Incidence and Prediction Nomogram for Metabolic Syndrome in a Middle-aged Vietnamese Population: a 5-year Follow-up Study

Tran Quang Thuyen

Vietnam Military Medical University

Dinh Hong Duong

Vietnam Military Medical University

Bui Thi Thuy Nga

National Institute of Nutrition

Nguyen Anh Ngoc

National Institute of Nutrition

Duong Tuan Linh

National Institute of Nutrition

Pham Tran Phuong

National Institute of Nutrition

Bui Thi Nhung

National Institute of Nutrition

Tran Quang Binh (✉ tranquangbinh@dinhduong.org.vn)

National Institute of Nutrition <https://orcid.org/0000-0003-3520-2131>

Research Article

Keywords: Metabolic syndrome, Incidence, Risk factor, Middle-aged, Vietnam

Posted Date: June 8th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-582331/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Version of Record: A version of this preprint was published at Endocrine on August 2nd, 2021. See the published version at <https://doi.org/10.1007/s12020-021-02836-5>.

Abstract

Purpose We aimed to determine the incidence and prediction nomogram for new-onset metabolic syndrome (MetS) in a middle-aged Vietnamese population.

Methods A population-based prospective study was conducted in 1150 participants aged 40-64 years without MetS at baseline and followed-up for 5 years. Data on lifestyle factors, socioeconomic status, family diabetes history, and anthropometric measures were collected. MetS incidence was estimated in general population and subgroup of age, gender, and MetS components. A Cox proportional hazards regression was used to estimate hazard ratios (HRs) with 95% confidence intervals (CI) for MetS. A prediction nomogram was developed and checked for discrimination and calibration.

Results During median follow-up of 5.14 years, the accumulate MetS incidence rate was 23.4% (95% CI: 22.2-24.7). The annual incidence rate (95%CI) was 52.9 (46.7-60.1) per 1000 person-years in general population and higher in women [56.6 (48.7-65.9)] than men [46.5 (36.9-59.3)]. The HRs (95% CI) for developing MetS were gender [females vs males: 2.04 (1.26-3.29)], advanced age [1.02 (1.01-1.04) per one year], waist circumference [1.08 (1.06-1.10) per one cm] and other obesity-related traits, and systolic blood pressure [1.02 (1.01-1.03) per one mmHg]. The prediction nomogram for MetS had a good discrimination (C-statistics = 0.742) and fit calibration (mean absolute error = 0.009) with a positive net benefit in the predicted probability thresholds between 0.13 and 0.70.

Conclusions The study is the first to indicate an alarmingly high incidence of MetS in a middle-aged population in Vietnam. The nomogram with simply applicable variables would be useful to qualify individual risk of developing MetS.

Introduction

Metabolic syndrome (MetS), a cluster composed of obesity, hypertension, insulin resistance, disturbed glucose and dyslipidemia [1], is an important risk factor for diabetes [2], cardiovascular diseases [3] and cancers [4] which are leading causes of deaths [5]. MetS is estimated to affect about 20–25% global [6] and 34.7% US adults [7]. In the Asia-Pacific region, the prevalence of MetS is about 20%, and continues to increase [8]. Fortunately, MetS can be prevented or delayed by lifestyle modifications such as healthy eating [9] and intensity of leisure time physical activity [10]. Thus, early identification of those who are at high risk of MetS may help to establish effective strategies for MetS prevention.

Developing the prediction model for incident MetS with appropriate factors are important and useful clinical practice for individual and community. In recent years, some models have been constructed using both non-invasive and invasive factors in China [11] and France [12]. However, these models are not usually suitable for low-resource settings. Furthermore, prediction models developed in one population may not be applied in other populations. Therefore, it is necessary to develop population-specific models for MetS prediction, especially non-invasive models which are more suitable for low-resource settings.

In Vietnam, there was a significant upward trend in the prevalence of MetS, from 10% in 2003 to 18.1% in 2011 [13–15]. Although the MetS prevalence has been investigated in several regions including both rural and urban settings, there has been no report on the MetS incidence. Moreover, Vietnam is experiencing a rapid change in both living environment and lifestyle which may lead to high risk of non-communicable diseases [16]. Precise estimation of MetS incidence can help high-risk individuals take interventions timely to reduce MetS-related morbidity and mortality. In this context, it is crucial to have a tool for predicting new-onset MetS that also promote an effective planning prevention and early treatment of MetS. Therefore, this five-year cohort study was conducted to estimate the incidence of MetS, and to develop a nomogram for MetS prediction among middle-aged Vietnamese population.

Materials And Methods

Study population

This study was an important part of the DiaMetS-VN population-based prospective study designed to identify the epidemiological patterns and genetics of MetS and type 2 diabetes in the middle-aged population in Vietnam. The participants of this study were Kinh Vietnamese aged 40–64 years, lived in Ha Nam, a typical rural province in the Red River Delta region. Further details of this population were previously reported [15]. Of 2042 participants without MetS at the baseline, 871 did not take part in the follow-up and 21 were missed glycemic and lipid profile. As a result, 1150 subjects were entered this analysis.

Data collection

The trained surveyors collected data through face-to-face interview with questionnaires. The participants in the follow-up 2016 survey were interviewed and measured with the same protocol in the baseline 2011 survey as described previously [17]. Briefly, all participants were asked fasting overnight for venous blood collection next morning. Blood sample was centrifuged immediately, then aliquots of plasma were stored at 2–8°C and transported to laboratory for analyzing biochemical index including glucose, total cholesterol, high-density lipoprotein (HDL-C), and

triglycerides (TG). Demographic data included current age, household income, education level, occupation, marital status, family history of diabetes, and history of using medicine for hypertension or dyslipidemia. A family history of diabetes was defined as having at least one parent or sibling with diabetes. In addition, occupation was categorized as heavy occupation (farmer and manual worker) and non-heavy occupation (office clerks, teacher, retired, and housework).

Anthropometric measurements including height, weight, waist circumference, hip circumference were done twice for each individual and the average of two values was used for data analysis. Waist circumference (WC) was measured at the midway between the lower rib margin and the iliac crest, whereas hip circumference was measured at the level of the largest circumference around the buttocks. From, body mass index (BMI), Waist-height ratio (WHtR) and waist-hip ratio (WHR) were calculated. In addition, blood pressure was manually also taken twice in a sitting position after at least 5 minutes of rest using a mercury sphygmomanometer and the mean of value was considered as participant's blood pressure.

To assess exposure, data on smoking habits, night sleeping duration, siesta, leisure time, alcohol consumption were obtained by interview. Smoking was defined in 3 groups (none smoker, ex-smoker and current smoker). Sleep duration was total of hours spend for sleeping at night daily. Participants were asked about the daily total of leisure-time including time for watching TV and sitting without physical activity. Alcohol intake was categorized in 5 groups: (none, < 1 drink/mo, ≥ 1 drink/mo to < 1 drink/wk, 1 drink/wk to ≤ 1 drink/d, and ≥ 2 drink/d, one drink was defined as a 50-ml cup of rice wine at about 30%).

Metabolic syndrome definition

MetS was defined according to the criteria of the US National Cholesterol Education Adult Treatment Panel III with adjusting waist circumference cutoff in Asian population [1, 18]. An individual was diagnosed MetS as the presence of three or more of the following: (1) waist circumference ≥ 90 cm for men and ≥ 80 cm for women; 2) fasting plasma glucose ≥ 100 mg/dL (5.6 mmol/L) or used of drug treatment of elevated glucose; 3) systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg or history of hypertension; 4) HDL-C < 40 mg/dL (1.04 mmol/L) for men and < 50 mg/dL (1.29 mmol/L) for women; 5) Triglycerides ≥ 150 mg/dL (1.7 mmol/L) or taking a lipid-lowering medication.

Statistical analysis

The MetS incidence was estimated using the weight based on the study design, the probability of sampling, finite population correction, and none-response rate. Incidence rates with 95% confidence interval (CI) were calculated by dividing the number of events by person-year at risk. Time at risk was estimated as the mid-time between of the two surveys in individuals who developed MetS and as the interval between the first and the last observation dates in participants without MetS. The age and sex-adjusted incidences were estimated using direct standardization method based on the 2019 Vietnam Population and Housing Census [19]. Baseline characteristics between two groups were compared using T-test or Mann-Whitney-U test or Chi-square test or Fisher's exact test when appropriate. The Cox proportional hazard regression model was used to estimate the hazard ratio (HR) for MetS.

The nomogram for estimating new-onset MetS was constructed according to the variables in prediction models resulting from multivariable logistic regression and Bayesian Model Average methods. The discrimination of the nomogram was evaluated by using the area under a receiver operating characteristic curve (AUC). Moreover, C-statistic was applied to quantify the discrimination ability of the nomogram and implementing internal validation of this model. In general, C-index > 0.7 is considered to present a good discrimination. Calibration of the nomogram was assessed by plotting the actual probability of MetS compared to the probabilities predicted by prediction model. The decision curve analysis of the model was built for using in the clinical utility [20]. In this study, we used bootstrap analysis with 500 subsamples for internal validation and with 1000 resamples for calibration. The statistical analyses were performed using SPSS version 16 (SPSS, Chicago, USA), Stata version 14 (Stata Corporation, College Station, TX, USA) and R version 3.5.3 for Windows. All of statistical tests were two-tailed and $P < 0.05$ was considered as significant.

Results

Table 1 shows the baseline characteristics of participants according to new-onset MetS at follow up. The subjects with MetS had higher baseline values of age, blood pressures, weight, BMI, WC, WHR, WHtR, and body fat percentage than those without MetS. No significant differences between the two groups were found in socioeconomic status (residence, marital status, education, occupation, and income level), sedentary time (watching TV and sitting), sleeping time, fasting plasma glucose, and lipid profile.

Table 1

Baseline characteristics of participants according to the development of metabolic syndrome at the end follow up

Variable	MetS (n = 280)	Non-MetS (n = 870)	P-value
Age (median, quartile) years	51.1 (46.0–56.0)	50. (45.6–55.3)	< 0.0001 ^a
Gender (n, %)			0.015 ^c
Male	84 (30.0)	331 (38.0)	
Female	196 (70.0)	539 (62.0)	
Body mass index (mean ± SD) kg/m ²	22.1 ± 2.6	20.8 ± 2.2	< 0.0001 ^b
Body fat (mean ± SD) %	29.2 ± 5.6	21.8 (22.5–30.2)	< 0.0001 ^a
Waist circumference (mean ± SD) cm	76.9 ± 7.3	72.0 (67.5–77.0)	< 0.0001 ^a
Systolic blood pressure (median, quartile) mmHg	110.0 (100.0–130.0)	110.0 (100.0–120.0)	< 0.0001 ^a
Diastolic blood pressure (median, quartile) mmHg	70.0 (70.0–80.0)	70.0 (60.0–80.0)	< 0.0001 ^a
Triglycerides (median, quartile) mmol/L	1.29 (1.00–2.00)	1.29 (0.97–1.91)	0.555 ^a
HDL-cholesterol (median, quartile) mmol/L	1.30 (1.05–1.66)	1.27 (1.00–1.66)	0.356 ^a
Fasting glucose (median, quartile) mmol/L	4.60 (4.00–5.09)	4.50 (4.00–5.00)	0.185 ^a
Region (n, %)			
Rural	265 (94.6)	844 (97.0)	0.063 ^c
Urban	15 (5.4)	26 (3.0)	
Education level (n, %)			0.828 ^c
Elementary	24 (8.6)	72 (8.3)	
Intermediate	178 (63.6)	542 (62.3)	
Secondary	31 (11.1)	115 (13.2)	
Post-secondary	47 (16.8)	141 (16.2)	
Income level (n, %)			0.506 ^c
< 25 percentiles	68 (24.3)	227 (26.1)	
< 25 percentiles	66 (23.6)	228 (26.2)	
50– < 75 percentiles	67 (23.9)	206 (23.7)	
≥ 75 percentiles	79 (28.2)	209 (24.0)	
Smoking (n, %)			< 0.0001 ^c
None	220 (78.6)	609 (70.0)	
Ex-smokers	34 (12.1)	92 (10.6)	
Current smokers	26 (9.3)	169 (19.4)	
Leisure time (median, quartile) hour/day	5.0 (3.3–7.0)	4.8 (3.0–7.0)	0.489 ^a
Sleeping time (median, quartile) hour/day	7.0 (6.0–7.0)	7.0 (6.0–7.0)	0.260 ^a

MetS metabolic syndrome^a Mann-Whitney U test^b T-test^c Chi-Square test

Variable	MetS (<i>n</i> = 280)	Non-MetS (<i>n</i> = 870)	<i>P</i> -value
Family history of diabetes (<i>n</i> , %)			
Yes	17 (6.1)	51 (5.9)	0.897 ^c
No	263 (93.9)	819 (94.1)	
<i>MetS</i> metabolic syndrome			
^a Mann-Whitney U test			
^b T-test			
^c Chi-Square test			

The comparison of baseline characteristics between participants and non-participants in the follow-up survey is shown in Additional Table. There were no significant differences between two groups in terms of anthropometrics, socioeconomic status, and lifestyles.

During a median follow-up of 5.14 years (quartile: 5.05–5.19 years), 280 (23.4%) subjects developed MetS. As shown in Table 2, the estimated incidences of MetS increased with age in general population. After 55 years of age, about a quarter of men and one third of women suffered from MetS during 5-year period. The MetS incidence was higher in groups: urban, non-heavy occupation, and overweight.

Table 2

Estimated 5-year incidence of metabolic syndrome in a Vietnamese middle-aged population according to baseline characteristics

Baseline characteristics	N° at risk	N° new-onset	Person-year	5 years cumulative incidence rate			Incidence density/1000 person-years		
				Total	Men	Women	Total	Men	Women
Total	1150	280	5224.2	23.4 (22.2–24.7)	20.1 (18.0–22.3)	25.3 (23.7–27.0)	52.9 (46.7–60.1)	46.5 (36.9–59.3)	56.6 (48.7–65.9)
Age group (years)									
40 – 44	220	42	1030.4	17.7 (15.3–20.4)	18.8 (13.9–24.9)	17.4 (14.7–20.4)	38.2 (28.0–53.1)	41.4 (21.9–85.6)	37.2 (26.1–54.6)
45 – 49	294	59	1368.1	18.7 (16.5–21.2)	15.4 (12.0–19.5)	20.5 (17.6–23.6)	42.7 (32.7–56.5)	36.0 (21.8–63.2)	46.0 (33.6–64.0)
50 – 54	282	63	1295.6	21.5 (19.1–24.2)	16.9 (13.8–20.6)	24.6 (21.2–28.3)	48.4 (37.2–64.0)	37.8 (24.5–60.7)	55.5 (39.9–79.0)
55 – 59	214	71	922.0	33.3 (29.8–36.9)	26.5 (21.3–32.4)	38.6 (34.0–43.4)	74.1 (57.5–96.4)	56.5 (35.4–95.1)	89.5 (66.3–122.0)
60 – 64	140	45	608.1	30.1 (26.3–34.3)	24.5 (19.1–30.9)	34.2 (29.1–39.7)	75.2 (55.1–104.5)	68.8 (39.4–128.8)	80.0 (55.4–118.2)
Region									
Rural	1109	265	5051.4	22.6 (21.4–23.9)	19.1 (17.1–21.3)	24.6 (23.0–26.2)	51.8 (45.6–58.9)	43.8 (34.9–55.8)	56.3 (48.5–65.7)
Urban	41	15	172.8	37.2 (29.9–45.0)	38.7 (25.9–53.3)	36.4 (27.9–46.0)	68.8 (37.6–133.7)	84.9 (30.2–292.0)	60.1 (28.2–139.5)
Occupation									
Heavy	915	214	4179.5	22.7 (21.3–24.2)	17.5 (15.1–20.2)	25.3 (23.5–27.1)	50.3 (43.6–58.2)	38.6 (28.6–53.2)	56.2 (47.9–66.2)
None heavy	235	66	1044.7	26.2 (23.5–29.2)	26.8 (23.0–31.1)	25.6 (21.8–29.9)	63.0 (48.3–83.1)	68.0 (47.5–99.9)	58.5 (39.7–88.5)
Nutrition status									
Underweight	160	23	768.1	12.9 (10.5–15.8)	9.6 (6.56–13.72)	15.3 (11.9–19.5)	28.9 (18.9–46.1)	22.6 (10.4–57.8)	33.3 (19.9–59.0)
Normal	749	154	3475.7	20.1 (18.7–21.7)	14.9 (12.7–17.4)	22.7 (20.8–24.7)	43.2 (36.6–51.4)	32.2 (22.8–47.0)	48.9 (40.4–59.5)
Overweight	162	64	672.7	38.7 (34.8–42.6)	37.1 (31.0–43.6)	39.6 (34.7–44.7)	97.3 (75.0–128)	107 (70.2–169)	92.4 (66.5–131)
Obesity	77	37	302.6	47.6 (41.3–53.8)	45.0 (36.1–54.3)	50.8 (42.4–59.2)	123 (88.9–172)	109 (67.6–183)	140 (90.7–222)
Severe obesity	2	2	5.2	N/A	N/A	N/A	N/A	N/A	N/A
MetS metabolic syndrome									
Data are weighted by the study design, the probability of sampling, finite population correction, and none-response rate. Data are shown as % (95% CI) for cumulative incidence rate and cases (95% CI) for incident density/1000 person-years. N/A, not applicable due to 2 participants with BMI ≥ 30 kg/m ² . Nutrition status was classified as underweight (BMI < 18.5 kg/m ²), normal (18.5 $\leq$ BMI < 23 kg/m ²), overweight (23 $\leq$ BMI < 25 kg/m ²), obesity (25 $\leq$ BMI < 30 kg/m ²), and severe obesity (BMI ≥ 30 kg/m ²). Occupation was categorized as heavy occupation (farmer and manual worker) or none heavy occupation (office clerks, teacher, retired worker, and houseworker).									

The sex- and age- standardized MetS incidences were 24.5% (95% CI: 24.3–24.7) in general population and significantly higher in women [27.3 (95% CI: 27.1–27.5)] than in men [20.4 (95% CI: 20.1–20.6)]. The corresponding new-onset MetS cases per 1000 person-years were 55.6 (95% CI: 54.7–56.5) in general population and much higher in women [62.2 (95% CI: 60.9–63.5)] compared to men [47.5 (95% CI: 46.4–48.7)].

Table 3 presents the development of MetS in participants with single component and pairwise combination of MetS components at the baseline. The more number of MetS component they had at baseline, the more MetS incidence rate they suffered at follow-up. In addition, among participants with one component at baseline, subjects with central obesity had the highest MetS incidence, while people with elevated blood glucose had the lowest incidence. Moreover, among 349 people with 2 MetS components, the highest incidence was seen in those with central obesity and raised blood pressure combination, while the lowest incidence was found in those with low HDL-C and elevated blood glucose combination.

Table 3
Incidence of metabolic syndrome according to the single and combination of baseline metabolic syndrome components

	At risk (<i>n</i>)	Person- years	Case (<i>n</i>)	5 years cumulative incidence rate (95% CI) (%)	Incidence/ 1000 person-years (95% CI)
The number of components					
0	243	1160.3	37	15.23 (11.25–20.28)	31.89 (23.22–43.64)
1	558	2605.1	109	19.53 (16.46–23.03)	41.84 (34.80–50.23)
2	349	1458.8	134	38.4 (33.45–43.60)	91.86 (78.09–107.8)
One of component					
CO	16	61.9	8	50.00 (28.00–72.00)	129.24 (66.79–234.8)
RBP	74	311.8	27	36.49 (26.44–47.87)	86.59 (60.19–123.1)
HTG	183	860.7	34	18.58 (13.61–24.84)	39.50 (28.40–54.69)
LHC	258	1237.9	37	14.34 (10.59–19.14)	29.89 (21.76–40.93)
EBG	27	132.7	3	11.11 (3.58–28.06)	22.61 (7.72–64.63)
Pairwise combination of components					
CO-RBP	18	59.3	13	72.22 (49.1–87.5)	219.2 (132.8–339.8)
LHC-CO	24	85.1	15	62.50 (42.71–78.84)	176.3 (109.8–270.7)
LHC-RBP	76	289.3	40	52.63 (41.55–63.46)	138.3 (103.2–182.8)
HTG-RBP	60	242.7	26	43.33 (31.57–55.90)	107.1 (74.16–152.3)
HTG-CO	35	142.7	15	42.86 (27.98–59.14)	105.1 (64.74–166.2)
RBP-EBG	11	49.3	3	27.27 (9.75–56.56)	60.85 (20.91–164.3)
HTG-EBG	19	85.8	5	26.32 (11.81–48.79)	58.28 (25.15–129.3)
LHC-HTG	91	434.4	14	15.38 (9.39–24.18)	32.23 (19.29–53.63)
LHC-EBG	14	67.6	2	14.29 (4.01–39.94)	29.59 (8.15–101.6)
CO-EBG	1	2.5	1	100.0 (20.65–100.0)	400.0 (74.5–846.6)
<i>HR</i> hazard ratio, <i>CI</i> confidence interval, <i>CO</i> central obesity, <i>RBP</i> raised blood pressure,					
<i>HTG</i> high triglycerides, <i>LHC</i> low HDL-Cholesterol, <i>EBG</i> elevated blood glucose					

Table 4 shows HR values of MetS according to candidate risk factors in multivariable analysis. Gender, age, blood pressures, fasting plasma glucose, and obesity-related measurements (WC, HC, WHtR, WHR, BMI, and body fat percentage) were significant risk factors for MetS. The HRs (95% CI) of MetS for gender (females vs males), advanced age, systolic blood pressure, fasting plasma glucose, and WC were 2.04 (1.26–3.29), 1.02 (1.01–1.04), 1.02 (1.01–1.03), 1.12 (1.02–1.40), and 1.08 (1.06–1.10), respectively. There was no significant association between incident MetS with levels of some lifestyle factors, socioeconomic conditions and family history of diabetes.

Table 4
Hazard ratio of metabolic syndrome according to candidate risk factors in multivariate analysis

Risk factors	Hazard ratio (95% CI)	P-value
Gender (female vs male)	2.04 (1.26–3.29)	0.004
Age (years)	1.02 (1.01–1.04)	0.021
Fasting plasma glucose (mmol/L)	1.12 (1.02–1.40)	0.025
Systolic blood pressure (mmol/L) ^a	1.02 (1.01–1.03)	< 0.0001
Diastolic blood pressure (mmol/L) ^b	1.03 (1.02–1.04)	< 0.0001
Triglycerides (mmol/L)	0.96 (0.85–1.07)	0.429
High density lipoprotein-cholesterol (mmol/L)	0.92 (0.73–1.16)	0.481
Each of the following obesity-related traits:		
Waist circumference (cm) ^c	1.08 (1.06–1.10)	< 0.0001
Waist height ratio (per 0.03) ^d	1.46 (1.31–1.64)	< 0.0001
Waist hip ratio (per 0.07) ^e	1.32 (1.19–1.46)	< 0.0001
Body mass index (kg/m ²) ^f	1.22 (1.15–1.27)	< 0.0001
Body fat (%) ^g	1.11 (1.08–1.15)	< 0.0001
Hip circumference (cm) ^h	1.10 (1.07–1.13)	< 0.0001
Family history of diabetes		
No	1.0	
Yes	0.88 (0.53–1.44)	0.605
Residence		
Rural	1.0	
Urban	1.26 (0.73–2.18)	0.413
Education level		
Elementary	1.0	
Intermediate	1.10 (0.70–1.71)	0.687
Secondary	0.99 (0.55–1.76)	0.964
Post-secondary	0.77 (0.43–1.39)	0.385
Marital status		
Married	1.0	
Never	0.84 (0.30–2.36)	0.739
Widowed	1.15 (0.72–1.85)	0.553
Others	1.16 (0.47–2.84)	0.746
Occupation		
Heavy	1.0	
None heavy	1.25 (0.88–1.78)	0.210
CI/ confidence interval		
^b replace ^a in multivariable analysis		
d, e, f, g, h step by step replace ^c in multivariable analysis		

Risk factors	Hazard ratio (95% CI)	P-value
Income level		
< 25 percentiles	1.0	
25– < 50 percentiles	1.06 (0.75–1.51)	0.727
50– < 75 percentiles	1.17 (0.82–1.67)	0.374
≥ 75 percentiles	1.09 (0.76–1.56)	0.644
Alcohol consumption		
None	1.0	
< 1 drink/mo	0.76 (0.44–1.29)	0.308
≥ 1 drink/mo to < 1 drink/wk	0.94 (0.55–1.60)	0.819
1 drink/wk to ≤ 1 drink/d	0.75 (0.43–1.30)	0.303
≥ 2 drink/d	1.01 (0.57–1.77)	0.987
Smoking status		
None	1.0	
Ex-smoker	0.72 (0.41–1.27)	0.259
Current smoker	1.12(0.66–1.93)	0.672
Leisure time/day (hour)	0.99 (0.94–1.03)	0.549
Sleeping time/day (hour)	0.96 (0.88–1.05)	0.419
CI/confidence interval		
^b replace ^a in multivariable analysis		
d, e, f, g, h step by step replace ^c in multivariable analysis		

A multivariable logistic regression analysis with backward stepwise and Bayesian Model Average approach were used to search for the most predictive MetS model with the highest AUC value and parsimonious variables. As a result, gender, age, WC, and SBP were considered in the final model (Table 5). The prediction nomogram for estimating the individual risk of MetS was constructed with above factors in the final model.

Table 5
The final model for prediction of 5-year incident metabolic syndrome in a middle-aged Vietnamese population

Predictor	Unit	β -coefficient (se)	P-value ^a
Gender	(female = 1, male = 0)	1.132 (0.178)	< 0.0001
Age	year	0.060 (0.019)	0.002
Waist circumference	cm	0.022 (0.005)	< 0.001
Systolic blood pressure	mmHg		
Intercept		-14.099 (1.191)	< 0.0001
^a Using multivariable logistic regression analysis			
CI/Confidence Interval.			

Figure 1 shows the nomogram for predicting new-onset MetS. The C-index before and after bootstrap was 0.742 and 0.7367 respectively, indicating a good discrimination of the nomogram. The calibration curve presented possibility of the nomogram-predicted probabilities versus the actual observation. As shown in Fig. 2a, both these lines were very close with the ideal line and the mean absolute error was 0.009. Thus, the prediction nomogram performed a good calibration. Figure 2b demonstrated that for the predicted probability thresholds between 0.13 and 0.70, the prediction nomogram showed a positive net benefit than strategies for all and none participant to treat.

Discussion

To the best of our knowledge, the study is the first to report the high MetS incidence in a middle-aged Vietnamese population with the annual incidence rate of 52.9 (95% CI: 46.7–60.1) per 1000 person-years. With almost similar range of age and equal criteria for diagnosed MetS, our finding was higher than that in Taiwan [21], Korea [22], and Thailand [23]. The current MetS incidence was relatively higher compared to a study in Japan with higher cut-off of WC criteria in both men and women [24]. Conversely, the incidence of MetS in current study was lower in Iran [25].

Regarding to sex difference in the MetS incidence, our study showed that the MetS incidence in women was higher than that in men, in line with previous studies [21, 25]. One study in Iran reported the reverse finding that the MetS incidence in men was higher than in women [27]. Another study in Portugal showed the similar MetS incidence in both gender [28]. A possible explanation for this discrepancy might result from the difference in socioeconomic status, lifestyle patterns, applied definition of MetS, and genetic background.

After adjustment for lifestyle factors, socioeconomic status, family history of diabetes and individual MetS components, the present study found that aging was an independent predictor of the development of MetS. The highest MetS incidence was found in 60–64 years men and 55–59 years women. This sex-difference should be interpreted with caution because 55–59 years is the postmenopausal period in women. A study in India showed that menopause was an independent risk factor of MetS and MetS incidence in postmenopausal women was higher about 2.5 times than in premenopausal women [29].

MetS might not often cause death directly, but MetS has been an important predictor to developing cardiovascular diseases and type 2 diabetes [30], which are the top four of all global deaths [5]. Recently, several prognostic models have been developed for predicting MetS in Asian populations [11, 32, 33] and Whites [34, 35]. Most of these models include both non-invasive and invasive factors such as age, measures of obesity (e.g. BMI, WC), blood pressures (SBP, DBP), lifestyle (e.g. smoking, dietary), biochemical indices (e.g. HDL-C, TG, FPG) and genetic background. The AUC values of these models vary from 0.67 to 0.94. There is only a nomogram for predicting the risk MetS among these models and this nomogram was constructed with six non-invasive factors [33]. In our study, the nomogram for the prediction of MetS was constructed base on only four non-invasive predictors including gender, age, WC and SBP with AUC in range of previous studies. Additionally, all of variables in our model are easy and cheap to collect, thus this model might be conveniently applied to qualify the risk of developing MetS for each middle-age person in entire population. Furthermore, the decision curve analysis of this nomogram presents a high application in clinical practice. When the probability thresholds of new-onset MetS were from 0.13 to 0.7, the net benefit of this nomogram is better than those of examination all participant or none participant strategies.

This study had some limitations. First, 43.1% of the subjects were lost to follow-up. Given that the significant difference between participants and non-participants was not found in terms of anthropometrics, socioeconomic status, and lifestyles, the possible participation bias was minimal. Second, physical activity and dietary intake were not included in analysis of risk factors for MetS. Lastly, as the study cohort included Kinh people living in rural areas of Vietnam, the findings cannot be generalised to either urban areas or other ethnic groups.

Conclusion

In summary, the study indicates an alarming high incidence of MetS among a middle-aged Vietnamese population. The non-invasive nomogram should be applied to estimate the personalized risk of new-onset MetS to help high-risk individuals take interventions timely to reduce MetS-related morbidity and mortality.

Declarations

Acknowledgments

The authors would like to thank all the participants and staffs of the Ha Nam Center for Preventive Medicine for their cooperation and assistance.

Funding

This study was supported by Vietnam's National Foundation for Science and Technology Development (NAFOSTED), grant no. 106.09–2010.29 and grant no. 106-YS.01-2015.10 from the Ministry of Science and Technology, Vietnam.

Conflicts of Interest

The authors declare that they have no competing interests

Availability of data and material

The datasets used and analyzed in this study are available from the corresponding author on reasonable request.

Author's contributions

TQT contributed to research design, data analysis, manuscript preparation, discussion and editing of the final draft for publication. TQB contributed to conceptualization of the study, data collection, data analysis, and the intellectual revision of the manuscript. DHD, BTTN, NAN, DTL, PTP, and BTN conceptualized the study, collected and entered data, interpreted and discussed the final draft for publication.

Ethics approval

The study was approved by the Ethics council of National Institute of Hygiene and Epidemiology, Vietnam (IRB-VN01057-34/2016).

Consent to participate

All of participants gave written informed consent with signatures before entering the study.

Consent to publication

Not applicable

References

1. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*. **120**, 1640–1645 (2009) <https://doi.org/10.1161/CIRCULATIONAHA.109.192644>
2. K. Kurotani, T. Miyamoto, T. Kochi, M. Eguchi, T. Imai, A. Nishihara, et al. Metabolic syndrome components and diabetes incidence according to the presence or absence of impaired fasting glucose: The Japan Epidemiology Collaboration on Occupational Health Study. *J. Epidemiol.* **27**, 408–412 (2017) <https://doi.org/10.1016/j.je.2016.08.015>
3. S. Mottillo, K.B. Filion, J. Genest, L. Joseph, L. Pilote, P. Poirier, et al. The Metabolic Syndrome and Cardiovascular Risk: A Systematic Review and Meta-Analysis. *J. Am. Coll. Cardiol.* **56**, 1113–1132 (2010). <https://doi.org/10.1016/j.jacc.2010.05.034>
4. K. Esposito, P. Chiodini, A. Colao, A. Lenzi, D. Giugliano. Metabolic Syndrome and Risk of Cancer: A systematic review and meta-analysis. *Diabetes Care*. **35**, 2402–2411 (2012). <https://doi.org/10.2337/dc12-0336>
5. World health Organization. Non communicable diseases. <https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases>. Accessed Dec 2 2020
6. Federation ID. The IDF consensus worldwide definition of the metabolic syndrome. (2006) <https://www.idf.org/e-library/consensus-statements/60-idf-consensus-worldwide-definition-of-the-metabolic-syndrome.html>. Accessed Dec 2 2020.
7. G. Hirode, R.J. Wong. Trends in the Prevalence of Metabolic Syndrome in the United States, 2011-2016. *JAMA*. **323** (24), 2526–2528 (2020). <https://doi.org/10.1001/jama.2020.4501>
8. P. Ranasinghe, Y. Mathangasinghe, R. Jayawardena, A.P. Hills, A. Misra.. Prevalence and trends of metabolic syndrome among adults in the asia-pacific region: a systematic review. *BMC public health*. **17**(1), 101 (2017). <https://doi.org/10.1186/s12889-017-4041-1>
9. J. Salas-Salvadó, J. Fernández-Ballart J, E. Ros, M.A. Martínez-González, M. Fitó M, R. Estruch, et al. Effect of a Mediterranean Diet Supplemented with Nuts on Metabolic Syndrome Status: One-Year Results of the PREDIMED Randomized Trial. *Arch. Intern. Med.* **168** (22), 2449–2458 (2008). <https://doi.org/10.1001/archinte.168.22.2449>
10. M. Hidalgo-Santamaria, A. Fernandez-Montero, M.A. Martinez-Gonzalez, L. Moreno-Galarraga, A. Sanchez-Villegas, M.T. Barrio-Lopez, et al. Exercise Intensity and Incidence of Metabolic Syndrome: The SUN Project. *Am. J. Prev. Med.* **52**, e95–101 (2017). <https://doi.org/10.1016/j.amepre.2016.11.021>
11. W. Zhang, Q. Chen, Z. Yuan, J. Liu, Z. Du, F. Tang, et al. A routine biomarker-based risk prediction model for metabolic syndrome in urban Han Chinese population. *BMC Public Health*. **15**, 64 (2015). <https://doi.org/10.1186/s12889-015-1424-z>
12. F. Szabo de Edelenyi, L. Goumidi, S. Bertrais, C. Phillips, R. MacManus, H. Roche, et al. Prediction of the metabolic syndrome status based on dietary and genetic parameters, using Random Forest. *Genes. Nutr.* **3**, 173–176 (2008). <https://doi.org/10.1007/s12263-008-0097-y>
13. T.V. Huy, M.T. Truong, N. Thach. Prevalence of metabolic syndrome in adults in Khanh Hoa, Viet Nam. *J Geriatr Cardiol.* **1**, 95–100 (2004)

14. T.T.H. Oanh, N.D. Nguyen, P. Phongsavon, Michael J. Dibley, and A.E. Bauman. *Metab. Syndr. Relat. Disord.* **8**, 69-78 (2010) <http://doi.org/10.1089/met.2009.0018>
15. T.Q. Binh, P.T. Phuong, B.T. Nhung, et al Metabolic syndrome among a middle-aged population in the Red River Delta region of Vietnam. *BMC Endocr. Disord.* **14**, 77 (2014). <https://doi.org/10.1186/1472-6823-14-77>
16. N.T. Tuyet, T. Maurizio. Vietnam a country in transition: health challenges. *BMJNPH.* **3**, 60–66 (2020) <http://dx.doi.org/10.1136/bmjnph-2020-000069>
17. T.Q. Binh, P.T. Phuong, B.T. Nhung, D.D. Thoang, P.V. Thang, T.K. Long, et al. Prevalence and correlates of hyperglycemia in a rural population, Vietnam: implications from a cross-sectional study. *BMC Public Health.* **12**, 939 (2012) <https://doi.org/10.1186/1471-2458-12-939>
18. Expert Panel on Detection E and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA.* **285**, 2486–2497 (2001) <https://doi.org/10.1001/jama.285.19.2486>
19. UNFPA Vietnam. Results of the 2019 Census on Population and Housing in Viet Nam (2020) <https://vietnam.unfpa.org/en/publications/results-2019-census-population-and-housing-viet-nam>. Accessed Jan 30 2021.
20. B.V. Calster, L. Wynants, J. Verbeek, J.Y. Verbakel, E. Christodoulou, A.J. Vickers, M.J. Roobol, & E.W. Steyerberg. Reporting and Interpreting Decision Curve Analysis: A Guide for Investigators. *Eur. Urol.* **74**(6), 796–804 (2018) <https://doi.org/10.1016/j.eururo.2018.08.038>
21. W.H. Sheu, S.Y. Chuang, W.J. Lee, S.T. Tsai, P. Chou, C.H. Chen. Predictors of incident diabetes, metabolic syndrome in middle-aged adults: a 10-year follow-up study from Kinmen, Taiwan. *Diabetes Res. ClinPract.* **74**(2), 162–168 (2006) <https://doi.org/10.1016/j.diabres.2006.03.011>
22. J.H. Hwang, S. Kam, J. Shin, J.Y. Kim, K.E. Lee, G.H. Kwon, et al. Incidence of Metabolic Syndrome and Relative Importance of Five Components as a Predictor of Metabolic Syndrome: 5-Year Follow-up Study in Korea. *J. Korean Med. Sci.* **28**, 1768–1773 (2013). <https://doi.org/10.3346/jkms.2013.28.12.1768>
23. J. Sangbangmud, B. Kaewthanasin, K. Jintabunyat, C. Pokabarl, C. Limcharoenchai, N. Kanchana-Udomkan, et al. Incidence and Risk Factors of Metabolic Syndrome and 9-year Follow-up in Na Yao Community, Sanam Chai Khet District, Chacheongsao, Thailand. *JSEAMED.* **2**, 7–15 (2018)
24. B. Zhu, Y. Haruyama, T. Muto, T. Yamazaki. Association Between Eating Speed and Metabolic Syndrome in a Three-Year Population-Based Cohort Study. *J. Epidemiol.* **25**(4), 332-336 (2015); <https://doi.org/10.2188/jea.JE20140131>.
25. S. Mohammadtaghi, M.S. Jalil, M. Masoud, N.S. Mahdih, S.M. Hossein, P. Ali, et al. The incidence of metabolic syndrome and the most powerful components as predictors of metabolic syndrome in central iran: a 10-year follow-up in a cohort study. *Iran Red. Crescent. Med. J.* **19**(7), e14934 (2017) <https://doi.org/10.5812/ircmj.14934>
26. N. Hosseini, M. Talaei, M. Dianatkhah, M. Sadeghi, S. Oveisgharan, N. Sarrafzadegan. Determinants of Incident Metabolic Syndrome in a Middle Eastern Population: Isfahan Cohort Study. *Metab. Syndr. Relat. Disord.* **15**(7), 354–362 (2017) <http://doi.org/10.1089/met.2016.0156>
27. F. Hadaegh, M. Hasheminia, M. Lotfaliany, R. Mohebi, F. Azizi, et al. Incidence of Metabolic Syndrome over 9 Years Follow-Up; the Importance of Sex Differences in the Role of Insulin Resistance and Other Risk Factors. *PLOS ONE* **8**(9): e76304 (2013) <https://doi.org/10.1371/journal.pone.0076304>
28. A.C. Santos, M. Severo, H. Barros. Incidence and risk factors for the metabolic syndrome in an urban South European population. *Prev. Med.* **50**, 99–105 (2010). <https://doi.org/10.1016/j.ypmed.2009.11.011>
29. N. Mehndiratta, S. Sharma, R.K. Sharma, S. Grover S. A Prospective study on the incidence of metabolic syndrome in premenopausal and postmenopausal women. *J. Mid-life Health.* **11**, 17–21 (2020). <https://www.jmidlifehealth.org/text.asp?2020/11/1/17/283783>
30. P.W. Wilson, R.B. D'Agostino, H. Parise, L. Sullivan, J.B. Meigs. Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. *Circulation.* **112**(20), 3066–3072. <https://doi.org/10.1161/CIRCULATIONAHA.105.539528>
31. T.T. Zou, Y.J. Zhou, X.D. Zhou, W.Y. Liu, S.V. Poucke, W.J. Wu, et al. MetS Risk Score: A Clear Scoring Model to Predict a 3-Year Risk for Metabolic Syndrome. *Horm. Metab. Res.* **50**, 683–689 (2018). <https://doi.org/10.1055/a-0677-2720>
32. J. Wang, C. Li, J. Li, S. Qin, C. Liu, J. Wang, et al. Development and internal validation of risk prediction model of metabolic syndrome in oil workers. *BMC Public Health.* **20**, 1828 (2020). <https://doi.org/10.1186/s12889-020-09921-w>
33. S. Wang, S. Wang, S. Jiang, Q. Ye. An anthropometry-based nomogram for predicting metabolic syndrome in the working population. *Eur. J. Cardiovasc. Nurs.* **19**, 223–229 (2020). <https://doi.org/10.1177/1474515119879801>
34. A. Scuteri, C.H. Morrell, S.S. Najjar, D. Muller, R. Andres, L. Ferrucci, et al. Longitudinal Paths to the Metabolic Syndrome: Can the Incidence of the Metabolic Syndrome Be Predicted? The Baltimore Longitudinal Study of Aging. *The Journals of Gerontology: Series A.* **64A**, 590–598 (2009) <https://doi.org/10.1093/gerona/glp004>

Figures

Figure 1

The nomogram for predicting new-onset MetS.

Figure 2

a, both these lines were very close with the ideal line and the mean absolute error was 0.009. Thus, the prediction nomogram performed a good calibration. b demonstrated that for the predicted probability thresholds between 0.13 and 0.70, the prediction nomogram showed a positive net benefit than strategies for all and none participant to treat.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [AdditionalTable.docx](#)