizes whole, unprocessed foods aligned with evolutionary dietary patterns, which may benefit metabolic health [8,9]. The EAT-Lancet score integrates health and environmental sustainability, addressing planetary health while also considering cardiometabolic risk [12]. Together, these indices capture diversity, evolutionary alignment, and sustainability, which are key dimensions of modern dietary recommendations.

2.8. Conceptual framework

Following a review of the existing scientific literature in the field of nutrition and metabolic disorders, a conceptual model was developed as reported in **Supplementary Methods**, **Table S3**. Modifiable risk factors are classified into seven groups including demographics (age, residential status, marital status), socioeconomic (education years, current employment status, and wealth index), behavioral (smoking status, physical activity, different diet quality indices [DDS, PDS, and Eat-Lancet Diet Score]), blood lipid (TC), obesity status (BMI, VAI), liver's health status (HSI) and health indicators (participant's health status, family history of three major metabolic disorders) **(Supplementary Fig. 2)**.

2.9. Statistical analysis

Frequency (percentage) and mean ± standard deviation (SD) were used for presenting categorical and continuous variables, respectively. Female and male participants were categorized based on median cut-off points of different dietary scores (DDS, PDS, Eat-Lancet). Qualitative risk factors were compared in each dietary score group by two independent samples t-tests. Significant differences in the quantitative risk factors across groups of different dietary scores were reported using a chi-square test. Simultaneous modeling and estimation of complicated relationships between multiple independent and dependent variables could be done by using the SEM [15]. Typically, a SEM comprises two components: a measurement model and a structural model [25]. In this study, a measurement model utilizing confirmatory factor analysis for identifying latent variables was not applicable. Therefore, the structural model with direct and indirect effects, a generalization of regression analysis, was employed to test the conceptual models within each gender group. A pathway that connects an exogenous variable to the outcome without considering any mediating factors is referred to as the direct effect. In contrast, a path that connects an exogenous variable to the outcome through mediating risk factors is known as an indirect effect. Indirect (mediated) effects were evaluated within the SEM framework using the product-of-coefficients methods. Mediation can be classified as complete when only a statistically significant indirect effect exists, or incomplete when both effects are statistically

significant. Details on model fit assessment are fully described in the **Supplementary Methods** file. All p-values were two-sided, and a p-value less than 0.05 was considered statistically significant.

3. Result

3.1. Descriptive statistics

The study included 8,086 participants, of whom 4,600 (56.9 %) were female and 3,486 (43.1 %) were male. The participants' ages ranged from 35 to 75 years, with a mean age of 48.41 ± 9.15 years. Tables 1 and 2 provide an overview of the baseline characteristics, including demographic and socioeconomic factors, lifestyle behaviors, anthropometric data, and metabolic variables, for female and male participants across the dietary score groups (DDS, PDS, and EAT-Lancet Diet Score). In addition, **Supplementary Table 1** shows baseline information between included and excluded participants.

3.2. Female participants

Descriptive statistics for female participants stratified by median dietary scores (DDS, PDS, EAT-Lancet) are presented in Table 1. Participants with higher DDS and PDS tended to have longer education durations (P-value < 0.001), higher rates of current employment (P-value = 0.007 for DDS), and greater physical activity levels (P-value = 0.007 for PDS), as well as elevated HDL-c levels (P-value < 0.001 for DDS). Additionally, lower DDS and PDS were more common among older individuals (P-value < 0.001) and those with higher SBP (P-value < 0.001), DBP (P-value = 0.01), FPG (P-value < 0.001), TG (P-value < 0.001), WC (P-value < 0.001), VAI (P-value < 0.001), and a greater number of chronic diseases (P-value = 0.003). For the EAT-Lancet score, lower adherence was observed in participants with higher TG (P-value < 0.001), WC (P-value < 0.001), BMI (P-value = 0.003), VAI (P-value < 0.001), HSI (P-value = 0.004), and weight (P-value = 0.001). However, no significant differences were noted for age or blood pressure.

3.3. Male participants

Table 2 outlines the characteristics of male participants across dietary score groups. Participants with high PDS had higher physical activity levels (P-value = 0.01), while lower DDS and PDS were more prevalent among older individuals (P-value = 0.02 for DDS) and those

Table 1
Baseline Characteristics of Female Participants in the Hoveyzeh Cohort Study, Stratified by Median Diet Quality Scores (n = 4600)[1].

	DDS			PDS			Eat-Lancet		
	≤ 4.97 n = 2284	> 4.97 n = 2316	P-value	≤ 38.57 n = 2326	> 38.57 n = 2274	P-value	≤ 10 n = 2287	> 10 n = 2313	P-value
Demographic									
Age, y	48.74 ± 9.19	47.60 ± 8.99	<0.001	48.67 ± 9.09	47.66 ± 9.10	<0.001	48.20 ± 8.97	48.14 ± 9.24	0.81
Urban Residents	1328 (58.1)	1376 (59.4)	0.19	1346 (57.9)	1358 (59.7)	0.10	1354 (59.2)	1350 (58.4)	0.29
Marital status	1839 (80.5)	1869 (80.7)	0.05	1870 (80.4)	1838 (80.8)	0.008	1849 (80.8)	1859 (80.4)	0.61
Socio-Economic									
Education years	2.19 ± 3.51	2.58 ± 3.95	<0.001	2.20 ± 3.62	2.58 ± 3.86	<0.001	2.40 ± 3.76	2.37 ± 3.73	0.78
Currently employed	95 (4.2)	132 (5.7)	0.007	110 (4.7)	117 (5.1)	0.54	2171 (94.9)	2189 (94.6)	0.25
Wealth index	1.90 ± 0.79	1.91 ± 0.77	0.72	1.89 ± 0.78	1.92 ± 0.78	0.19	1.91 ± 0.77	1.89 ± 0.79	0.51
Lifestyle Behaviors									
Sleep duration, h	7.97 ± 1.48	7.91 ± 1.45	0.17	7.97 ± 1.47	7.91 ± 1.46	0.16	7.96 ± 1.46	7.92 ± 1.47	0.29
Smoking status	166 (7.3)	172 (7.4)	0.44	133 (8.5)	103 (6.9)	0.09	169 (7.4)	169 (7.3)	0.47
PA, MET-h/wk	36.49 ± 4.18	36.71 ± 4.04	0.06	36.44 ± 4.11	36.77 ± 4.12	0.007	36.63 ± 4.13	36.57 ± 4.10	0.59
Clinical parameters									
SBP, mmHg	111.75 ± 18.48	109. 84 ± 18.26	<0.001	111.87 ± 18.65	109.68 ± 18.06	<0.001	111.01 ± 18.77	110.57 ± 18.01	0.41
DBP, mmHg	70.40 ± 11.08	69.61 ± 10.93	0.01	70.62 ± 11.26	69.37 ± 10.71	<0.001	70.06 ± 11.16	69.94 ± 10.87	0.69
FPG, mg/dL	114.03 ± 49.86	107.83 ± 46.55	<0.001	113.50 ± 49.94	108.26 ± 46.46	<0.001	112.14 ± 50.28	109.69 ± 46.27	0.08
TG, mg/dL	157.46 ± 93.11	141.94 ± 96.52	<0.001	157.54 ± 95.16	141.57 ± 94.48	<0.001	155.30 ± 96.96	144.06 ± 93.00	<0.001
TC, mg/dL	191.21 ± 40.10	189.91 ± 41.41	0.28	191.80 ± 40.01	189.29 ± 41.50	0.03	191.56 ± 41.20	189.56 ± 40.31	0.09
HDL-c, mg/dL	52.23 ± 11.83	53.87 ± 12.22	<0.001	52.85 ± 11.70	53.27 ± 12.40	0.23	52.74 ± 11.79	53.37 ± 12.31	0.07
AST, mg/dL	17.58 ± 7.97	17.51 ± 11.30	0.78	17.67 ± 8.36	17.42 ± 11.06	0.40	17.76 ± 11.74	17.33 ± 7.36	0.13
ALT, mg/dL	18.22 ± 12.44	17.63 ± 12.49	0.11	18.27 ± 12.78	17.56 ± 12.14	0.05	18.20 ± 13.18	17.64 ± 11.72	0.12
Obesity Status									
Weight, kg	74.90 ± 14.83	74.17 ± 15.01	0.10	74.98 ± 14.74	74.07 ± 15.10	0.04	75.28 ± 14.96	73.79 ± 15.12	0.001
BMI, kg/m^2	29.59 ± 5.49	29.36 ± 5.51	0.16	29.59 ± 5.40	29.36 ± 5.60	0.15	29.72 ± 5.45	29.23 ± 5.54	0.003
WC, cm	101.39 ± 11.98	100.08 ± 12.18	<0.001	101.49 ± 11.89	99.96 ± 12.26	<0.001	101.38 ± 11.90	100.09 ± 12.26	<0.001
VAI	2.97 ± 2.20	2.56 ± 2.09	<0.001	2.95 ± 2.28	2.58 ± 2.01	<0.001	2.88 ± 2.26	2.64 ± 2.04	<0.001
Liver's health status									
HSI	37.69 ± 6.49	37.32 ± 6.56	0.05	37.68 ± 6.39	37.32 ± 6.66	0.06	37.78 ± 6.50	37.22 ± 6.54	0.004
Health Indicators									
Family history*	1623 (71.1)	1644 (71.0)	0.49	1656 (71.2)	1611 (70.8)	0.41	1624 (71.0)	1643 (71.0)	0.50
Health Status	1.15 ± 1.38	1.03 ± 1.30	0.003	1.16 ± 1.38	1.01 ± 1.30	<0.001	1.15 ± 1.38	1.03 ± 1.30	0.003

[a]Values are means ± SDs unless otherwise indicated. P-values were computed by Student's *t*-test for continuous variables and chi-square test for categorical variables. **Residential status** denotes urban compared with rural. **Marital status** denotes a married person compared with a single person (single, widow, divorced). **Currently employed** denotes employed compared with jobless (retired, broken-down, and housewife). **Smoking status** denotes smokers (a person who has smoked more than 100 cigarettes in their lifetime) compared with Non-smokers.

ALT: Alanine aminotransferase; **AST**: Aspartate aminotransferase; **BMI**: Body mass index; **cMetS-S:** Continuous Metabolic Syndrome Severity Score; **DBP**: Diastolic blood pressure; **DDS**: Dietary diversity score; **FPG**: Fasting plasma glucose; **HDL-c**: High-density lipoprotein cholesterol; **HSI**: Hepatic steatosis index; **MET**: Metabolic equivalent of the task; **PDS**: Paleolithic diet score; SBP: Systolic blood pressure; **TC**: Total cholesterol; **TG**: Triglycerides; **VAI**: Visceral adipose index; **WC**: Waist circumference.*Type 2 diabetes mellitus, hypertension, and ischemic heart disease.

Table 2
Baseline Characteristics of Male Participants in the Hoveyzeh Cohort Study, Stratified by Median Diet Quality Scores (n = 3486)[1].

	DDS			PDS			Eat-Lancet		
	≤ 5.14 n = 1739	> 5.14 n = 1747	P-value	≤ 39.14 n = 1725	> 39.14 n = 1761	P-value	≤ 10 n = 1714	> 10 n = 1772	P-value
Demographic									
Age, y	49.08 ± 9.25	48.38 ± 9.14	0.02	48.72 ± 9.12	48.73 ± 9.28	0.97	48.53 ± 9.10	48.92 ± 9.30	0.20
Urban Residents	1126 (64.7)	1092 (62.5)	0.09	1101 (63.8)	1117 (63.4)	0.41	1106 (64.5)	1112 (62.8)	0.14
Marital status	1705 (98.0)	1711 (97.9)	0.76	1694 (98.2)	1722 (97.8)	0.40	1681 (98.1)	1735 (97.9)	0.68
Socio-Economic									
Education years	6.47 ± 5.40	6.77 ± 5.45	0.09	6.53 ± 5.47	6.71 ± 5.39	0.32	6.80 ± 5.44	6.44 ± 5.42	0.05
Currently employed	1289 (74.1)	1345 (77.0)	0.27	1310 (75.9)	1324 (75.2)	0.96	1305 (76.1)	1329 (75.0)	0.19
Wealth index	2.08 ± 0.73	2.11 ± 0.70	0.25	2.10 ± 0.72	2.09 ± 0.71	0.94	2.10 ± 0.71	2.09 ± 0.72	0.46
Lifestyle Behaviors									
Sleep duration, h	7.20 ± 1.62	7.11 ± 1.52	0.10	7.14 ± 1.59	7.17 ± 1.56	0.51	7.14 ± 1.54	7.17 ± 1.60	0.49
Smoking status	685 (39.4)	682 (39.0)	0.42	674 (39.1)	693 (39.4)	0.44	681 (39.7)	686 (38.7)	0.28
PA, MET-h/wk	37.91 ± 7.37	38.35 ± 7.47	0.08	37.83 ± 7.18	38.42 ± 7.64	0.01	38.00 ± 7.23	38.26 ± 7.60	0.31
Clinical parameters									
SBP, mmHg	117.11 ± 17.81	114.49 ± 15.71	<0.001	116.99 ± 17.50	114.64 ± 16.08	<0.001	115.93 ± 17.13	115.67 ± 16.56	0.65
DBP, mmHg	73.97 ± 11.54	72.71 ± 10.65	0.001	74.26 ± 11.36	72.43 ± 10.80	<0.001	73.59 ± 11,22	73.09 ± 11.01	0.18
FPG, mg/dL	114.20 ± 49.69	109.54 ± 47.96	0.005	113.29 ± 48.52	110.47 ± 49.20	0.08	112.01 ± 47.12	111.73 ± 50.53	0.86
TG, mg/dL	190.49 ± 123.35	173.06 ± 113.70	<0.001	191.55 ± 132.53	172.16 ± 103.00	<0.001	182.45 ± 116.81	181.08 ± 120.94	0.73
TC, mg/dL	187.28 ± 39.24	187.69 ± 38.80	0.75	188.07 ± 38.99	186.90 ± 39.04	0.37	188.04 ± 39.80	186.95 ± 38.24	0.41
HDL-c, mg/dL	45.66 ± 10.32	46.49 ± 10.35	0.01	45.91 ± 10.47	46.24 ± 10.22	0.35	45.91 ± 10.20	46.24 ± 10.48	0.35
AST, mg/dL	20.61 ± 8.76	20.51 ± 8.93	0.72	20.59 ± 8.56	20.52 ± 9.12	0.81	20.60 ± 8.66	20.52 ± 9.02	0.78
ALT, mg/dL	27.38 ± 17.47	26.70 ± 17.78	0.25	27.39 ± 17.26	26.60 ± 17.97	0.24	27.51 ± 17.75	26.58 ± 17.50	0.12
Obesity Status									
Weight, kg	83.24 ± 15.37	81.04 ± 14.72	<0.001	83.16 ± 15.03	81.14 ± 15.13	<0.001	82.55 ± 15.33	81.74 ± 14.89	0.11
BMI, kg/m^2	27.76 ± 4.63	27.03 ± 4.49	<0.001	27.74 ± 4.61	27.06 ± 4.52	<0.001	27.53 ± 4.67	27.27 ± 4.48	0.09
WC, cm	97.90 ± 11.65	95.74 ± 11.25	<0.001	97.65 ± 11.53	95.99 ± 11.42	<0.001	97.12 ± 11.55	96.52 ± 11.45	0.12
VAI	2.72 ± 2.34	2.40 ± 2.15	<0.001	2.72 ± 2.51	2.40 ± 1.96	<0.001	2.57 ± 2.23	2.55 ± 2.27	0.73
Liver's health status									
HSI	38.10 ± 6.58	37.16 ± 6.97	<0.001	38.11 ± 7.04	37.15 ± 6.51	<0.001	37.90 ± 6.64	37.37 ± 6.93	0.02
Health Indicators									
Family history*	1121 (64.5)	1140 (65.3)	0.32	1119 (64.9)	1142 (64.8)	0.50	1112 (64.9)	1149 (64.8)	0.50
Health Status	0.98 ± 1.20	0.88 ± 1.15	0.01	0.96 ± 1.20	0.91 ± 1.15	0.27	0.94 ± 1.19	0.93 ± 1.17	0.71

[a]Values are means ± SDs unless otherwise indicated. P values were computed by Student's *t*-test for continuous variables and chi-square test for categorical variables. **Residential status** denotes urban compared with rural. **Marital status** denotes a married person compared with a single person (single, widow, divorced). **Currently employed** denotes employed compared with jobless (retired, broken-down, and housewife). **Smoking status** denotes smokers (a person who has smoked more than 100 cigarettes in their lifetime) compared with Non-smokers.

ALT: Alanine aminotransferase; **AST**: Aspartate aminotransferase; **BMI**: Body mass index; **cMetS-S:** Continuous Metabolic Syndrome Severity Score; **DBP**: Diastolic blood pressure; **DDS**: Dietary diversity score; **FPG**: Fasting plasma glucose; **HDL-c**: High-density lipoprotein cholesterol; **HSI**: Hepatic steatosis index; **MET**: Metabolic equivalent of the task; **PDS**: Paleolithic diet score; **SBP**: Systolic blood pressure; **TC**: Total cholesterol; **TG**: Triglycerides; **VAI**: Visceral adipose index; **WC**: Waist circumference. *Type 2 diabetes mellitus, hypertension, and ischemic heart disease.

with elevated SBP (P-value < 0.001), DBP (P < 0.001), FPG (P-value = 0.005 for DDS), TG (P-value < 0.001), weight (P-value < 0.001), BMI (P-value < 0.001), WC (P-value < 0.001), VAI (P-value < 0.001), and HSI (P-value < 0.001). Participants with lower EAT-Lancet scores had higher HSI (P-value = 0.02), but no other significant trends emerged.

3.4. Structural equation Modelling

Figs. 1-3 present the best-fit hypothesized models, displaying standardized path coefficients stratified by gender. Figs. 1-3 and **Supplementary Table 2-7** showed that the DDS exhibited significant inverse associations with the severity of MetS. These associations included direct effects ($\beta_{Females}$ = -0.04; β_{Males} = -0.04), indirect effects ($\beta_{Females}$ = -0.06; β_{Males} = -0.09), and total effects ($\beta_{Females}$ = -0.11; β_{Males} = -0.14). Similarly, the PDS showed significant inverse relationships with MetS severity, including direct effects ($\beta_{Females}$ = -0.03, βMales = -0.02), indirect effects (βFemales = -0.05, βMales = -0.07), and total effects (βFemales = -0.09, β_{Males} = -0.09). The EAT-Lancet Diet Score demonstrated significant inverse relationships with MetS severity only through indirect effects ($\beta_{Females}$ = -0.04; β_{Males} = -0.03) and total effects ($\beta_{Females}$ = -0.06; β_{Males} = -0.04), underscoring its role in mitigating MetS severity through mediating pathways. **Supplementary Figs. 3-5** present the direct, indirect, and total effects linking diet quality scores to metabolic syndrome severity, with simplified pathways stratified by sex.

Diet quality influenced the severity of MetS through multiple mediators, including adiposity and metabolic dysfunction. In both genders, DDS, PDS, and the EAT-Lancet diet score had significant indirect effects on MetS severity through mediators such as higher BMI (except for the EAT-Lancet diet score), higher VAI (except for the EAT-Lancet diet score), higher HSI, and a higher number of individuals' diseases (only in females for the EAT-Lancet diet). Notably, in males, all three diet scores exhibited additional indirect effects via prolonged sleep duration and elevated TC, suggesting gender-specific metabolic interactions.

Demographic and lifestyle factors further modified these associations. Older age and urban residence were linked to higher MetS severity, with indirect effects mediated by smoking, physical inactivity, poor diet quality (DDS and PDS), and adverse metabolic profiles. Interestingly, urban residency did not significantly correlate with diet quality indices, though its association with TC was male-specific. Marriage was associated with greater MetS severity, partly mediated by

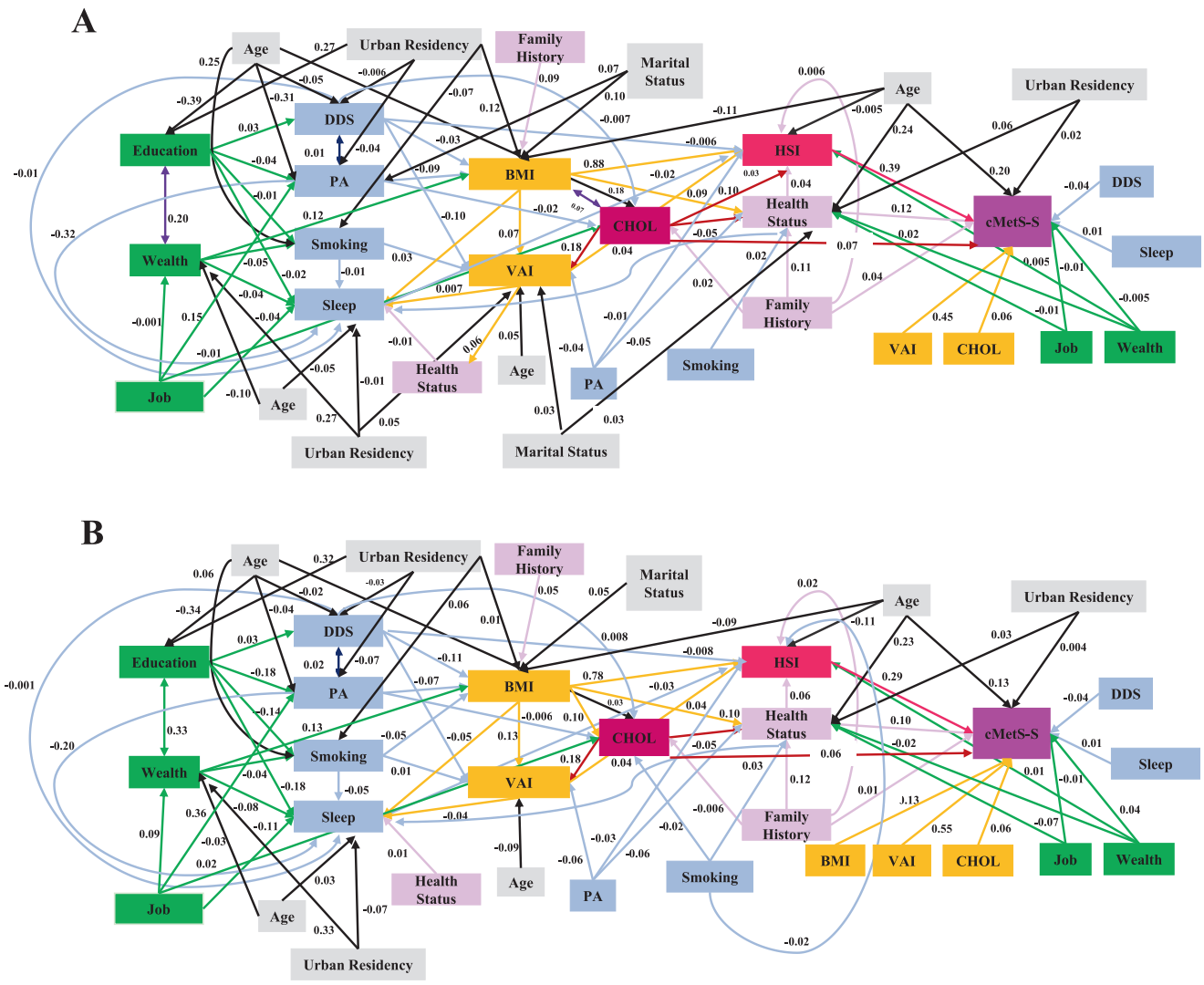

Fig. 1. Best-fit conceptual model illustrating pathways of risk factors to the severity of metabolic syndrome for **(A)** female participants [Comparative Fit Index (CFI) = 0.961, Tucker-Lewis Index (TLI) = 0.888, Root Mean Square Error of Approximation (RMSEA) = 0.058 [90 % CI: 0.055, 0.062], Standardized Root Mean Square Residual (SRMR) = 0.028] and **(B)** male participants (CFI = 0.994, TLI = 0.982, RMSEA = 0.022 [90 % CI: 0.017, 0.027], SRMR = 0.014). Several factors are repeated at different locations, with different pathways depicted for easy reading, but they do not differ significantly from their identical counterparts. BMI: body mass index; cMetS-S: continuous metabolic syndrome severity score; CHOL: total cholesterol; DDS: dietary diversity score; HSI: hepatic steatosis index; PA: physical activity; VAI visceral adiposity index.

lower physical activity (in females), shorter sleep, dyslipidemia (in males), and higher adiposity.

Lifestyle behavioral factors, including smoking and physical inactivity, exhibited gender-dependent effects. Smoking worsened MetS severity in females but showed paradoxical inverse associations in males, mediated by longer sleep, elevated TC, and higher BMI. Physical activity indirectly reduced the risk of MetS by improving sleep and lowering adiposity. Sleep duration itself influenced MetS severity through its impact on HSI.

Clinical parameters, such as TC, BMI, VAI, and HSI, were directly associated with MetS severity, with TC and VAI exerting additional indirect effects through hepatic and metabolic dysfunction. These findings reinforce the central role of diet quality in metabolic health, with its effects being amplified or attenuated by lifestyle and clinical risk factors.

For further details on the associations between other modifiable risk factors and MetS severity, please see Figs. 1-3 and **Supplementary Table 2-7**.

4. Discussion

This study represents the first investigation to simultaneously evaluate a broad range of diet quality scores and other critical modifiable risk factors with the MetS severity in female and male populations, using SEM as the analytical framework. By quantifying the complex interrelationships among these simultaneous risk factors and their impact on MetS, our findings provide valuable evidence to inform the prioritization of management and prevention efforts. These include three distinct diet quality scores, measured by the DDS, PDS, and EAT-Lancet Diet Score, alongside demographic variables (age, residential status, marital status), socioeconomic indicators (education years, job status, wealth index), lifestyle behaviors (sleep duration, physical activity levels, and smoking), clinical parameters like lipid markers (TC), obesity status (assessed through BMI and VAI), liver health status (HSI), as well as family history and overall health status.

4.1. Diet quality scores

Our key findings revealed that the DDS and PDS had significant

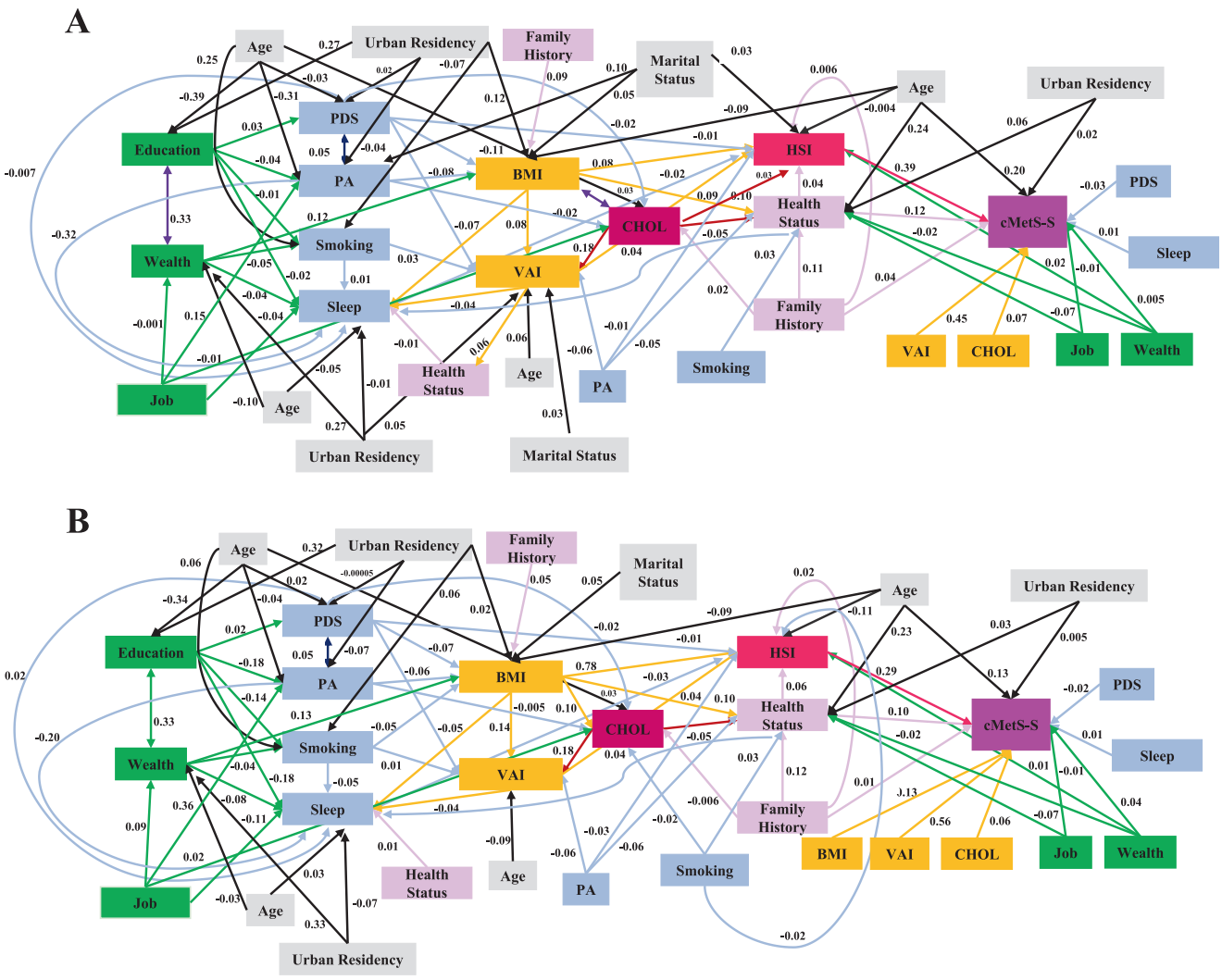

Fig. 2. Best-fit conceptual model illustrating pathways of risk factors to the severity of metabolic syndrome for **(A)** female participants [Comparative Fit Index (CFI) = 0.961, Tucker-Lewis Index (TLI) = 0.890, Root Mean Square Error of Approximation (RMSEA) = 0.058 (90 %CI [0.054, 0.061]), and Standardized Root Mean Square Residual (SRMR) = 0.028] and **(B)** male participants (CFI = 0.994, TLI = 0.982, RMSEA = 0.022 (90 %CI [0.018, 0.027]), and SRMR = 0.014). Several factors are repeated at different locations, with different pathways depicted for easy reading, but they do not differ significantly from their identical counterparts. BMI: body mass index; cMetS-S: continuous metabolic syndrome severity score; CHOL: total cholesterol; HSI: hepatic steatosis index; PA: physical activity; PDS: paleolithic dietary score; VAI visceral adiposity index.

direct effects on the severity of MetS. Also, each of the three quality scores indirectly influences the severity of MetS by mediating their positive impact on key health indicators, including reduced TC levels, lower BMI and VAI, reduced HSI, and a decrease in the total number of individual comorbid conditions.

The DDS demonstrated significant direct and indirect inverse associations with MetS severity in both genders. This aligns with evidence suggesting that diverse diets, as captured by the DDS, provide a broader spectrum of essential nutrients and phytochemicals, which collectively improve metabolic health by reducing inflammation, oxidative stress, and dyslipidemia [11,26]. The DDS's holistic assessment of food-group variety may explain its robust association, as it transcends the limitations of single-nutrient approaches and reflects adherence to traditional dietary guidelines [11].

Similarly, the PDS exhibited significant direct and indirect effects, reinforcing its potential as a therapeutic dietary pattern for metabolic disorders. The PDS's emphasis on unprocessed plant-based foods, lean meats, and nuts, while excluding refined grains, dairy, and processed foods, may mitigate MetS components by improving insulin sensitivity, lipid profiles, and visceral adiposity [8,9,27]. Mechanistically, the PDS's alignment with evolutionary dietary patterns could reduce postprandial glycemic spikes and systemic inflammation, as evidenced by *meta*-analyses linking Paleolithic diets to improved glucose metabolism and lipid regulation [27,28].

In contrast, the EAT-Lancet Diet Score influenced MetS severity exclusively through indirect pathways ($\beta \sim$ Females$\sim = -0.04$; $\beta \sim$ Males$\sim = -0.03$), mediated by reductions in BMI, visceral adiposity (as measured by VAI), and hepatic steatosis (as measured by HSI). Unlike traditional dietary scores (e.g., Mediterranean diet, Dietary Approaches to Stop Hypertension score, and Healthy Eating Index), the EAT-Lancet score uniquely integrates environmental sustainability and human health considerations into its framework. Evidence from two extensive prospective cohort studies suggests that following the EAT-Lancet diet is associated with improved cardiometabolic health [29,30]. In our study, the absence of a direct effect for the EAT-Lancet Diet Score may stem from its unique design, which prioritizes planetary health alongside metabolic outcomes. Unlike DDS (focused on food-group diversity) and PDS (emphasizing evolutionary alignment), the EAT-Lancet score integrates sustainability goals (e.g., reduced red meat, plant-based emphasis) that may not directly target metabolic pathways

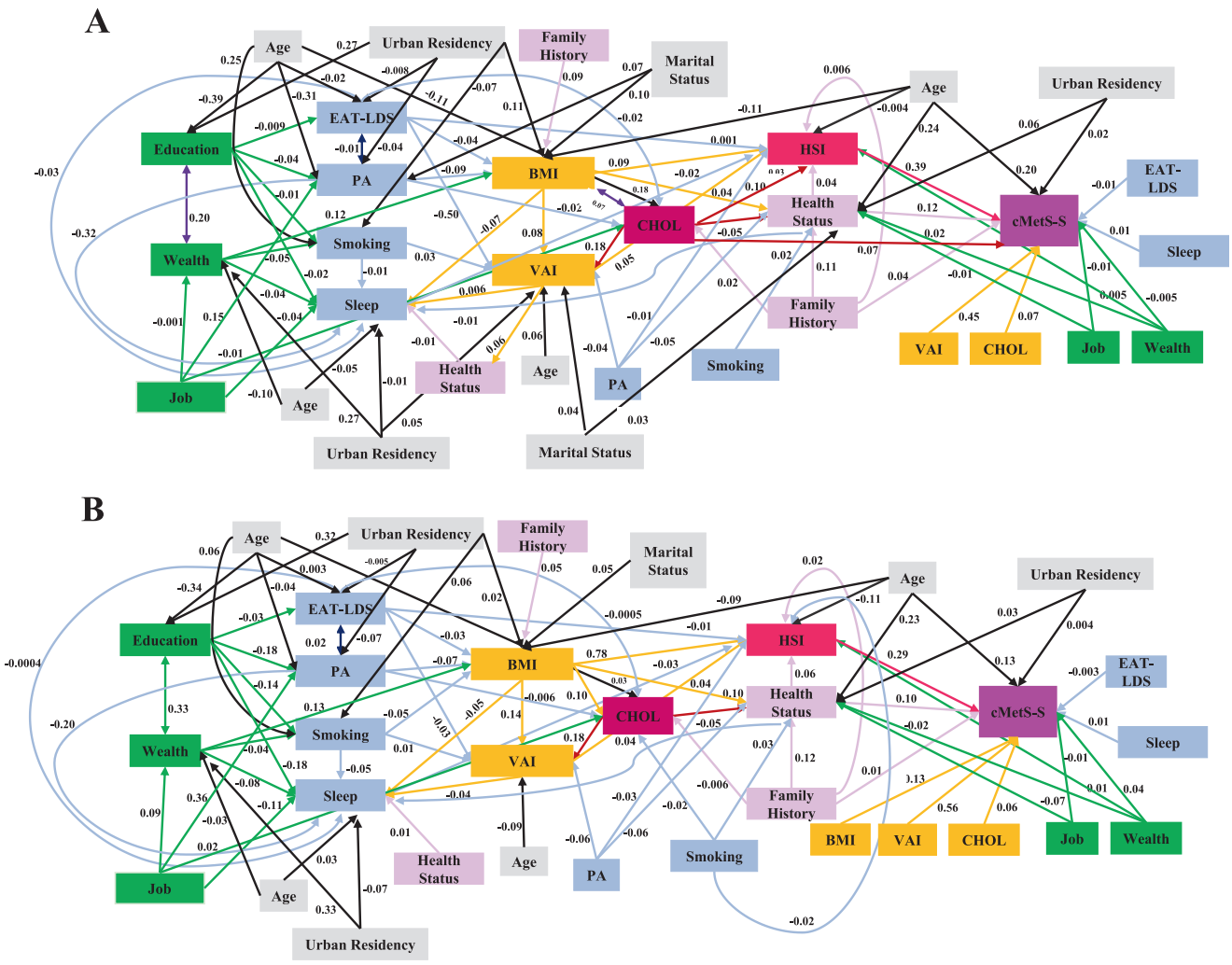

Fig. 3. Best-fit conceptual model illustrating pathways of risk factors to the severity of metabolic syndrome for **(A)** female participants [Comparative Fit Index (CFI) = 0.960, Tucker-Lewis Index (TLI) = 0.889, Root Mean Square Error of Approximation (RMSEA) = 0.058 (90 %CI [0.054, 0.062]), and Standardized Root Mean Square Residual (SRMR) = 0.028] and **(B)** male participants (CFI = 0.994, TLI = 0.982, RMSEA = 0.022 (90 %CI [0.017, 0.027]), and SRMR = 0.014). Several factors are repeated at different locations, with different pathways depicted for easy reading, but they do not differ significantly from their identical counterparts. BMI: body mass index; cMetS-S: continuous metabolic syndrome severity score; CHOL: total cholesterol; HSI: hepatic steatosis index; PA: physical activity; VAI visceral adiposity index.

[11,12,24]. For instance, the EAT-Lancet's emphasis on plant-based proteins and limited animal products might minimize saturated fat intake (beneficial for dyslipidemia) [12]. Still, it could also lower bioavailability of specific nutrients (e.g., heme iron), potentially offsetting direct metabolic benefits [31]. Prior studies report similar findings, where its benefits emerge only when mediated by weight management or inflammation reduction [29,30]. Additionally, the score's environmental metrics (e.g., food carbon footprint) may not fully align with biomarkers of MetS, which explains its indirect influence via lipid profile and liver health rather than direct metabolic regulation. In contrast, DDS and PDS, being more metabolically targeted, offer dual advantages.

4.2. *Mediating roles of clinical and lifestyle factors*

Our results indicated that blood lipid, assessed as an elevated level of TC, played a crucial role, both directly and indirectly, in influencing the severity of MetS in men and women. The indirect effect of elevated TC on the severity of MetS is mediated through increased VAI, higher HSI, and a greater number of overall comorbid conditions. The findings are in agreement with previous research from two studies that focused on the direct influence of dyslipidemia on metabolic risk factors [32,33]. Additionally, this study emphasizes the critical role of managing visceral adiposity and BMI in preventing and managing metabolic disorders [34].

It is suggested that non-alcoholic fatty liver disease (NAFLD) reflects the liver-specific expression of MetS, with insulin resistance serving as the primary underlying pathogenic mechanism [35]. This further implies that the HSI could serve as a valuable tool for identifying individuals at risk of developing metabolic abnormalities [36]. Our study found that a higher HSI directly worsened MetS severity in both genders, while lifestyle factors, such as sleep, indirectly mitigated MetS by lowering HSI. Physical activity reduced MetS severity indirectly by improving TC, BMI, VAI, HSI, and comorbidities [37], consistent with prior research on cardiometabolic risk [38–40].

Our study found that smoking indirectly worsened MetS severity in females, mediated by higher VAI, HSI, and comorbidities. In males, smoking was linked to reduced MetS severity, potentially due to lower TC, VAI, BMI, and HSI. A *meta*-analysis showed smokers have a 26 % higher MetS risk (42 % for heavy smokers) [41], though some studies report no association [42,43] or even a protective effect [44]. Confounding factors, such as study design and lifestyle, may explain

discrepancies. Male smokers often exhibit lower weight and better body composition [45]. Smoking may alter metabolism via sympathetic nervous system activation and hormonal changes, influencing fat distribution [46]. Nicotine stimulates lipolysis, suppresses appetite, and raises metabolic rate [47], yet paradoxically may increase abdominal adiposity [48]. The exact reasons for this paradoxical increase in abdominal fat despite weight loss remain unclear, but these mechanisms provide some insight.

4.3. Demographic and socioeconomic influences

Regarding demographic and socio-economic factors, our analysis revealed direct or indirect effects on the severity of MetS. Specifically, older age, urban residency, married people, higher education levels, unemployment, and a higher wealth score were associated with increased MetS severity. In the findings from the Hoveyzeh Cohort Study, which investigated the association between socioeconomic factors and MetS, logistic regression analysis revealed no significant associations between wealth status or educational level and the prevalence of MetS [49]. Interestingly, in our study of the male population, a higher education level was indirectly associated with increased severity of MetS, mediated by lower physical activity level, elevated TC, higher BMI and VAI, increased HSI, and a greater number of comorbid conditions. This observation is likely explained by the fact that individuals living in urban areas, those with higher incomes, and those with higher education levels often adopt less healthy lifestyles, primarily influenced by the pressures and time constraints associated with their professional commitments [50].

4.4. Core modifiable targets for primary prevention of MetS

In the context of primary prevention, the simultaneous quantification of multiple risk factors and their interconnected pathways consolidates scattered evidence, facilitating the identification of key upstream targets for preventing and managing metabolic disorders. According to our results: (1) promoting compliance with healthy dietary indices should be emphasized as a primary dietary strategy to prevent MetS; (2) increasing physical activity levels may serve as a key behavioral target; (3) managing BMI and VAI should be central obesity-related targets; (4) controlling hepatic disorders and cholesterol levels may be essential clinical parameter targets. Future studies are needed to confirm this conceptual model in diverse populations.

4.5. Strengths and limitations

The present study has several limitations that should be taken into account when interpreting the findings. First, causality cannot be inferred due to its cross-sectional design, and longitudinal studies would be necessary for any inference of true causality. Second, due to self-reported dietary intake and other lifestyle factors, measurement error was inevitable. Third, the observed associations may not be fully explained because this study did not consider other dietary factors, including dietary habits and meal and snack patterns. Fourth, the presence of residual confounding cannot be entirely ruled out, as unmeasured or unknown factors may have influenced the findings. Fifth, another limitation is that we were unable to include a measure of psychological state due to the lack of data from validated questionnaires in the HCS. Finally, as dietary intake, lifestyle behaviors, sociodemographic parameters, and severity of MetS may differ between ethnic groups, the generalizability of our results may be limited.

Despite these potential limitations, to our knowledge, this is the first study to investigate the mediating role of diet quality, including the PDS, DDS, and EAT-Lancet Diet Score, in the relationship between lifestyle, sociodemographic factors, clinical and biochemical variables, and the severity of MetS in the adult population. Additionally, the current study employed SEM, a robust statistical technique that enabled the simultaneous examination of multiple relationships among variables. Furthermore, we addressed the limitations of traditional MetS criteria by utilizing a continuous MetS severity score rather than a binary classification. This severity score was developed by analyzing the clustering of MetS components, weighting each component through confirmatory factor analysis, and accounting for variations across gender groups. Additional strengths of our study include a large sample size and the incorporation of both urban and rural populations, which improves the generalizability of the results. Additionally, the use of a reliable and validated questionnaire to collect dietary and other relevant information further strengthens the study's methodological approach.

5. Conclusions

This study investigated modifiable risk factors as an interconnected system related to the severity of MetS by analyzing integrated pathways within a large population-based cohort. In primary prevention, assessing multiple interrelated risk factors is crucial for identifying key targets for the effective management of metabolic disorders. Our findings highlight the importance of prioritizing a healthy diet to prevent MetS, promoting physical activity as a behavioral intervention, managing BMI and VAI to address obesity-related risks, and improving liver health and cholesterol levels as critical clinical targets.

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Author contributions

EM, SJ, and FB designed the study, analyzed the data, and drafted the manuscript. SJ, AMH, and BC contributed to the discussion and critically reviewed/edited the manuscript. All authors have read and agreed to the published version of the manuscript. All authors have primary responsibility for the final content.

Ethical approval and consent to participate

The Jundishapur University of Medical Sciences Ethics Committee approved the study in Ahvaz, Iran (IR.AJUMS.REC.1402.686).

Consent for publication

Not applicable.

Clinical trial number

Not applicable.

CRediT authorship contribution statement

Farnush Bakhshimoghaddam: Writing – original draft, Methodology. **Elham Maraghi:** Writing – review & editing, Supervision, Methodology, Formal analysis, Conceptualization. **Ali Mohammad Hadianfard:** Writing – review & editing. **Bahman Cheraghian:** Writing – review & editing. **Sima Jafarirad:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2025.112436.

Data availability

Data will be made available on request.

The data supporting the findings of this study were obtained from the Hoveyzeh Cohort Study (HCS). However, due to licensing restrictions, the data are not publicly accessible. They are available from the corresponding author upon reasonable request for research purposes.

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