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Development of a Nomogram for Predicting Metabolic Syndrome in South Korean Adults Focusing on Alameda 7: A Preliminary Study †

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Abstract: This study identified high-risk groups for metabolic syndrome based on the "Alameda 7" model using national survey data on adults conducted in South Korea and developed a nomogram allowing medical personnel to visually examine the predictive path of high-risk groups for metabolic syndrome in primary care settings easily. This study targeted 11,868 adults between the ages of 19 and 80 living in the community. Metabolic syndrome, an outcome variable, was based on the five criteria of the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) and a subject was defined as having metabolic syndrome when the subject met three or more of them. This study constructed a metabolic syndrome, predictive model (a multivariate model after adjusting all confounding variables) to understand the relationship (influence) between variables regarding metabolic syndrome by using logistic regression analysis. The developed predictive model for metabolic syndrome (final model) provided a nomogram so that clinicians can easily interpret the prediction result (prediction probability). The results of multivariate logistic regression analysis revealed that physical inactivity, maintaining desirable weight for height, binge drinking, smoking, breakfast frequency, and sleeping hours were independently ($p < 0.05$) associated with metabolic syndrome in South Korean adults. It is required to continuously manage high-risk groups for metabolic syndrome with these multiple risk factors at the same time to prevent metabolic syndrome.

Keywords: Alameda 7; multiple risk factors; nomogram; metabolic syndrome; predictive model

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1. Introduction

Metabolic syndrome is a cluster disease group of obesity, lipid metabolic abnormality, diabetes, or disturbed glucose tolerance, and hypertension, which were risk factors of cardiovascular disease and type II diabetes, previously known as insulin resistance syndrome or syndrome X [1]. Chronic diseases such as hypertension, diabetes, and cardiovascular disease are showing an increasing trending along with the increase of obese population in modern society [2]. A common clinical characteristic of these diseases is that they are closely related to metabolic syndrome [2]. The obesity rate has been steadily increasing over the past 10 years in South Korea: the prevalence of obesity increased from 29.7% in 2009 to 35.7% in 2019 [3]. If this trend of obesity rate continues, it is believed that the prevalence of metabolic syndrome, directly related to obesity, will steadily increase in the future. Consequently, it is critical to detect and manage the high-risk groups for metabolic syndrome in primary care.

Complex factors including sociodemographic factors, genetic factors, occupational (working environment) factors, health behaviors, psychological factors, smoking, drinking, exercise, diet, and lifestyle can induce metabolic syndrome [4,5]. It is necessary to

prevent metabolic syndrome including the changes in holistic health-promoting behaviors as soon as possible rather than changing individual factors. Numerous studies have reported that lifestyle-related health behaviors such as overeating, obesity, and lack of exercise due to a sedentary lifestyle are closely related to the onset of metabolic syndrome [6,7]. Obesity is particularly known to be an important causal factor of metabolic syndrome. Therefore, studies have focused on reducing obesity. However, these previous studies have two limitations. First, most of them used regression analysis to identify individual risk factors (independent risk factors) of metabolic syndrome. Poortinga [8] and Byeon [9] identified the clustering of health behaviors targeting community population groups and showed that an individual had two or more living habits (health risk behaviors) rather than one living habit and these many health risk factors tended to cluster with each other. Second, studies on the multiple health risk behaviors of metabolic syndrome were mainly conducted for European and North American populations, and there are limitations in applying the results of these studies to Asians who have different physical conditions and lifestyles. In addition, since Asians are composed of very diverse ethnic groups, races, and cultures, it is difficult to apply models for predicting metabolic syndrome for Southeast Asian populations [10,11] to South Korean local populations and interpret the results. Therefore, it is necessary to develop a metabolic syndrome predictive model with excellent predictive performance, such as sensitivity and specificity using epidemiological data representing the South Korean community to clinically discover metabolic syndrome at an early stage efficiently in South Korea.

On the other hand, previous studies that identified multiple health risk factors of physical health status [12,13] mainly used the "Alameda 7" model [14] (7 living habits: smoking, drinking, obesity (weight control), exercise, breakfast and snack, and sleep), which was included in the large-scale epidemiological investigation in Alameda County, California, USA. Since it is possible to control or alter living habits by oneself to some extent, metabolic syndrome can be prevented and health can be improved by changing health risk behaviors. This study identified high-risk groups for metabolic syndrome based on the "Alameda 7" model using national survey data on adults conducted in South Korea and developed a nomogram allowing medical personnel to visually examine the predictive path of high-risk groups for metabolic syndrome in primary care settings easily.

2. Method

2.1. Data Source

This is a secondary data analysis study using the raw data of the 7th Korea National Health and Nutrition Examination Survey (KNHANES) conducted from 2016 to 2018 under the supervision of the Korea Centers for Disease Control and Prevention under the Ministry of Health and Welfare. The administration and design of KNHANES data are described in detail elsewhere [15]. This study targeted 11,868 adults between the ages of 19 and 80 living in the community.

2.2. Variable Measurement

Metabolic syndrome, an outcome variable, was based on the five criteria of the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) and a subject was defined as having metabolic syndrome when the subject met three or more of them [16]. The five criteria of metabolic syndrome presented by NCEP-ATP III are (1) men's waist measurement ≥ 90 cm and women's waist measurement ≥ 80 cm, (2) fasting blood glucose ≥ 100 mg/dL or taking medications related to hypoglycemic, (3) fasting triglycerides > 150 mg/dL or taking drugs related to lowering blood lipids, (4) HDL-C of men < 40 mg/dL, HDL-C of women < 50 mg/dL, or taking drugs related to lowering blood lipids, and (5) systolic blood pressure ≥ 130 mmHg, diastolic blood pressure ≥ 85 mmHg, or taking hypotensive drugs.

Health risk behaviors, explanatory variables, were, based on health behaviors presented in "Alameda7", smoking (current smoker, former smoker, and non-smoker), binge drinking experience in the past year (yes or no), maintaining desirable weight for height (based on the World Health Organization (WHO) Asia-Pacific region body mass index (BMI) criteria: underweight (BMI < 18.5 kg/m^2), normal (18.5 kg/m^2 ≤ BMI < 23 kg/m^2), pre-obesity stage (23 kg/m^2 ≤ BMI < 25 kg/m^2), class 1 obesity (25 kg/m^2 ≤ BMI < 30 kg/m^2), class 2 obesity (30 kg/m^2 ≤ BMI < 35 kg/m^2), and class 3 obesity (35 kg/m^2≤)), sleeping hours (<5 h, 5 h≤ and <6 h, 6 h≤ and <7 h, 7 h≤ and <8 h, 8 h≤ and <9 h, and 9 h≤), mean number of having a breakfast per week for the past year (rarely, "1–2 times a week", "3–4 times a week", or "5–7 times per week"), and physical inactivity (yes or no), which were survey items included in the National Health and Nutrition Examination Survey. Binge drinking was defined as two times or more per week and seven glasses per time for men and two times or more per week and five glasses per time for women according to the WHO standards [References]. Physical inactivity was defined as not conducting a vigorous physical activity that was very difficult or made one out of breath at least for 20 min a day at least three days a week or a moderate physical activity that was a little harder than usual or made one breath harder at least for 30 min a day at least five days a week according to the criteria of the Global Physical Activity Questionnaire (GPAQ) developed by the WHO. Confounding variables included sociodemographic characteristics (e.g., education level, monthly average household income, age, gender, and occupation) and health status (e.g., subjective health status and depression).

2.3. Developing a Model for Predicting Metabolic Syndrome for South Korean Adults

This study constructed a metabolic syndrome, predictive model (a multivariate model after adjusting all confounding variables) to understand the relationship (influence) between variables regarding metabolic syndrome by using logistic regression analysis. The developed predictive model for metabolic syndrome (final model) provided a nomogram so that clinicians can easily interpret the prediction result (prediction probability). The nomogram consists of a point line, a risk factor line, a probability line, and a total point line. Figure 1 presents an example of a nomogram.

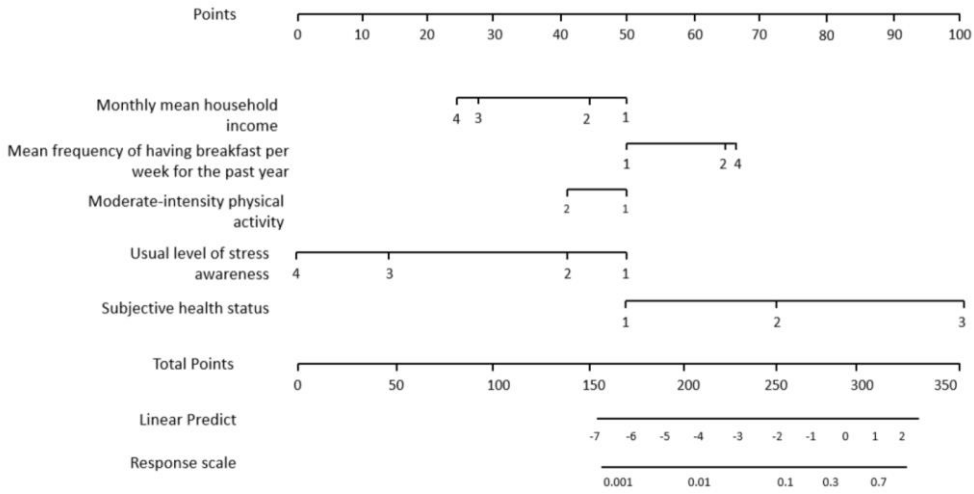

Figure 1. Example of nomogram [15].

2.4. Nomogram Validation

This study used the 10-fold cross-validation to validate the predictive performance of the developed metabolic syndrome predictive model (nomogram). AUC, general accuracy, balanced accuracy, F1 score, sensitivity, and specificity were presented. R version 4.0.3 (Foundation for Statistical Computing, Vienna, Austria) was used for analyses and significance level was 0.05 in two-tailed test.

3. Results

3.1. Characteristics of Subjects According to the Prevalence of Metabolic Syndrome

Among the total subjects (n = 11,868), 3508 adults (29.6%) had metabolic syndrome. This study conducted a chi-square test (nominal variable) and an independent sample t-test (continuous variable) to identify the characteristics of subjects according to the prevalence of metabolic syndrome. The results showed that monthly mean household income, subjective health status, gender, education level, occupation, depression, physical inactivity, maintaining desirable weight for height, binge drinking, smoking, breakfast frequency, sleeping hours, and age significantly ($p < 0.05$) affected metabolic syndrome. The Scatterplot metrics of the variables is presented in Figure 2.

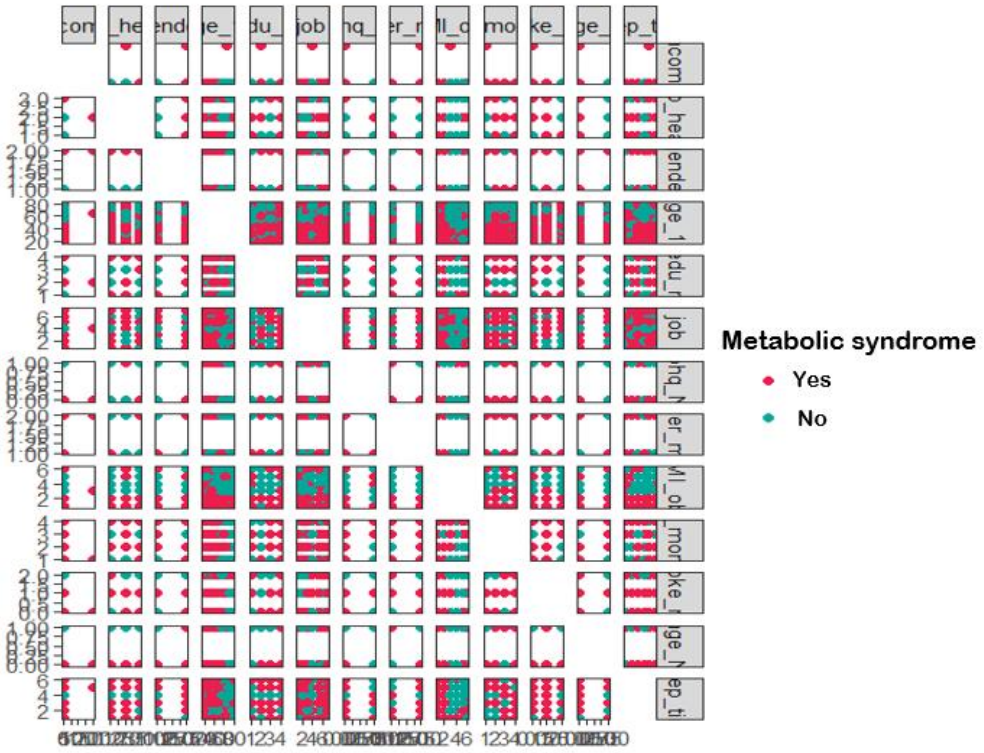

Figure 2. Scatterplot metrics of the variables.

3.2. Developing a Model for Predicting Metabolic Syndrome in South Korean Adults

The results of multivariate logistic regression analysis revealed that physical inactivity, maintaining desirable weight for height, binge drinking, smoking, breakfast frequency, and sleeping hours were independently ($p < 0.05$) associated with metabolic syndrome in South Korean adults when all confounding variables (education level, mean monthly household income, age, gender, occupation, subjective health status, depression, and maintaining desirable weight for height) were adjusted.

Figure 3 presents the nomogram for predicting metabolic syndrome in South Korean adults developed in this study. The risk factors for metabolic syndrome in South Korean adults were BMI, smoking, breakfast frequency, binge drinking, physical inactivity, and sleeping hours, presented in the order of influence's magnitude. Among them, BMI (maintaining desirable weight for height) was the most influential variable, and class 3 obesity had the highest risk of metabolic syndrome. For example, when high-risk groups for metabolic syndrome were identified based on the multiple factors using this nomogram, those who were in class 3 obesity, were smokers, rarely had a breakfast in the past one year, experienced binge drinking, and had been physically inactive, and had slept more than

nine hours, had the total nomogram score of 149.48 points and the metabolic syndrome risk probability of 87% (Figure 4).

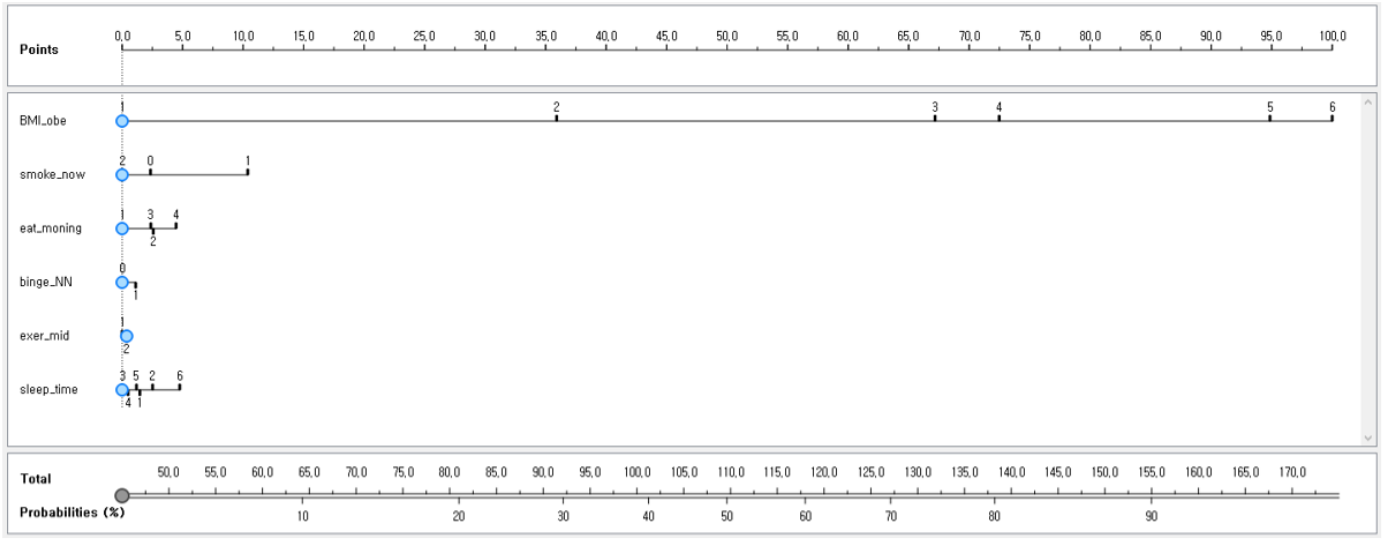

Figure 3. The nomogram for predicting metabolic syndrome in South Korean adults.

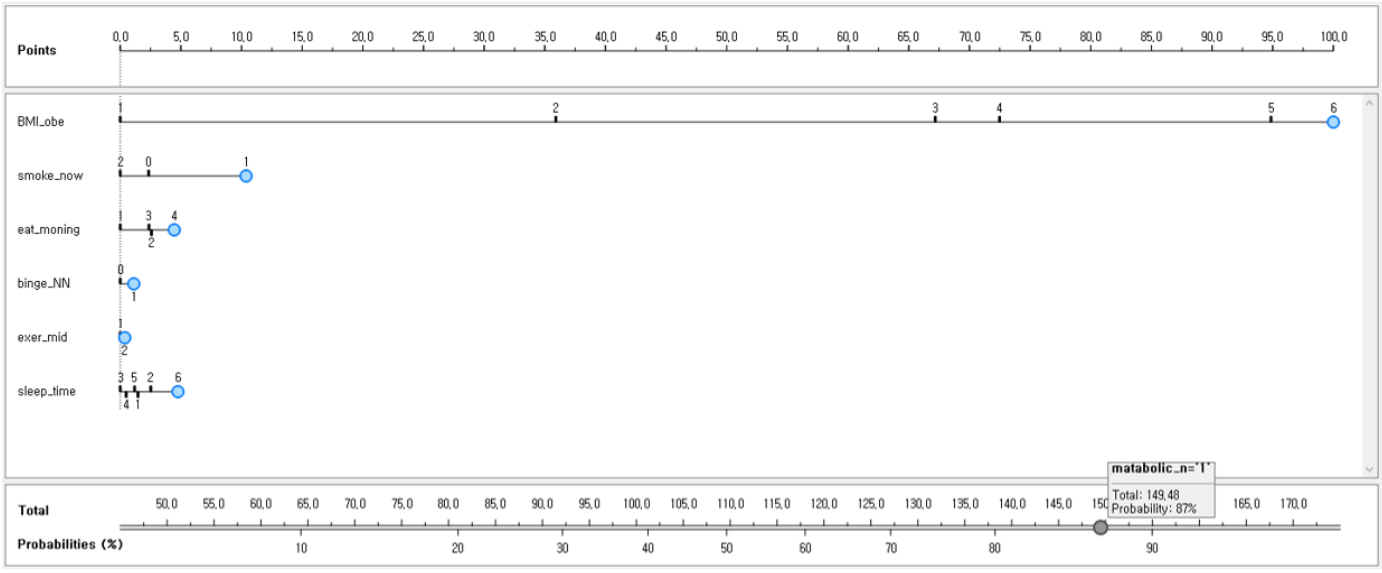

Figure 4. Application example of metabolic syndrome predictive nomogram for Korean adults.

When the developed metabolic syndrome predictive nomogram was validated with 10-fold cross validation, the AUC of the nomogram was 0.74 and the general accuracy of it was 0.73. The calibration plot of the developed metabolic syndrome predictive nomogram is presented in Figure 5.

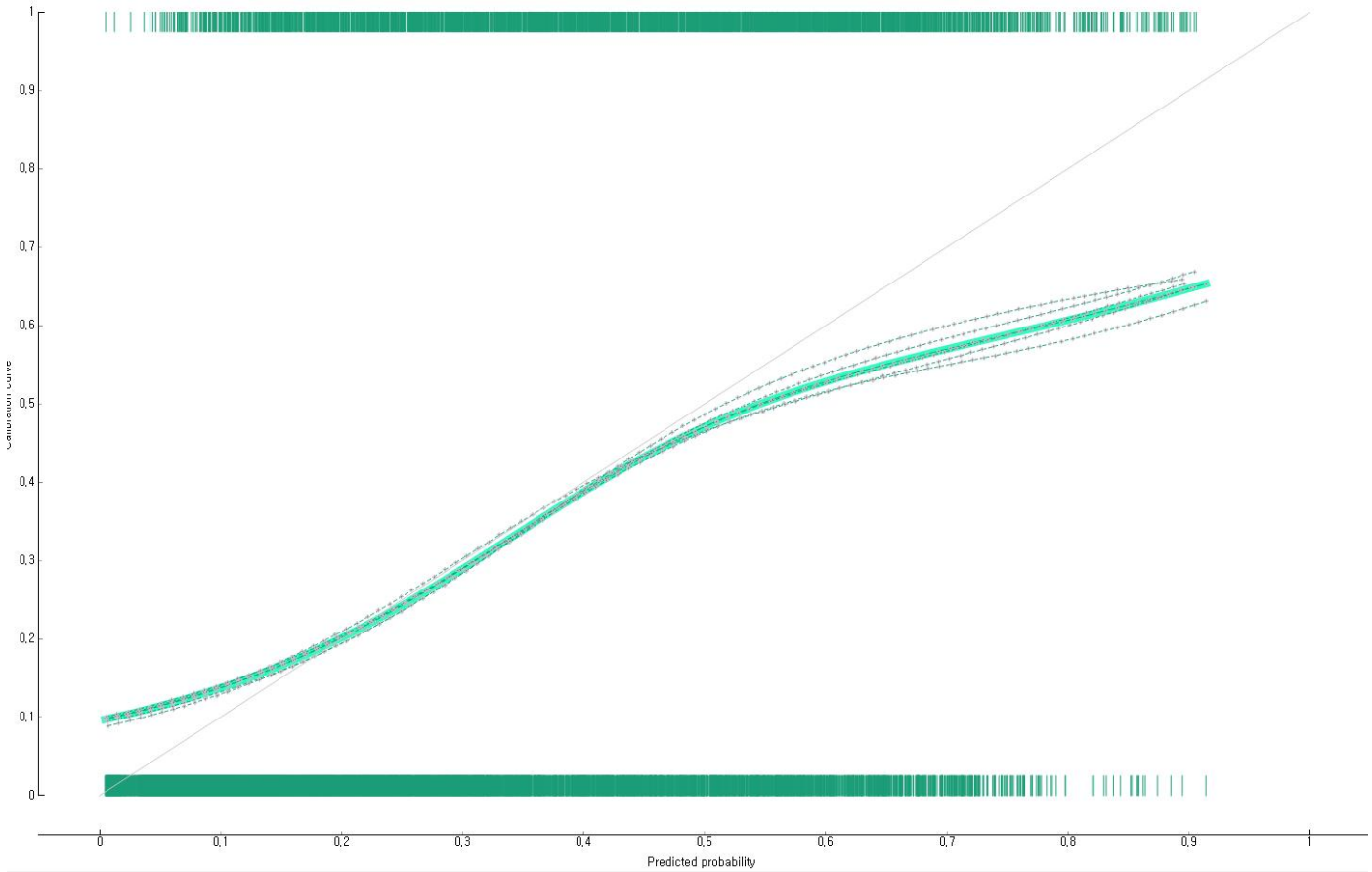

Figure 5. The calibration plot of the developed metabolic syndrome predictive nomogram.

4. Discussion

This study identified risk factors for metabolic syndrome in South Korean adults based on multiple health risk behaviors and found that physical inactivity, maintaining desirable weight for height, binge drinking, smoking, breakfast frequency, and sleeping hours were independent predictors of metabolic syndrome. It has been generally assumed that insulin resistance is the root cause of metabolic syndrome but the pathogenesis of it has not been clearly understood. Similar to the results of this study, many studies [4] have reported that obesity, inactive lifestyle, diet, smoking, and genetic factors cause metabolic syndrome. Particularly, Prasad et al. [17] argued that a person with an abnormally large waist measurement had a 46% chance of developing metabolic syndrome within 5 years, indicating a high risk of metabolic syndrome. The results of this study also confirmed that obesity, measured by BMI, was the most critical factor for predicting metabolic syndrome among health risk behaviors. These results indicated the importance of maintaining desirable weight for height in metabolic syndrome.

Moreover, the results of previous studies showed that the onset rate of metabolic syndrome was higher in former smokers and current smokers than non-smokers [18], in those who drank more than two glasses per day or binge drinking at least once a week than Fan et al. [19], and in those who did not exercise than in those who exercised regularly [20].

Nevertheless, only a few studies have evaluated multiple risk factors for metabolic syndrome. This study identified high-risk groups based on multiple risk factors in South Korean adults using the nomogram. It was predicted that the risk probability of adults who were in class 3 obesity, smoked, rarely had a breakfast in the past year, experienced binge drinking, had been physically inactive, and had slept over 9 h was 87% after adjusting gender, education level, occupation, depression, and subjective health status.

Therefore, it is required to continuously manage high-risk groups for metabolic syndrome with these multiple risk factors at the same time to prevent metabolic syndrome.

It is necessary to develop a highly accurate model for predicting high-risk groups for metabolic syndrome with high explanatory power based on the results of this study by adding genomic data, disease history, and family history to the metabolic syndrome predictive model. It is also required to develop a model for predicting high-risk groups for metabolic syndrome by gender, age, and occupation and a predictive model customized for a subject to prevent metabolic syndrome.

Author Contributions: For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used. Conceptualization, B.H.; methodology, B.H.; software, B.H.; validation, B.H.; formal analysis, B.H.; writing—original draft preparation, B.H.; writing—review and editing, B.H; visualization, B.H. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of National Biobank of Korea under Korea Centers for Disease Control and Prevention (protocol code KBN-2019-1327).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement:

Conflicts of Interest: The authors declare no conflict of interest.

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