Interaction between overweight, obesity and smoking on the risk of pre-diabetes and type 2 diabetes in Guangdong, China

Zhuanping Zeng
Guangdong Pharmaceutical University
Yinghua Jin
Guangdong Pharmaceutical College: Guangdong Pharmaceutical University
Yingying Zheng
Guangdong Pharmacial university
Lei Xiang
Guangdong Pharmaceutical College: Guangdong Pharmaceutical University
Jin Yang
Guangdong Pharmaceutical College: Guangdong Pharmaceutical University
Liufen Peng
Gaungdong Pharmicial university
Qin Wei
Guangdong Pharmaceutical College: Guangdong Pharmaceutical University
Meng Yang
Guangdong Pharmaceutical University
Qiuting Cheng
Guangdong Pharmaceutical College: Guangdong Pharmaceutical University
Xianglu Rong
Guangdong Pharmaceutical College: Guangdong Pharmaceutical University
Shenghua Piao
Guangdong Pharmacial university
Jiao Guo (gyguoyz@163.com)
Guangdong Pharmaceutical College: Guangdong Pharmaceutical University

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Abstract

Background

Pre-diabetes mellitus (PDM) is considered an early warning signal of type 2 diabetes mellitus (T2DM). However, most studies only analyze the risk factors of diabetes, ignore the exploration of PDM. The aim of this study was to investigate the independent and combined impacts of overweight obesity and smoking on the risk of PDM and T2DM.

Methods

28,208 patients with T2DM were selected from 5 cities in the Pearl River Delta, Guangdong Province, China. According to the same region, gender and age difference less than 5 years old, 28208 patients with PDM and 28208 patients with normal glucose tolerance (NGT) were randomly selected. We analyzed the influential factors of PDM,T2DM and the interaction between smoking and overweight and obesity on using ordered multi-class logistic regression and multi-class results non-conditional logistic regression.

Results

Overweight and obesity (OR = 1.427,95%CI:1.388 ~ 1.468; OR = 1.829,95%*CI*:1.753 ~ 1.908) and smoking (OR = 1.161,95%CI:1.113 ~ 1.212) were risk factors for the onset of T2DM by ordered multiple Logistic regression. Furthermore, both in the comparison of NGT, PDM and NGT, T2DM, the results showed that overweight, obesity and smoking were risk factors for both PDM and T2DM too. And we found there was an additive interaction between overweight obesity and smoking in the developing of T2DM. Moreover, there would be 0.196(0.051 ~ 0.341) relative excess risk due to the additive interaction, 9.1% (2.0%-16.1%) of T2DM exposed to both risk factors was attributable to the additive interaction, and the risk of T2DM in overweight and obese smokers was 1.203(1.004–1.402) times as high as the sum of risks in the participants exposed to a single risk factor alone too.

Conclusions

Overweight obesity and smoking are the risk factors for the onset of T2DM. The risk of the coexistence of both factors is greater than that of single factors. Early weight control and positive smoking control are beneficial to prevent and delay the occurrence of T2DM.

Background

Pre-diabetes was defined as blood glucose concentrations higher than normal but not high enough to be classified as diabetes, which was the state between normal and diabetes, categorized into either impaired fasting glucose (IFG) or/and impaired glucose tolerance (IGT)[1,2,3] and was called impaired glucose Regulation (IGR).Pre-diabetes was considered to be a necessary stage of T2DM, and was an early warning signal of T2DM.

Several national or regional studies have found that the prevalence of diabetes in China is on the rise, and the prevalence of pre-diabetes is getting higher and higher, showing a significant trend of increase and has far exceeded the prevalence of diabetes. In 1994, the prevalence of diabetes in China was 2.5%, and the prevalence of pre-diabetes was 3.2%[4]. In 2007, the New England Journal reported that the prevalence of diabetes in Chinese adults increased to 9.7%, while the prevalence of pre-diabetes increased to 15.5%[5]. The literature data of JAMA in 2017 showed that the prevalence of diabetes in Chinese adults reached 10.9%, and the prevalence of pre-diabetes reached 35.7%[6]. The rising prevalence of diabetes poses a great crisis to China's public health and economy. It’s known that early intervention in high-risk groups might reduce the incidence of PDM and T2DM. However, the risk factors and the mechanism of their interaction were not clear.

Several factors such as overweight, obesity, hyperlipidemia and hypertension are prevalent in T2DM.Among them, obesity is an important risk factor for T2DM[7]. The number of overweight and obese people is increasing with the improvement of living standards. In 2014, China's obese population ranked first in the world[8]. Smoking is another important risk factor for diabetes too. The risk of diabetes in smokers is 1.2 times higher than that in non-smokers[9]. Relevant studies have shown that the occurrence of diabetes caused by overweight, obesity and smoking is related to insulin resistance[10,11]. Therefore, there may be some synergistic effect in the mechanism leading to diabetes.

At present, most of the studies only analyze the risk factors of diabetes, ignore an important stage of reversing the onset of diabetes in the process of diabetes, and ignore the exploration of risk factors of pre-diabetes. At present, there are few studies on the interaction between overweight, obesity and smoking on pre-diabetes and diabetes. Hence, in this study, we aimed to explore the influence of overweight, obesity and smoking on incident T2DM, and the independent and comprehensive effects on pre-diabetes and T2DM respectively.

Methods

Participants

This study based on a health checkup of chronic non-communicable diseases among residents aged 18 in the Pearl River Delta region of Guangdong Province in 2017. It covered Dongguan, Guangzhou, Shenzhen, Zhuhai, and Jiangmen cities in the Pearl River Delta, Guangdong Province. Five cities, each of which was divided into layers according to the overall population size, urban population ratio, mortality and complex multi-stage sampling. The samples were collected by surveyors with uniform training, who conducted a comprehensive questionnaire survey including general demographic characteristics, disease history, life style and other factors. Laboratory tests and physical measurements were carried out by professionals and the information was recorded in the physical examination records. According to the principle of same-gender, age difference less than 5 years, living in the same region, 28,208 patients with PDM and 28,208 NGT were matched with T2DM, respectively.

The questionnaire content

The health examination questionnaire were covered (1) General situation investigation: gender, age, marriage, physical exercise, smoking: smoking during the examination and smoking history before the examination is defined as smoking, never smoking is defined as no smoking, etc. ; (2) Laboratory tests: fasting intravenous blood glucose test and oral glucose tolerance test to diagnose diabetes, and detect Total cholesterol (TC), Triglyceride (TG), Low Density Lipoprotein Cholesterol (LDL-C), High-Density Lipoprotein Cholesterol (HDL-C); (3) Physical examination: measurement of Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), height, weight, Body Mass Index (BMI) = weight (Kg) / height (m).

Related diagnostic criteria：

： WHO definition was used to diagnose diabetes and pre-diabetes (intermediate hyperglycaemia)[2]：

T2DM group：Fasting venous blood glucose (FPG)≥7.0 mmol/L or 2h plasma glucose concentration (2hPG) after OGTT≥11.1 mmol/L.

PDM group: Impaired Fasting Glucose (IFG) is 6.1≤FPG＜7.0mmol/L, or Impaired Glucose Tolerance (IGF) is 7.8≤2hPG ＜11.1mmol / L.

NGT group: FPG＜6.1 mmol/L and 2hPG after OGTT＜7.8 mmol/L

： Overweight and obesity: According to the "Guidelines for the Prevention and Control of Overweight and Obesity in Chinese Adults" [12], develop standards:

Overweight: 24.0≤BMI＜28.0kg/m^2, Obesity: BMI≥28.0kg/m2.

Statistical analysis

Continuous variables conforming to the normal distribution were expressed as mean standard deviation：`c±s：, non-conforming variables were expressed as the median interquartile range (MQ), and the categorical variables were analyzed by chi-square test for continuous variable analysis of variance. The development process of diabetes was an ordered categorical variable, so an ordered multi-class logistic regression model was used: NGT was used as the control group, PDM and T2DM were the case groups, and univariate analysis was performed first to incorporate the statistically significant variables into the multifactorial in the model. Then the unconditional logistic regression models of NGT-T2DM and NGT-PDM were established respectively to study the independent and comprehensive effects of smoking and overweight and obesity and diabetes. The multiplicative interaction was determined by *P* value less than 0.05, and the additive interaction was conducted by nonlinear mixed effect model by the relative excess risk ratio (RERI), attribution ratio (AP) and interaction index (S). These three indicators determined the additive interaction of smoking, overweight and obesity on impaired glucose tolerance and diabetes.

Results

Characteristics of study participants

A total of 84,624 subjects were enrolled, with 28,208 subjects in each group. There were statistical difference in age, education, marriage, occupation, smoking, drinking, exercise, diet and BMI among the three groups. By pairwise comparison there were no difference in the distribution of education and marriage in the comparison NGT and PDM. In the comparison of NGT and T2DM, there were no significant difference in the distribution of occupations between the two groups too (Table 1).

Biochemical indicators of NGT, PDM, T2DM

Table 2 shows the biochemical indicators between the three groups of NGT, PDM and T2DM. From the indicators, it might be found that HDL-C level decreased the risk to development PDM and T2DM, however, other indicators like TC, TG and SBP increase the risk of PDM and T2DM.

Analysis the risk factors of NGT, PDM, T2DM by ordered Multi-Classification Logistic Results

NGT, PDM, T2DM were be regarded as dependent variables, and age, education, marriage, occupation, sports, alcohol, diet, BMI, hypertension and other factors were be regarded as risk factors, we utilized an orderly multi-class logistic regression analysis to find the risk factors of PDM and T2DM. Smoking and BMI have an impact on the development of diabetes. Adjusting factors such as age, education, marriage, exercise, alcohol, diet, hypertension, and other factors show that smoking also affects the development of diabetes (P <0.001, OR (95% CI) = 1.161 (1.113 ~ 1.212)), BMI were influential factors for the progression of diabetes too(P <0.05, $OR_{overweight}$ (95% CI) = 1.427 (1.388 ~ 1.468), $OR_{obesity}$(95% CI) = 1.829 (1.753 ~ 1.908)) (Table 3).

Unconditional Logistic Regression results between NGT-PDM and NGT-T2DM

Table 4 showed the results of unconditional logistic regression between NGT-PDM and NGT-T2DM. In the NGT-PDM group, adjusting for age, education and other confounding factors showed that smoking, obesity, and overweight were risk factors for PDM (P < 0.001), in the NGT-T2DM group, adjusting for mixed factors such as age and education showed that smoking, obesity and overweight were risk factors for T2DM (P <0.001). By comparing the two models, we found that smoking and obesity affect the development both PDM and T2DM.

Results of multiplicative and additive interactions between NGT-PDM and NGT-T2DM

Table 4 showed that overweight and obesity were correlated with PDM and T2DM, and the risk had a dose-response relationship. While underweight was a protective factor of PDM in the NGT-PDM, but it was insignificance by comparison NGT-T2DM groups. Therefore, overweight and obesity were considered as risk group, and normal and underweight were considered as control group for additive interaction and multiplicative interaction model analysis.

Table 5 showed the multiplicative and additive interactions effects of obesity and smoking on PDM after stratification. The risk of PDM among overweight/ obesity and smokers was 2.262(2.091~2.448) times than that of non-overweight/non obesity and non-smokers. The results showed that overweight/ obese and smoking increased the risk of PDM than those exposed single risk factor alone. However, we did not find an multiplicative and additive interactions between overweight/ obesity and smoking on PDM.

To found multiplicative and additive interactions of overweight/ obesity and smoking to develop T2DM, the risk of T2DM among overweight/obesity and smokers was 2.2(2.036~2.377) times than that of non-overweight /non obesity and non-smokers. We found that subjects who were overweight/ obesity and smoking had greater risk to develop T2DM than those exposed to a single risk factor alone. However, there was no multiplicative interaction between smoking and overweight/obesity and T2DM, but an additive interaction was existence (Table 6).

Discussion

This study found that smoking, overweight and obesity were independent factors of PDM and T2DM. Moreover, overweight/obesity and smoking might affect the development of T2DM. These results were consistent with other previous studies. For example[13], the Strong Heart Study conducted among 1677 American Indians found that obesity significantly increased the risk for T2DM in those with PDM by 2.7 times after 7.8 years of follow-up. A systematic review of 25 prospective cohort studies (1.2 million participants) showed that smoking was associated with 44% increased risk of developing T2DM (relative risk [RR] 1.44, 95%CI 1.31–1.58)[14].However, the interaction between obesity and smoking on incident of T2DM is still unclear, so we studied the interaction between overweight obesity and smoking on PDM and on T2DM. In this study, we did not find an interaction between overweight/obesity and smoking on PDM, but the risk of PDM among overweight and obese smokers was 2.262 times than that of non-overweight and obese non-smokers. Previous studies had shown that smoking increases blood glucose concentration after oral glucose tolerance[15] and may impair insulin sensitivity[16].However, smoking is associated with higher energy expenditure and decreased appetite, which might cause smokers to lose weight and gain weight after quitting smoking[17].But, smoking and body mass index interact to influence the diabetes, and the interactions are complex. A follow-up study in Japan suggests that, light smoking reduced the risk for T2DM in lean men[18].Furthermore,a prospective cohort study conducted among 3,598 Chinese found that although there was a significant interaction between smoking and abdominal obesity in patients with T2DM, even no significant interaction was found between smoking and overall obesity, but T2DM was also associated with a higher incidence among overall obese smokers[19].

In this study, there was an additive interaction between smoking, overweight obesity and T2DM, and the interaction between smoking and overweight obesity accounted for 9.1% of the occurrence of diabetes. Furthermore, overweight and obese smokers was 2.2 times to develop T2DM than non-overweight /non obesity and non-smokers. Multiple biological mechanisms could explain the link between overweight obesity, smoking and diabetes.

First, smoking affects the neuroendocrine system. Smoking and nicotine directly act on the surrounding tissues (mainly mediated by catecholamines) and indirectly affect the neuroendocrine circuit in the central nervous system[20], reducing food intake by inhibiting the signal of hypothalamus appetite, and increasing energy consumption, thus reducing body weight. However, smoking increases the risk of central obesity by increasing the 2-hydroxylation of estradiol or by inducing an imbalance of androgen to estrogen activity in smokers[21].Central obesity in the form of abdominal fat accumulation is closely related to insulin resistance and diabetes [22].Smoking is associated with increased levels of anti-regulatory hormones and increased sympathetic activity, which may be the cause of impaired insulin sensitivity caused by smoking [23].

Secondly, the insulin resistance of most obese patients [24] is related to the significantly increased level of free fatty acids in the blood[25]. Smoking aggravates the insulin resistance of obese patients by increasing free fatty acids. Smoking has been shown to be associated with insulin resistance in non-diabetic[26] and type 2 diabetic[27], with long-term smokers having insulin resistance, hyperinsulinemia and dyslipidemia. Nicotine promotes adipobreakdown and transports free fatty acids to the liver and skeletal muscles, which are associated with the secretion of very low density lipoprotein in the liver, lipid saturation in muscle cells, and peripheral insulin resistance[28].

Third, both smoking and obesity might affect mitochondrial function. Smoking increases oxidative stress and inflammation, thereby impairs endothelial function, leading to insulin resistance and diabetes[29]. Smoking is associated with carbon monoxide exposure[30]. It had been reported that carbon monoxide exposure increases oxidative stress, leading to impaired mitochondrial function, inflammation, and endothelial function. A series of studies had found that in the obesity-induced IR population, the mRNA level and protein content of mitochondrial genes, the size and number of mitochondria, and the activity of oxidase [31–32] were all lower than those in the normal control group.

Fourth, inflammation plays a role in the development of T2DM. Prospective nested case-control studies[33] showed that the baseline levels of IL-6 and CRP in DM cases were significantly higher than those in the control group, and the elevated levels of CRP and IL-6 predicted the development of T2DM. Adipose tissue produces about 25% of systemic il-6 in the body[34]. Inflammatory properties of IL-6 include stimulating the liver to produce acute phase proteins [35, 36]. The release of IL-6 from adipose tissue may lead to low-level systemic inflammation in people with excessive body fat. Another sensitive marker of systemic inflammation is acute c-reactive protein (CRP). A higher BMI[37] was found to be associated with a higher CRP concentration, even in young people aged 17–39 years, suggesting a low-grade systemic inflammatory state in overweight and obese people. Studies had shown[38] that current smokers had significantly higher CRP levels (2.53 vs 1.35 mg/L) than those who had never smoked. The double effects of overweight and obesity and smoking increase chronic inflammatory responses then led to PDM or T2DM.

Advantage:

The mechanisms by which overweight, obesity and smoking contribute to diabetes are still being investigated. It has been documented that smoking is a risk factor for diabetes[39, 40], and overweight and obesity may affect the occurrence of diabetes[41].However, there is few literatures on the influence of overweight/obesity and smoking on the progression of the disease, there is few reports on whether overweight/obesity and smoking are risk factors for PDM. The combined effects of overweight and smoking on pre-diabetes and T2DM have been less well reported. The main advantage of this study is a large sample case-control study design. In this study, we aimed to explore the influence of overweight, obesity and smoking on incident T2DM,and the independent and comprehensive effects on PDM and T2DM respectively, so as to provide reference for early controlling diabetes risk factors.

Limitations

The limitation of this study is that the smoking status is collected through self-report of the respondents, and there may be smokers who do not admit that they smoke. Secondly, fewer women are smokers, so the interaction between smoking and overweight and obesity among female smokers might be verified by expanding the sample. Third, smokers, including former and current smokers, have been reported to reduce the risk of diabetes after quitting smoking. Fourth, smoking intensity was not recorded. Fifth, the selection of The Pearl River Delta region in Guangdong has certain limitations, which might expand the sample to increase the representation of other Cities and regions in China.

Conclusions

The main findings of this study is that the overweight/obesity and smoking are important influence factors of PDM and T2DM, which affect the degree of disease development. It also found an interaction between overweight/obesity and smoking for T2DM.It is suggested that early weight control and active control is helpful to prevent and delay the onset of T2DM. Overweight and obese people should control their weight in a reasonable range. Smokers take quitting smoking as an important way to improve their lifestyle. In other words, people with smoking habits and overweight and obese should not only stop smoking and control their weight, but also reduce the inhalation of second-hand smoke, so as to reduce the occurrence of diabetes.

Abbreviations

T2DM:type 2 diabetes mellitus; PDM:pre-diabetes mellitus; NGT:normal glucose tolerance; IFG:impaired fasting glucose; IGT: impaired glucose tolerance;IGR: impaired glucose Regulation; TC:Total cholesterol; TG:Triglyceride ; LDL-C:Low Density Lipoprotein Cholesterol;HDL-C:High-Density Lipoprotein Cholesterol; DBP:Diastolic Blood Pressure;SBP:Systolic Blood Pressure;BMI:Body Mass Index ;FPG:Fasting venous blood glucose;2hPG:2h plasma glucose concentration.

Declarations

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Authors' contributions

JG,XL,SP and ZZ contributed to the conception and design of the study. ZZ,YZ,JY,LP,MQ,YM and QC participated in the data acquisition and the analyses of data. All authors contributed to the interpretation of data. YJ, YZ and ZZ were involved in drafting the manuscript. All authors have read and approved the final manuscript.

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Consent to publish

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethics Committee of the First Affiliated Hospital of Guangdong Pharmaceutical University. All subjects signed informed consent.

Competing interests

The authors declare that they have no competing interests.

Author details

1. Guangdong Metabolic Diseases Research Center of Integrated Chinese and Western Medicine; Key Laboratory of Glucolipid Metabolic Disorder, Ministry of Education of China; Institute of Chinese Medicine, Guangdong Pharmaceutical University; School of public health, Guangdong Pharmaceutical University; Guangdong TCM Key Laboratory for Metabolic Diseases, Guangzhou 510006, China.

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Tables

Table 1 Basic situation of NGT,PDM, T2DM

Variables	NGT (n= 28208)	PDM (n= 28208)	T2DM (n= 28208)	P_a	P_b	P_c
Age				<0.001	<0.001	<0.001
18~43	5065(17.96)	3383(11.99)	3336(11.83)			
44~59	8322(29.5)	8613(30.53)	9548(33.85)			
≥60	14821(52.54)	16212(57.47)	15324(54.33)			
Education				<0.001	0.081	<0.001
Below primary school	4698(16.65)	4822(17.09)	5039(17.86)			
middle school	3625(12.85)	3450(12.23)	3453(12.24)			
Above high school	4168(14.78)	4110(14.57)	3917(13.89)			
Others	15717(55.72)	15826(56.1)	15799(56.01)			
Marriage				0.004	0.092	0.004
Unmarried/widowed/divorced	2079(7.37)	1910(6.77)	1903(6.75)			
Married	26129(92.63)	26298(93.23)	26305(93.25)			
Occupation				<0.001	<0.001	0.128
Mental workers	2620(9.29)	2804(9.94)	2609(9.25)			
Manual workers	6283(22.27)	5871(20.81)	6090(21.59)			
Other	19305(68.44)	19533(69.25)	19509(69.16)			
Smoking				<0.001	<0.001	
No	3052(10.82)	3721(13.19)	3736(13.24)			
Yes	25156(89.18)	24487(86.81)	24472(86.76)			
Drinking				<0.001	<0.001	<0.001
No	2193(7.77)	2527(8.96)	2510(8.9)			
Yes	26015(92.23)	25681(91.04)	25698(91.1)			
Fitness				<0.001	<0.001	<0.001
No	16878(59.83)	16980(64.13)	17758(62.95)			
Yes	11330(40.17)	9499(35.87)	10450(37.05)			
diet				<0.001	<0.001	<0.001
Vegetarian equilibrium	23125(81.98)	23003(81.55)	22980(81.47)			
Vegetarian imbalance	776(2.75)	1028(3.64)	992(3.52)			
Others	4307(15.27)	4177(14.81)	4236(15.02)			
BMI				<0.001	<0.001	<0.001
Normal	17214(61.03)	13418(47.57)	13424(47.59)			
Underweight	1505(5.34)	866(3.07)	1257(4.46)			
Overweight	7602(26.95)	10226(36.25)	9850(34.92)			
Obesity	1887(6.69)	3698(13.11)	3677(13.04)			
hypertension				<0.001	<0.001	<0.001
No	1575(5.58)	1836(6.51)	2007(7.12)			
Yes	26633(94.42)	26372(93.49)	26201(92.88)			

Note: a: represents the differences between the three groups of NGT, PDM, and T2DM, b: represents the differences between the two groups of NGT,PDM, and c: represents the differences between the two groups of NGT, T2DM

Table 2 Biochemical indicators of NGT, PDM, T2DM[`c±s or M±Q]

variables	NGT (n=28208)	PDM (n=28208)	T2DM (n=28208)	*F* or *H*	*P* value
waistline(cm)	82.00±9.00	84.00±10.00	85.00±10.00	2155.033	<0.001
SBP(mmHg)	129.06±16.40	132.28±16.21	132.30±16.81	352.580	0.001
DBP(mmHg)	78.35±9.72	79.52±9.62	80.00±13.00	107.228	<0.001
TC(mol/L)	5.01±1.18	5.28±1.20	5.40±1.21	736.137	<0.001
TG(mol/L)	1.29±0.72	1.46±1.00	1.69±1.35	1665.199	<0.001
LDL-C(mol/L)	2.85±1.12	3.00±1.17	3.06±1.22	346.301	<0.001
HDL-C(mol/L)	1.37±0.44	1.33±0.47	1.30±0.47	325.210	<0.001

Table 3 logistic regression analysis of T2DM risk factors

Variables	*β*	*sc*	z	*P value*	Gross OR(95%CI)	Adjusted OR(95%CI)
Age						
18~43	1.000	-	-	-	-	-
44~59	0.3796	0.021	326.4986	<0.001	1.564(1.503~1.628)	1.462(1.403~1.523)
≥60	0.3024	0.0201	225.1918	<0.001	1.443(1.39~1.498)	1.353(1.301~1.408)
Education						
Below primary school	1.000	-	-	-	-	-
Middle school	-0.0785	0.0242	10.5703	0.0011	0.914(0.873~0.957)	0.924(0.882~0.969)
Above high school	-0.0488	0.0235	4.2895	0.0383	0.906(0.867~0.947)	0.952(0.909~0.997)
Others	-0.0263	0.0182	2.0763	0.1496	0.952(0.92~0.985)	0.974(0.940~1.010)
Marriage						
Unmarried/widowed/ divorced/	1.000	-	-	-	-	-
Married	-0.0216	0.0255	0.7193	0.3964	1.075(1.024~1.128)	0.979(0.931~1.029)
Physical exercise						
No	1.000	-	-	-	-	-
Yes	0.0667	0.014	22.6892	<.0001	1.106(1.078~1.135)	1.069(1.040~1.099)
Drinking						
No	1.000	-	-	-	-	-
Yes	-0.0011	0.0255	0.0019	0.9654	1.113(1.064~1.163)	0.999(0.950~1.050)
Diet						
Vegetarian Equilibrium	1.000	-	-	-	-	-
Vegetarian imbalance	0.0951	0.0357	7.0801	0.0078	1.19(1.11~1.276)	1.100(1.025~1.180)
Others	-0.0473	0.0196	5.7965	0.0161	0.992(0.958~1.027)	0.954(0.918~0.991)
Smoking						
No	1.000	-	-	-	-	-
Yes	0.1496	0.0216	48.1665	<0.001	1.179(1.136~1.225)	1.161(1.113~1.212)
BMI						
Normal	1.000	-	-	-	-	-
Underweight	0.0601	0.0322	3.4807	0.0621	1.033(0.971~1.099)	1.062(0.997~1.131)
Overweight	0.3559	0.0144	611.6245	<.0001	1.459(1.419~1.5)	1.427(1.388~1.468)
Obesity	0.6037	0.0216	780.167	<.0001	1.851(1.776~1.93)	1.829(1.753~1.908)
Hypertension						
No	1.000	-	-	-	-	-
Yes	0.1132	0.0271	17.4629	<0.001	1.21(1.151~1.273)	1.12(1.062~1.181)

Table 4 Unconditional Logistic Results Between NGT-PDM and NGT-T2DM

Variables	NGT-PDM				NGT-T2DM			
	β	*P value*	Crude OR (95%CI)	Regulated OR (95%CI)	*B*	*P*值	Crude OR (95%CI)	Regulated OR (95%CI)
Age								
18~43	1.000	-	-	-	1.000	-	-	-
44~59	0.329	<0.001	1.55 (1.47~1.634)	1.39 (1.315~1.469)	0.490	<0.001	1.742 (1.653~1.836)	1.633 (1.546~1.724)
≥60	0.364	<0.001	1.638 (1.56~1.72)	1.439 (1.364~1.517)	0.378	<0.001	1.57 (1.494~1.649)	1.459 (1.385~1.538)
Education								
Below primary school	1.000	-	-	-	1.000	-	-	-
middle school	-0.093	0.005	0.927 (0.872~0.986)	0.911 (0.854~0.972)	-0.112	0.001	0.888 (0.835~0.944)	0.895 (0.84~0.953)
Above high school	0.021	0.512	0.961 (0.906~1.019)	1.021 (0.959~1.088)	-0.072	0.023	0.876 (0.826~0.929)	0.931 (0.875~0.99)
others	-0.020	0.415	0.981 (0.937~1.027)	0.98 (0.933~1.029)	-0.033	0.174	0.937 (0.896~0.981)	0.967 (0.922~1.015)
marriage								
Unmarried/ widowed/ divorced	1.000	-	-	-	1.000	-	-	-
married	-0.058	0.092	1.095 (1.027~1.168)	0.943 (0.881~1.01)	-0.021	0.535	1.1 (1.031~1.173)	0.979 (0.916~1.047)
Smoking								
No	1.000	-	-	-	1.000	-	-	-
Yes	0.195	<0.001	1.25 3(1.19~1.318)	1.215 (1.146~1.288)	0.204	<0.001	1.258 (1.196~1.324)	1.226 (1.158~1.299)
Drinking								
No	1.000	-	-	-	1.000	-	-	-
Yes	-0.013	0.703	1.167 (1.099~1.239)	0.987 (0.921~1.057)	- 0.007	0.837	1.158 (1.091~1.23)	0.993 (0.928~1.063)
Fitness								
No	1.000	-	-	-	1.000	-	-	-
Yes	0.20	<0.001	1.2 (1.159~1.242)	1.223 (1.178~1.27)	0.080	<0.001	1.141 (1.103~1.18)	1.083 (1.044~1.124)
diet								
Vegetarian equilibrium	1.000	-	-	-	1.000	-	-	-
Vegetarian imbalance	0.174	0.001	1.332 (1.211~1.464)	1.19 (1.08~1.311)	0.155	0.002	1.286 (1.169~1.416)	1.168 (1.059~1.287)
Others	-0.651	<0.001	0.975 (0.931~1.021)	0.521 (0.493~0.552)	-0.061	0.016	0.99 (0.945~1.036)	0.941 (0.896~0.989)
BMI								

normal	1.000	-	-	-	1.000	-	-	-
Underweight	-0.181	<0.001	0.738 (0.677~0.805)	0.835 (0.763~0.913)	0.103	0.011	1.071 (0.99~1.158)	1.109 (1.024~1.2)
Overweight	0.515	<0.001	1.726 (1.663~1.791)	1.674 (1.611~1.74)	0.477	<0.001	1.662 (1.6~1.725)	1.61 (1.551~1.672)
Obesity	0.902	<0.001	2.514 (2.368~2.669)	2.464 (2.318~2.62)	0.890	<0.001	2.499 (2.353~2.653)	2.434 (2.291~2.585)
hypertension								
No	1.000	-	-	-	1.000	-	-	-
Yes	0.068	0.074	1.177 (1.098~1.262)	1.07 (0.994~1.152)	0.145	<0.001	1.295 (1.21~1.387)	1.156 (1.077~1.242)

Table 5 Addition and multiplication of overweight/obesity and smoking in PDM after stratification

Overweight and obesity	Smoking	PDM		OR(95%*CI*)	P_{mult}	P_{add}	RERI(95%CI)	AP(95%CI)	S(95%CI)
		No	Yes						
No	No	16784	12469	1.000	0.609	0.069	0.151 (-0.012~0.314)	0.065 (-0.007~0.138)	1.129 (-0.962~1.295)
No	yes	1935	1815	1.229(1.147~1.318)					
Yes	No	8372	12018	1.892(1.823~1.964)					
Yes	yes	1117	1906	2.262(2.091~2.448)					

Table 6 Addition and multiplication of overweight and obesity and smoking in T2DM after stratification

Overweight and obesity	Smoking	T2DM		OR(95%CI)	P_{mult}	P_{add}	RERI(95%CI)	AP(95%CI)	S(95%CI)
		no	yes						
No	No	16542	12582	1.000	0.757	0.008	0.196 (0.051~0.341)	0.091 (0.020~0.161)	1.203 (1.004~1.402)
No	Yes	1887	1823	1.213(1.133~1.299)					
Yes	No	8249	11494	1.784(1.720~1.85)					
Yes	Yes	1098	1877	2.200(2.036~2.377)					

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