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Sex- and Age-Specific Body Composition Indices as Predictors of New-Onset Type 2 Diabetes Mellitus in Koreans: A Nationwide Cohort Study

Short running title: Body composition index and T2DM risk in Korean

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Strengths and limitation of this study

- The large-scale study using NHIS database representing almost the entire Korean population with 10-year longitudinal follow-up result.
- Sex and age-groups stratified risk of new onset type 2 diabetes mellitus was estimated, which previous studies did not conduct.
- Due to the lack of laboratory data such as glycated hemoglobin or oral glucose tolerance test results, the severity of diseases could not be evaluated.
- Because only data of Koreans were included, external validation was not conducted with other ethnicities.

Abstract

Objectives: Hormonal and age-related differences in body composition require tailored approaches for predicting new-onset type 2 diabetes (NODM). Previous studies lacked in-depth stratified analyses. We investigate sex- and age-specific body composition indices associated with NODM.

Design and setting: Retrospective, nationwide, population-based cohort study.

Participants: We analyzed 4,058,891 adults who underwent a health examination in year 2009 and 10-year follow-up data of from the National Health Insurance Service (NHIS).

Outcome measure: NODM risk stratified by sex and age-groups in 20-year intervals according to quartiles or per 1standard-deviation (SD) increase in BMI, WC, WHtR, VAI, ABSI, and WWI

Results: Among the total subjects, 625,715 (15.4%) developed NODM during median 10-year follow-up. The fourth quartile of WHtR showed the highest hazard ratio (HR) for NODM compared to the first quartile among various indices across the entire population (HR 2.54, 95% CI 2.52–2.57). In men, WHtR consistently exhibited the strongest association with NODM across all age-groups in analysis based on 1-SD increase; ages 20–39 (HR 1.54, 95% CI 1.53–1.55), ages 40–59 (HR 1.39, 95% CI 1.38–1.39), ages 60–79 (HR 1.23, 95% CI 1.22–1.24). In women, different indices exhibited the closest association with NODM; BMI for ages 20–39 (HR 1.48, 95%CI 1.47–1.49), WHtR for ages 40–59 (HR 1.46, 95% CI 1.45–1.47), and WC for ages 60–79 (HR 1.23, 95%CI 1.22–1.24).

Conclusion: WHtR was the strongest predictor of NODM in men across all ages, while in women, the relevant indices varied by age-groups. These findings highlight the need for sex- and age-specific body composition assessments in predicting NODM risk.

Keywords: Type 2 diabetes mellitus; anthropometric index; body composition; body mass

index; waist circumference

1. Introduction

The number of patients diagnosed with type 2 diabetes mellitus (T2DM) has been rapidly growing. In 2021, 540 million patients were diagnosed with T2DM worldwide, which is five-fold the number of patients with DM in 1980 [1]. Similarly, in a T2DM epidemiologic study in Korea, 16.7% of adults ≥ 30 years had T2DM in 2020 whereas the prevalence of T2DM in 2018 was 13.8% [2]. Because DM is associated with cerebro-cardiovascular complications and mortality, discovering a screening tool for T2DM is important for early diagnosis. Body composition indices provide simple, rapid, and inexpensive ways to evaluate risks of metabolic disease by simply measuring anthropometric parameters.

Since its development in 1932, body mass index (BMI) has been a cornerstone for measuring obesity [3]. However, with the discovery of different metabolic risks associated with visceral and subcutaneous fat [4], alternatives like waist circumference (WC), waist-hip ratio (WHR), and waist-height ratio (WHtR) emerged, highlighting central obesity more effectively [5]. Later, more complex indices such as a body shape index (ABSI) and visceral adiposity index (VAI) were introduced, showing strong links to cardio-metabolic risk and insulin sensitivity [6 7]. Recognizing the metabolic risks of sarcopenia, researchers developed the weight-adjusted waist index (WWI) to reflect low muscle mass [8]. Unique in its negative association with muscle mass, WWI stands out as no other existing body composition parameter captures the reduction in muscle mass as effectively [9].

In previous studies, these body composition indices were investigated in terms of new onset T2DM (NODM) prediction [10]; however, tailored age- and sex-related risk stratification was not performed. However, increasing prevalence of sarcopenia exert significant impact on metabolic risk as people get aged. Not only that, but changes in body

composition also differ between the sexes. Menopause causes 15–20% of additional abdominal fat accumulation and decreasing testosterone in men induces muscle mass reduction [11]. Therefore, we hypothesized that different body composition indices would be associated with NODM between a young muscular population and sarcopenic older population, or between men and women. In the present study, body composition indices regarding prediction of NODM were compared in different age and sex groups using 10-year longitudinal national comprehensive cohort data.

Methods

Data source and study population

In the present study, claims data from the National Health Insurance Service (NHIS) database from January 1, 2004 to December 31, 2019 were used. Korea has a universal single-payer national health system and the NHIS maintains national records of all covered inpatient and outpatient visits, procedures, and prescriptions. The International Classification of Disease version 10 (ICD-10) codes were used to identify past medical history and new onset of disease. The study included men and women between 20 and 80 years of age who underwent a health examination between January 1, 2009 and December 31, 2009 and satisfied the following criteria: no history of DM (E10–14), liver disease (K70–77), pancreas disease (K85–87), pancreatectomy (E89.1), or cancer (C00–97) within 5 years or who used a glucocorticoid within 1 year from the date of health checkup at the time of data collection, all of which might affect onset of DM as a secondary cause. Participants with fasting blood glucose ≥ 126 mg/dL at the health examination in 2009, participants with missing and outlier values for height, weight, WC, triglyceride (TG), and high-density lipoprotein cholesterol

(HDL-C) for the calculation of anthropometric index, and subjects who were deceased at baseline, were excluded**.** Ultimately, a total of 4,058,891patients were included in the analysis. For the examination of body composition indices reflecting age and sex dependent DM risk stratification, we divided the study total population into three groups: young-adult (20-39 years), middle-aged (40-59 years), and elderly (60-79 years). Individuals in their 40s and 50s often experience change in body composition due to childbirth and the perimenopausal period, while those in their 60s and 70s typically face a loss of muscle mass and strength [12]. The detailed study flow is shown in **Supplementary Figure 1**. The Korea University Institutional Review Board approved this study (No. 2022GR0041) which was conducted in accordance with the Declaration of Helsinki of the World Medical Association. We were permitted to use the NHIS data by the NHIS review committee (NHIS-2022-1-704). The need for informed consent was waived because anonymous and de-identified information was used for analysis.

Definition of body composition index and variables

The characteristics of NHIS databases were presented in previous studies [13]. Among various body composition parameters, six body composition indices were selected for the present study: BMI, WC, WHtR, VAI, ABSI, and WWI, which have been widely studied in large cohorts. Because NHIS has no data on hip circumference, the effect of WHR could not be analyzed in this study. The body composition indices were calculated with the following equations: BMI as weight/height^{2} [3], WHtR as WC/height [4,5], ABSI as $1000 \times WC \times weight^{-2/3} \times height^{5/6}$ [14], VAI as $WC/[39.68 + (1.88 \times BMI)] \times TG/1.03 \times 1.31/HDL$ (for men) and $WC/[36.58 + (1.89 \times BMI)] \times TG/0.81 \times 1.52/HDL$ (for women) [7], and WWI as WC/√weight

[15]. Age, sex, residential area, and income percentile were obtained from the insurance eligibility database. Smoking status, alcohol consumption, regular exercise, height, weight, family history of diabetes, TG, and HDL-C were obtained from the health screening examination database. An area with a population > 0.3 million was classified as urban. Alcohol consumption was classified as none, moderate (1–14 cups per week for men, 1–7 cups per week for women), heavy (≥ 15 cups per week for men, ≥ 8 cups per week for women), or unknown. Regular exercise was defined as none, regular (vigorous activity for ≥ 3 days or moderate-intensity activity for ≥ 5 days), irregular (other activities including walking), or unknown.

Study outcomes

The study outcome was the incidence of NODM defined either by searching for ICD-10 codes E11–14, usage of oral hypoglycemic agent (OHA), or a fasting plasma glucose (FPG) level of ≥ 126 mg/dL [16]. The duration of follow-up was defined as the time interval between the health examination date and the date of the study outcome, death, or censoring or the end of the study period (December 31, 2019). We evaluated the relationship between six body composition indices—BMI, WC, WHtR, VAI, ABSI and WWI—and the onset of diabetes mellitus (NODM) over a 10-year period. These indices were compared based on their association with NODM across different 20-year age intervals and between sexes.

Statistical analysis

The baseline characteristics of the study population are presented as mean ± standard deviation (SD) for continuous variables and number (percentage) for categorical variables. The ANOVA and chi-square test were used to compare the characteristics between men and women with different age-groups and between subjects with and without T2DM. Incidence rate of NODM was calculated by dividing the number of subjects diagnosed with NODM with person-years. Cox proportional hazards regression was used to identify association between anthropometric indices and NODM. Calculated hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated based on the quartiles and 1-SD of each body composition index. To account for additional potential confounding factors at the baseline health examination, age, sex, smoking status, alcohol consumption, regular exercise, family history of diabetes, residential area, and income percentile were adjusted (Model 1~5). Additional adjustment with systolic blood pressure, diastolic blood pressure, TG and HDL-C was presented in supplementary material (Model 6). Not only does the VAI formula contain TG and HDL-C, but also main purpose of our study is to estimate NODM risk by measuring body composition without laboratory test. As a result, we presented result of model 1 through 5 in the main findings. *P*-value < 0.05 was considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Patient and public involvement

Since this study utilized publicly available datasets, there was no direct patient or public involvement in the planning, execution, or analysis steps. Nevertheless, we understand the value of integrating patients and public insights into research. We plan to disseminate our finding to patients and public as valuable information for the T2DM prevention.

Results

Baseline characteristics of study population and 10-year cumulative incidence of NODM

For the 10-year follow-up period, 625,715 subjects were diagnosed with NODM (15.4% of the total population). The mean age of the study population was 41.9 ± 12.2 years and 60.7 % of participants were men. The incidence rate of NODM for the 10-year period was 16.2% in men and 13.3% in women. When age was stratified by two decades, 10-year T2DM incidence in both men and women markedly increased almost 2-fold in the middle-aged group (40–59 years) compared with the young adult group (20–39 years) (men: 14.0% in 20–39 age group, 27.4% in 40–59 age group; women: 10.4% in 20–39 age group, 22.7% in 40–59 age group; **Figure 1**). In the elderly group, 32.9% of men and 30.7% of women progressed to T2DM during the 10-year follow-up period. The detailed baseline characteristics of men and women with age groups were presented in **Table 1.** In obesity classification based on BMI, percentage of obese men decreases in ages 60-79, while percentage of obese women increases in age 60-79. Comparison of baseline characteristics of patients with or without incidental NODM are shown in **Supplementary table 1**.

Association of the quartiles of body composition indices and NODM incidence across different 20-year age interval and between sexes

Of the various body composition indices, WHtR exhibited the highest HR for the NODM in the fourth quartile group compared with the first quartile in all models of Cox-regression.

NODM HR of WHtR in the fully adjusted model was 2.54 (95% CI 2.52–2.57) followed by WC, BMI, VAI, WWI, and ABSI with HRs of 2.54, 2.52, 2.31, 2.19, 1.78, and 1.18, respectively (**Table 2).** When we further adjusted for systolic blood pressure, diastolic blood pressure, triglycerides (TG), and high-density lipoprotein (HDL), which are directly influenced by anthropometric parameter, WHtR still showed the highest HR for NODM among all body composition indices **(Supplementary table 2**).

Subgroup analysis was performed to examine the best body composition indices associated with NODM in different sex and 20-year interval age groups. As shown in **Figure 2A**, in men, WHtR had the highest HR for NODM across all age groups compared with other indices. The impact of body composition indices on NODM was most significant in men aged 20-39, showing a gradual reduction in HR with aging. However, in women, the effect of body composition indices on NODM was greatest in middle-aged group (ages 40–59), with HR value numerically higher than those in both young adult women (ages 20–39) and elderly women (ages 60-79) (**Figure 2B)**. Similar to men, the WHtR had the highest HR for NODM in women, except in the elderly group.

Association of 1 SD increment of body composition indices with NODM across different 20-year age interval groups and sex groups

In the regression analysis based on quartiles of indices, HRs of NODM were markedly increased in the fourth quartile of indices compared with risk increment observed in the second and third quartiles. To avoid overestimating the association between NODM and the body composition indices, which might occur due to high correlations observed in the fourth quartile, we also evaluated the association between NODM and a 1 standard deviation (SD)

increase in each index. The relative risk of NODM with 1 SD increase of body composition indices in each sex and age group is shown in **Figure 3A and 3B**. In men, WHtR had the highest HR across all age groups with 54% increased risk in young adults, 39% in middle-aged, and 23% in the elderly per 1 SD increase, showing sequential decrease in HR values as age increased **(Figure 3A and supplementary table 3)**. Conversely, in women, differential indices showed the highest risk of NODM with 1 SD increase in each age group; BMI had the highest HR in young adults, WHtR in middle-aged subjects, and WC in the elderly. The association of indices related to waist circumference (WC) and waist-to-height ratio (WHtR) remained significant up to middle age but diminishes in older age groups. **(Figure 3B and supplementary table 3)**.

Discussion

The present research included a nationwide cohort database and found that a distinct body composition index adequately predicted the risk of 10-year NODM in different age and sex groups. The incidence of NODM increased 2-fold from the young adult group to the middle-aged group. WHtR was strongly associated with NODM in men across all age groups. In women, BMI in young adult (ages 20–30), WHtR in middle-aged (ages 40–50), and WC in elderly (ages 60–70) showed the strong association with NODM based on 1 SD increase of each index. In men, the influence of body composition indices on NODM was greatest in the young adult group, with a sequential decrease as age increased. In women, the significant effect of body composition indices was maintained in the middle-aged group but showed a decreased impact in the elderly group. Although predictive power of body composition index

for NODM was not generally high, we emphasize that consistent application of BMI for assessing metabolic risk in all age and sex groups should be avoided.

Since Bray et al. warned a crisis of diabetes incidence in 2014 [17], the prevalence of T2DM rapidly grew worldwide updating the number of individuals with T2DM every year. In addition to traditional risk factors for T2DM such as obesity, age, ethnicity, and familial history of DM, frequent exposure to highly processed food and sedentary lifestyle warrants periodic screening for T2DM regardless of age. In the Laiteerapong study group, immediate glycemic control after the onset of DM was shown important for reduction of vascular complications and mortality [18]. The legacy effect evidenced in this study emphasizes the significance of early detection and management of DM. BMI has been used as an easy and rapid method to screen DM risk and evaluate the degree of obesity. To compensate for the limitations of BMI in discriminating between visceral and subcutaneous fat, WC, WHtR, and ABSI were suggested [4-6]. Laboratory data such as TG and HDL-C were adopted in the VAI equation [7] and development of WWI was used to discriminate between muscle and fat mass [9].

In several studies, comparison of new indices to BMI for DM screening has been reported. In a Chinese study that included 8,121 subjects 35–60 years of age, WHtR was reported more effective than BMI or WC for T2DM prediction [19]. In the meta-analysis of 31 studies, WHtR was significantly associated with T2DM compared with BMI in both men and women [20]. In another meta-analysis including 22 prospective studies, WHtR and WC showed similar predictability for DM and were superior to BMI [21]. Furthermore, Maryam et al. reported WC predicted T2DM development better than BMI, ABSI, WHtR, and WHR in their prospective study with 9,354 subjects [22]. In a study that included 3,461 Chinese participants, VAI was reported an effective index for DM prediction compared with WC, WHtR, and BMI [23]. Differences in study results might be due to the heterogeneity of the

study populations and characteristics. Unlike previous studies, risk stratification was performed in the present study with subjects of different age and sex because they may have different metabolic risks and body composition.

Based on the study results, in women, age had a significant effect on body composition index that is most relevant to incidental DM. Women experience significant changes in hormones and body composition during pregnancy, childbirth, and menopause. Cho et al. showed weight gain in women during perinatal period mostly resulted from visceral fat deposition [24], and in other studies, the number of parity was positively associated with abdominal obesity [25]. Furthermore, in previous research, fat mass volume doubled, and lean mass decreased at the start of menopause with reduction in estrogen level [25]. In several studies, body fat distribution was shown to change from the extremities to the trunk during the perimenopausal period [26]. These undesirable body composition changes are strongly associated with cardiometabolic disease risks, increasing incidence of DM, dyslipidemia, and cardiovascular disease (CVD) in postmenopausal women [27]. Therefore, the significant increase of DM incidence in women in the 40–59 group compared with the 20–39 group in the present study was likely because women undergo a decrease in estrogen in their mid-to-late 40's and 50's. Regarding the body composition index associated with DM, we demonstrated that every 1SD increase in BMI exhibited the strongest HR for NODM in the young women, however in the middle-aged women, that of WHtR showed the highest HR for NODM. This result may be due to visceral fat accumulation and undesirable body compositional changes after women experience pregnancy and delivery through their 40's and menopause in their 50's.

However, in men, the WHtR had the closest relationship with NODM across all age groups. In numerous literatures, WHtR was shown superior to BMI for DM prediction [21 23].

The reason why WHtR is better than BMI for DM prediction is due to the inclusion of visceral obesity in the WHtR index. Visceral adiposity induces insulin resistance, dysregulation of adipokines, and malfunction of adipocytes, resulting in NODM [28]. However, the reason WHtR is better than WC for NODM prediction remains unknown although several theories have been suggested. A plausible explanation is short stature, which is largely due to genetic factors, might affect visceral obesity, insulin resistance, and vulnerability to metabolic diseases [29]. In addition, because WHtR adjusts for the effect of height on WC, it reflects a different body fat distribution based on individual height [11].

Notably, in the young adult group, BMI of women and WHtR of men had the highest HRs for NODM with 1SD increase, indicating body composition associated with NODM differs between sexes. Women store excess fat first in a metabolically healthy fat region such as subcutaneous fat and lower extremities and then in visceral adipose tissue (VAT), whereas men predominantly accumulate fat more rapidly as VAT [30]. For women, the importance of VAT starts to appear in the postpartum and perimenopausal period. The present study showed that WHtR was significantly associated with the risk of NODM, especially in young adult men with a sequential decrease with aging; however, in women, the clinically significant effect of WHtR for NODM was obvious around the perimenopausal period. Considering the emerging trend in early-onset DM leading higher incidence of microvascular and macrovascular complications, intervention that reverses or reduces abdominal obesity, especially in young adult men and perimenopausal women, is critical.

The present study had several limitations. Because claims data from NHIS were analyzed, subjects were included and excluded based on ICD-10 codes that clinicians reported to the insurance service. Although we tried to exclude subjects with secondary causes of DM (diseases or medication), undefined cases may have been included or

incorrectly eliminated. Furthermore, due to the lack of laboratory data such as glycated hemoglobin or oral glucose tolerance test results, the severity of diseases could not be evaluated. In addition, any causal relationship could not be evaluated due to the intrinsic restriction of observational studies. Additionally, although we performed receiver operating characteristics (ROC) analysis to compare predictive power of each body composition index, the onset of DM in elderly tend to be multifactorial beyond the effect of body composition, resulting in a decrease in the area under the curve with increasing age. This reduction in predictive power was insufficient to compare the superiority of the indices, so we did not proceed to pairwise comparison of indices. Finally, because only data of Koreans were included, age- and sex-stratified DM risk should be evaluated in different ethnicities. However, this is the first and most recent large-scale study in which significant body composition indices for NODM were compared using 10-year longitudinal follow-up NHIS database representing almost the entire Korean population. Subjects with probable secondary causes for DM were excluded and multiple variables adjusted that could affect the onset of DM to examine the effect of body composition indices on NODM incidence.

Conclusion

In conclusion, WHtR in men of all age groups, BMI, WHtR, and WC in young adults, middle-aged, and elderly women, respectively, had the strongest association with the 10-year incidence of NODM in Korean population. Applying an age- and sex-specific body composition index is important to appropriately screen for the risk of NODM. Because the incidence of NODM significantly increased in the middle-aged group in both men and women, active surveillance for NODM risk by measuring WC and height is necessary for effective prevention.

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Conflict of interest

The authors declare that they have no competing interests.

Data availability

Study protocol, raw data that support the findings are available from the corresponding author upon reasonable request.

Author contribution

Conceptualization and design: H.J.Y., M.J.P., M.K.

Data acquisition, analysis: M.K.

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Figure legends

Figure 1. 10-year incidence of T2DM stratified by 10-year age groups in (A) Men and (B) Women

Figure 2. HRs of T2DM across quartiles of body composition indices according to 20-year age group in men (A) and women (B)

HR, hazard ratio; T2DM, type 2 diabetes mellitus; BMI, body mass index; WC, waist circumference; WHtR, waist height ratio

Figure 3. HR of new onset T2DM in fully adjusted model according to 1SD increase of anthropometric indices stratified by 20-year age groups in men (A) and women (B)

HR, hazard ratio; T2DM, type 2 diabetes mellitus; SD, standard deviation; BMI, body mass index; WC, waist circumference; WHtR, waist height ratio; VAI, visceral adiposity index; WWI, weight adjusted waist index; ABSI, A body shape index

Table legends

Table 1. Baseline Characteristics of patients with or without incident T2DM

Table 2. Hazard ratios (HRs) and 95% Confidence interval (95%CI) of T2DM across quartiles of body composition indices in total population

BMI, body mass index; WC, waist circumference; WHtR, waist height ratio; VAI, visceral adiposity index; WWI, weight adjusted waist index; ABSI, A body shape index

Table 1. Baseline Characteristics of patients with or without incident T2DM

	Men (N=2,463,811)				Women (N=1,595,080)			
	Age 20-39	Age 40-59	Age 60-79	*p*-value	Age 20-39	Age 40-59	Age 60-79	*p*-value
No. participants	1258327	992621	212863		563530	826450	205100	
BMI, kg/m^2	23.9 ± 3.2	24.0 ± 2.8	23.4 ± 2.8	<0.001	21.4 ± 3.1	23.2 ± 2.9	24.0 ± 3.1	<0.001
Underweight	35006 (2.8)	18533 (1.9)	7902 (3.7)		72860 (12.9)	21004 (2.5)	5474 (2.7)	
Normal	488605 (38.8)	342039 (34.5)	85976 (40.4)		359414 (63.8)	403581 (48.8)	71525 (34.9)	
Overweight	315404 (25.1)	284633 (28.7)	58937 (27.7)		67955 (12.1)	201009 (24.3)	54453 (26.6)	
Obese	419312 (33.3)	347416 (35.0)	60048 (28.2)		63301 (11.2)	200856 (24.3)	73648 (35.9)	
Income percentile				<0.001				<0.001
Medical aid	1073 (0.1)	698 (0.1)	487 (0.2)		722 (0.1)	1796 (0.2)	738 (0.4)	
≤ 30th	234504 (18.6)	160323 (16.2)	64376 (30.2)		186337 (33.1)	264646 (32.0)	48687 (23.7)	
31st–70th	646329 (51.4)	342703 (34.5)	72448 (34.0)		289033 (51.3)	289447 (33.9)	65071 (31.7)	
> 70th	318804 (25.3)	468547 (47.2)	74038 (34.8)		84574 (15.0)	271104 (33.2)	88603 (43.2)	
Unknown	57617 (4.6)	20350 (2.1)	1514 (0.7)		2864 (0.5)	6657 (0.7)	2001 (1.0)	
Residency area				<0.001				<0.001
Urban	952413 (75.7)	770384 (77.6)	146653 (68.9)		446470 (79.2)	649886 (77.6)	131129 (63.9)	
Rural	305598 (24.3)	221942 (22.4)	66132 (31.1)		116906 (20.8)	185208 (22.4)	73891 (36.0)	
Unknown	316 (0)	295 (0)	78 (0)		154 (0)	356 (0)	80 (0)	
Family history of DM	95941 (7.6)	75935 (7.7)	5822 (2.7)	<0.001	49880 (8.9)	72913 (9.2)	8350 (4.1)	<0.001
Smoking status				<0.001				<0.001
Never smoker	364532 (29.0)	263588 (26.6)	82287 (38.7)		511139 (90.7)	785970 (95.1)	197053 (96.1)	
Ex-smoker	181767 (14.5)	261163 (26.3)	60755 (28.5)		19931 (3.5)	11606 (1.4)	1911 (0.9)	
Current	704877 (56.0)	462090 (46.6)	68553 (32.2)		28889 (5.1)	22682 (2.7)	4535 (2.2)	
Unknown	7151 (0.6)	5780 (0.6)	1268 (0.6)		3571 (0.6)	6792 (0.8)	1601 (0.8)	

Heavy drinking				<0.001				<0.001
None	314855 (25.0)	283718 (28.6)	94373 (44.3)		298791 (53.0)	60[illegible]534 (73.4)	181677 (88.6)	
Moderate	572886 (45.5)	402993 (40.6)	70875 (33.3)		172935 (30.7)	15[illegible]281 (18.3)	14497 (7.1)	
Heavy	342328 (27.2)	282280 928.4)	42639 920.0)		76051 (13.5)	[illegible]794 (5.9)	3793 (1.9)	
Unknown	28258 (2.3)	23630 (2.4)	4976 92.3)		15753 (2.8)	[illegible]841 (2.4)	5133 (2.5)	
Regular exercise				<0.001				<0.001
None	224755 (17.9)	204722 (20.6)	55883 (26.3)		117228 (20.8)	[illegible]703 (26.0)	67356 (32.8)	
Irregular	826539 (65.7)	584212 (58.9)	102190 (48.0)		390425 (69.3)	[illegible]541 (56.8)	101561 (49.5)	
Regular	195008 (15.5)	195416 (19.7)	53336 (25.1)		50809 (9.0)	[illegible]577 (16.5)	34821 (17.0)	
Unknown	12025 (1.0)	8271 (0.8)	1454 (0.7)		5068 (0.9)	[illegible]29 (0.7)	1362 (0.7)	
WC, cm	81.5 ± 7.9	83.1 ± 7.2	83.5 ± 7.7	<0.001	70.8 ± 7.5	[illegible]5.4 ± 7.5	80.2 ± 7.9	<0.001
WHtR	0.5 ± 0	0.5 ± 0	0.5 ± 0	<0.001	0.4 ± 0	[illegible]0.5 ± 0.1	0.5 ± 0.1	<0.001
ABSI	347884.1 ± 17515.9	357304.7 ± 18253.6	369448.7 ± 20420.1	<0.001	337529.8 ± 21711.5	[illegible]4381.8 ± [illegible]0926.5	363581.9 ± 24347.6	<0.001
WWI	9.7 ± 0.5	10 ± 0.5	10.5 ± 0.6	<0.001	9.5 ± 0.6	[illegible]0 ± 0.7	10.8 ± 0.8	<0.001
VAI	431320.6 ± 300187.2	471715.6 ± 311853.9	404461.7 ± 255281.4	<0.001	399669.1 ± 257236.4	[illegible]2165.7 ± [illegible]01931.2	630556 ± 343916.3	<0.001
SBP, mmHg	121.9 ± 12.2	124.2 ± 14.3	129.7 ± 16.3	<0.001	111.7 ± 11.3	[illegible]8.6 ± 14.8	128.3 ± 16.5	<0.001
DBP, mmHg	76.4 ± 8.9	78.6 ± 10.0	79.4 ± 10.3	<0.001	70.1 ± 8.4	[illegible]4.0 ± 10.1	77.9 ± 10.2	<0.001
AST, IU/L	25.4 ± 22.7	26.7 ± 23.2	26.8 ± 15.7	<0.001	19.2 ± 11.2	[illegible]2.2 ± 16.8	24.8 ± 14.7	<0.001
ALT, IU/L	28.9 ± 28.1	28.2 ± 23.6	23.7 ± 16.9	<0.001	15.2 ± 13.7	[illegible]9.3 ± 17.9	20.7 ± 16.8	<0.001
FBS, mg/dL	90.5 ± 11.1	94.7 ± 11.7	95.8 ± 11.9	<0.001	87.6 ± 9.9	[illegible]1.7 ± 10.5	94.2 ± 11.1	<0.001
eGFR	86.8 ± 57.1	81.3 ± 47.8	78.5 ± 34.4	<0.001	90.0 ± 50.0	[illegible]2.8 ± 27.3	75.8 ± 27.1	<0.001
T-chol, mg/dL	189 ± 34.9	199.7 ± 36.6	194.2 ± 37.3	<0.001	178.2 ± 31.3	[illegible]7.7 ± 36.4	209.9 ± 38.9	<0.001
TG, mg/dL	139.8 ± 96.6	154.9 ± 101.7	134.5 ± 82.9	<0.001	82.1 ± 47.4	[illegible]4.7 ± 62.3	132.9 ± 72.9	<0.001
LDL-C, mg/dL	122.0 ± 302.3	117.9 ± 72.2	115.6 ± 60.1	<0.001	125.8 ± 430.0	[illegible]9.8 ± 84.6	129.5 ± 64.5	<0.001
HDL-C, mg/dL	53.1 ± 11.9	52.3 ± 12.1	52.7 ± 12.6	<0.001	61.8 ± 12.9	[illegible]3.3 ± 12.8	54.8 ± 12.5	<0.001

Data were presented Mean ± SD or n (%)

T2DM, type 2 diabetes mellitus; No, number; BMI, body mass index; WC, waist circumference; WHtR, waist height ratio; ABSI, a body shape index; WWI, weight adjusted waist index; VAI, visceral adiposity index; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; FBG, fasting blood glucose; eGFR, estimated glomerular filtration rate; T-chol, total- cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol

Table 2. Hazard ratios (HRs) and 95% Confidence interval (95%CI) of NODM across quartiles of body composition indices in total population

	T2DM (n) (n=625715)	Person year	Incidence rate	Model 1	Model 2	Model 3	Model 4	Model 5
BMI								
Q1 (n=1,005,153)	91,517	9,827,735.2	9.3	1	1	1	1	1
Q2 (n=1,016,249)	128,239	9,778,783.8	13.1	1.41 (1.40-1.42)	1.21 (1.20-1.22)	1.22 (1.21-1.23)	1.22 (1.21-1.23)	1.22 (1.21-1.23)
Q3 (n=1,038,875)	171,369	9,788,956.5	17.5	1.88 (1.87-1.90)	1.52 (1.50-1.53)	1.53 (1.52-1.55)	1.53 (1.51-1.54)	1.54 (1.52-1.55)
Q4 (n=998,614)	234,590	9,031,690.8	26.0	2.80 (2.78-2.82)	2.30 (2.28-2.31)	2.31 (2.29-2.33)	2.29 (2.27-2.31)	2.31 (2.29-2.33)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
WC								
Q1 (n=965,392)	78,371	9,534,939.2	8.2	1	1	1	1	1
Q2 (n=1,100,752)	138,929	10,600,570.5	13.1	1.60 (1.58-1.61)	1.36 (1.35-1.37)	1.35 (1.34-1.37)	1.35 (1.34-1.36)	1.35 (1.34-1.36)
Q3 (n=1,034,301)	176,385	9,698,250.5	18.2	2.22 (2.20-2.24)	1.77 (1.75-1.79)	1.76 (1.74-1.77)	1.75 (1.73-1.76)	1.76 (1.74-1.78)
Q4 (n=958,446)	232,030	8,593,406.1	27.0	3.30 (3.27-3.32)	2.55 (2.53-2.57)	2.52 (2.50-2.55)	2.51 (2.48-2.53)	2.52 (2.50-2.54)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
WHtR								
Q1 (n=1,014,803)	73,264	10,069,987.3	7.3	1	1	1	1	1
Q2 (n=1,015,850)	117,355	9,843,068.3	11.9	1.64 (1.63-1.66)	1.35 (1.34-1.37)	1.35 (1.34-1.36)	1.34 (1.33-1.35)	1.35 (1.33-1.36)
Q3 (n=1,011,915)	171,833	9,499,797.5	18.1	2.49 (2.47-2.51)	1.80 (1.79-1.82)	1.79 (1.78-1.81)	1.78 (1.76-1.80)	1.79 (1.77-1.81)
Q4 (n=1,016,323)	263,263	9,014,313.2	29.2	4.03 (4.00-4.06)	2.58 (2.55-2.60)	2.56 (2.54-2.58)	2.54 (2.52-2.56)	2.54 (2.52-2.57)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
VAI								
Q1 (n=1,014,722)	100,176	9,894,725.8	10.1	1	1	1	1	1
Q2 (n=1,014,723)	125,088	9,780,992.2	12.8	1.26 (1.25-1.27)	1.23 (1.22-1.24)	1.22 (1.21-1.23)	1.22 (1.21-1.23)	1.22 (1.21-1.23)
Q3 (n=1,014,723)	163,206	9,584,646.6	17.0	1.68 (1.67-1.70)	1.56 (1.55-1.57)	1.53 (1.52-1.54)	1.53 (1.51-1.54)	1.53 (1.52-1.54)
Q4 (n=1,014,723)	237,245	9,166,801.7	25.9	2.56 (2.54-2.58)	2.27 (2.25-2.28)	2.20 (2.18-2.21)	2.18 (2.17-2.20)	2.19 (2.17-2.21)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
ABSI								
Q1 (n=1,014,710)	110,242	9,903,776.6	11.1	1	1	1	1	1
Q2 (n=1,014,752)	138,228	9,741,236.9	14.2	1.28 (1.27-1.29)	1.09 (1.08-1.10)	1.08 (1.07-1.09)	1.08 (1.07-1.09)	1.09 (1.08-1.09)
Q3 (n=1,014,964)	166,745	9,559,615.0	17.4	1.57 (1.56-1.58)	1.16 (1.15-1.17)	1.15 (1.14-1.16)	1.15 (1.14-1.16)	1.16 (1.15-1.17)

Q4 (n=1,014,465)	210,500	9,222,537.8	22.8	2.06 (2.04-2.07)	1.20 (1.19-1.21)	1.18 (1.17-1.19)	1.19 (1.18-1.20)	1.18 (1.17-1.19)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
WWI								
Q1 (n=1,011,717)	86,064	9,994,386.9	8.6	1	1	1	1	1
Q2 (n=1,021,449)	126,085	9,868,208.8	12.8	1.49 (1.47-1.50)	1.25 (1.24-1.26)	1.25 (1.23-1.26)	1.24 (1.23-1.25)	1.25 (1.23-1.26)
Q3 (n=1,011,449)	170,662	9,503,139.9	18.0	2.09 (2.07-2.11)	1.51 (1.50-1.52)	1.50 (1.49-1.51)	1.49 (1.48-1.51)	1.50 (1.49-1.51)
Q4 (n=1,014,276)	242,904	9,061,430.7	26.8	3.12 (3.10-3.15)	1.81 (1.79-1.82)	1.79 (1.77-1.80)	1.78 (1.77-1.80)	1.78 (1.76-1.79)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

Model 1: Unadjusted
Model 2: Adjusted for age, sex
Model 3: Adjusted for age, sex, smoking habit, alcohol drinking, physical activity
Model 4: Adjusted for age, sex, smoking habit, alcohol drinking, physical activity, family history of DM
Model 5: Adjusted for age, sex, smoking habit, alcohol drinking, physical activity, family history of DM, income percentile, residence area

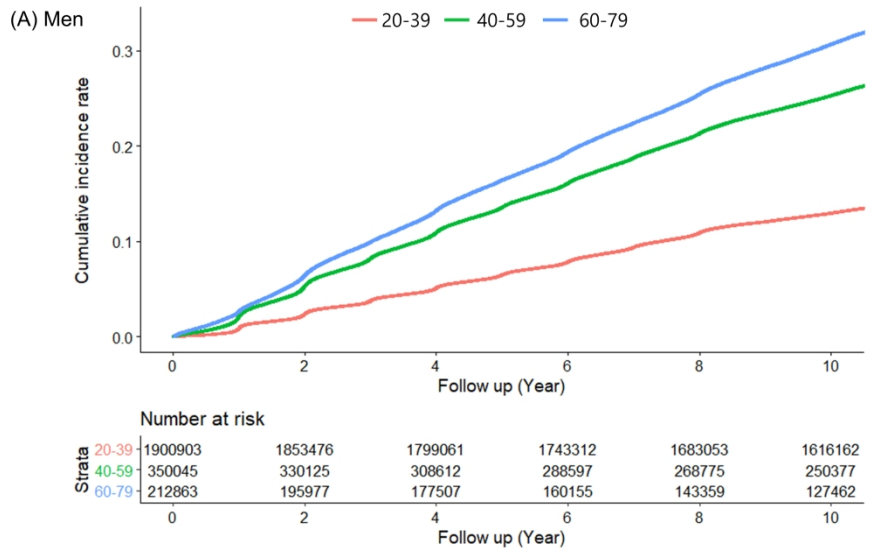

Figure 1-A. 10-year incidence of T2DM stratified by 10-year age groups in men

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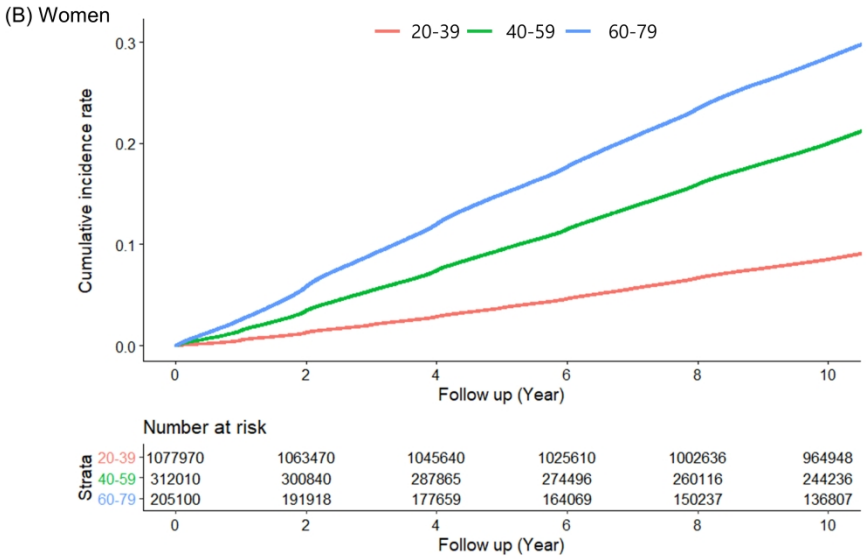

Figure 1-B. 10-year incidence of T2DM stratified by 10-year age groups in women

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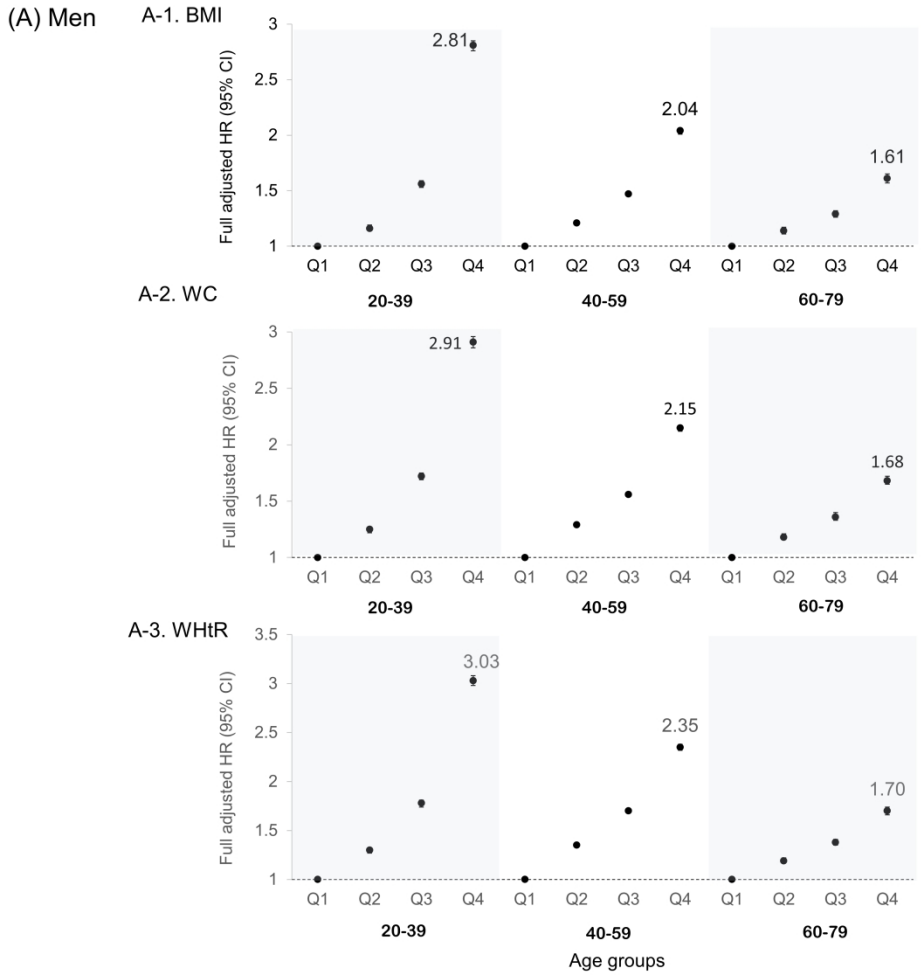

Figure 2-A. HRs of T2DM across quartiles of body composition indices according to 20-year age group in men

338x330mm (300 x 300 DPI)

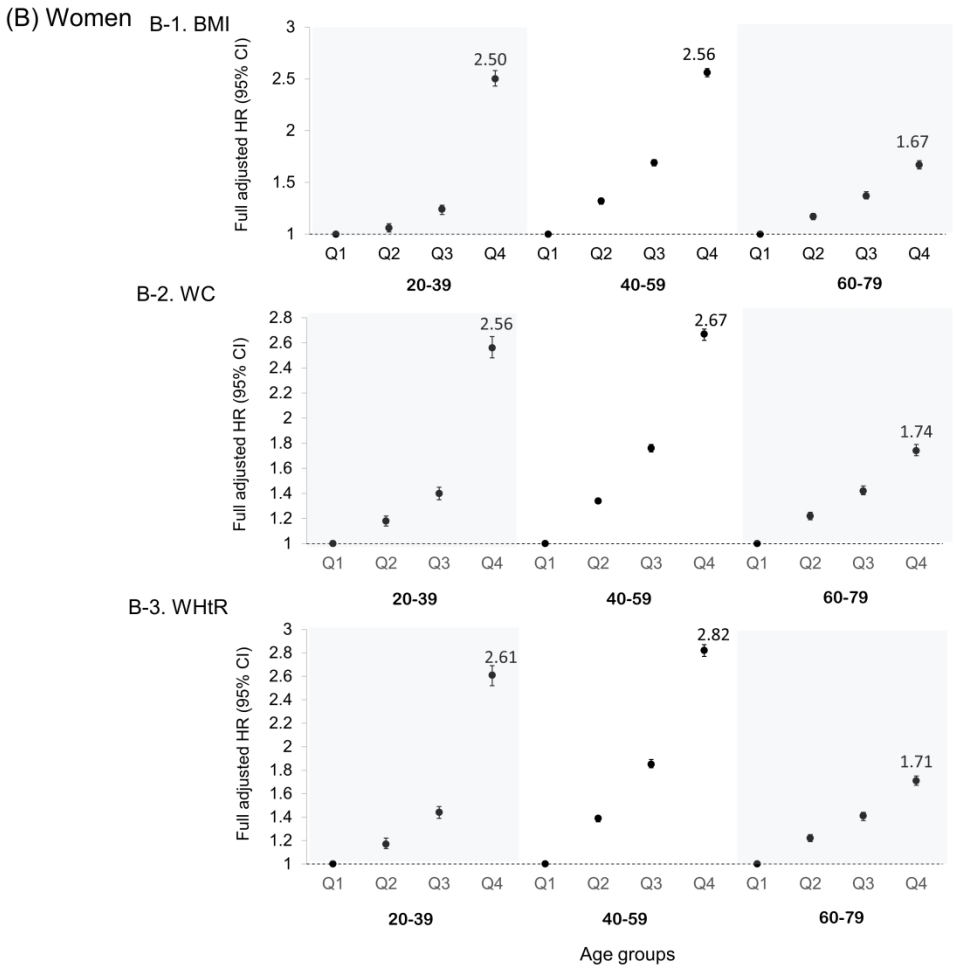

Figure 2-B. HRs of T2DM across quartiles of body composition indices according to 20-year age group in women

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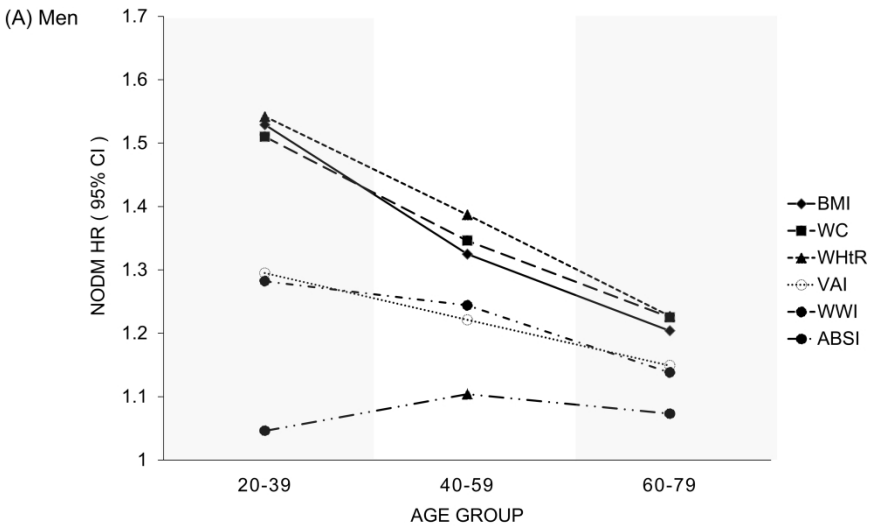


Figure 3-A. HR of new onset T2DM in fully adjusted model according to 1SD increase of anthropometric indices stratified by 20-year age groups in men

338x190mm (300 x 300 DPI)

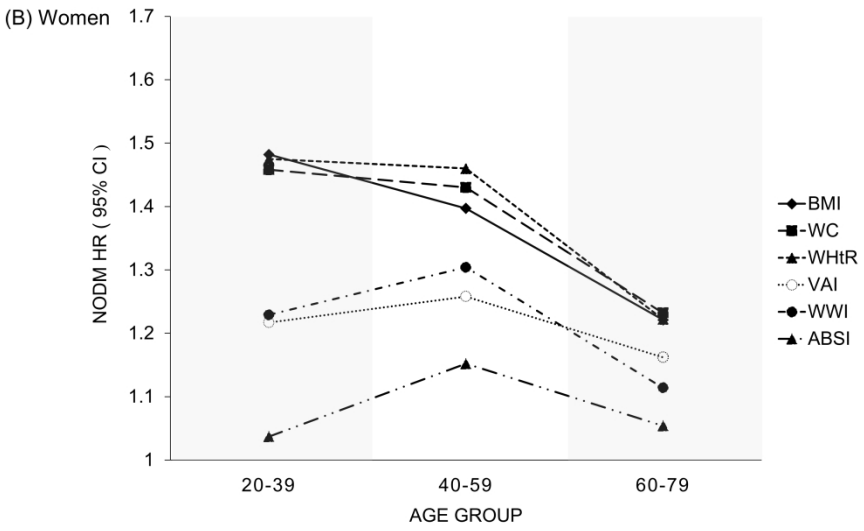
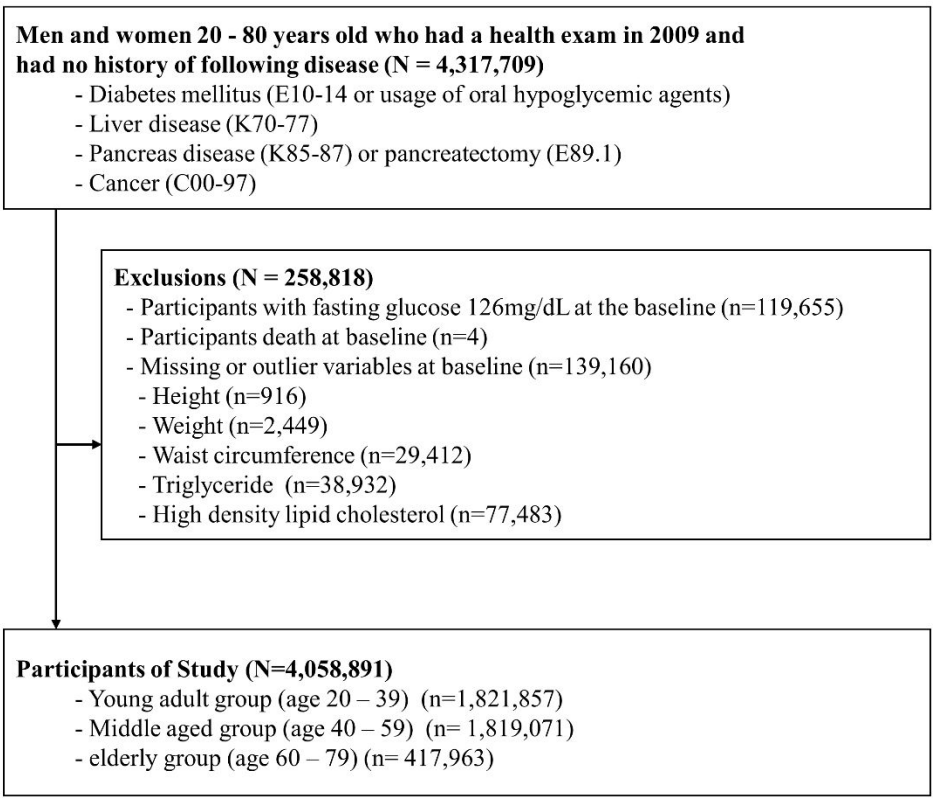


Figure 3-B. HR of new onset T2DM in fully adjusted model according to 1SD increase of anthropometric indices stratified by 20-year age groups in women

338x190mm (300 x 300 DPI)

Supplementary Figure 1. Flow diagram for selection of study population



Supplementary table 1. Baseline Characteristics of patients with or without incident NODM

	Overall (N=4,058,891)		
	Non-Diabetes	New onset Diabetes	*P*-value
No. participants	3,433,176	625,715	
Age, years	40.9 ± 12.1	47.9 ± 12.5	<0.001
20-29	707,113 (20.6)	47,752 (7.6)	
30-39	951,882 (27.7)	115,110 (18.4)	
40-49	972,192 (28.3)	184,824 (29.5)	
50-59	507,212 (14.8)	154,843 (24.7)	
60-69	212,964 (6.2)	88,690 (14.2)	
70-79	81,813 (2.4)	34,496 (5.5)	
Sex (n, %)			<0.001
Men	2,058,003 (59.9)	405,808 (64.9)	
Women	1,375,173 (40.1)	219,907 (35.1)	
BMI, kg/m^2	23.2 ± 3.1	24.6 ± 3.3	<0.001
Underweight	147,883 (4.3)	12,896 (2.1)	
Normal	1,559,794 (45.4)	191,346 (30.6)	
Overweight	826,187 (24.1)	156,204 (25.0)	
Obese	899,312 (26.2)	265,269 (42.4)	
Income percentile			<0.001
Medical aid	4,363 (0.1)	951 (0.2)	
≤ 30th	808,739 (23.6)	150,134 (24.0)	
31st–70th	1,444,830 (42.1)	251,201 (40.1)	
> 70th	1,096,557 (31.9)	212,113 (33.9)	
Unknown	78,687 (2.3)	11,316 (1.8)	
Residency area			<0.001
Urban	2,627,635 (76.5)	460,300 (73.6)	
Rural	804,433 (23.4)	165,244 (26.4)	
Unknown	1,108 (0)	171 (0)	
Family history of DM	251,318 (7.3)	60,523 (9.7)	<0.001
Smoking status			<0.001
Never smoker	1,894,045 (55.2)	310,524 (49.6)	
Ex-smoker	443,578 (12.9)	93,555 (15.0)	
Current	1,073,833 (31.3)	217,793 (34.8)	
Unknown	21,720 (0.6)	3,843 (0.6)	
Heavy drinking			<0.001
None	1,500,879 (43.7)	279,069 (44.6)	
Moderate	1,193,151 (34.8)	192,316 (30.7)	
Heavy	656,085 (19.1)	139,800 (22.3)	

Unknown	83,061 (2.4)	14,530 (2.3)	
Regular exercise			<0.001
None	735,567 (21.4)	149,080 (23.8)	
Irregular	211,6047 (61.6)	358,421 (57.3)	
Regular	552,695 (16.1)	113,272 (18.1)	
Unknown	28,867 (0.8)	4,942 (0.8)	
WC, cm	78.6 ± 8.6	82.7 ± 8.8	<0.001
WHtR	0.47 ± 0.05	0.50 ± 0.05	<0.001
ABSI	349,029.1 ± 21,153.0	355,076.7 ± 21,522.2	<0.001
WWI	9.9 ± 0.7	10.2 ± 0.7	<0.001
VAI	443,097.2 ± 284,260.8	565,230.4 ± 373,858.6	<0.001
SBP, mmHg	120.2 ± 14.1	126.0 ± 15.6	<0.001
DBP, mmHg	75.3 ± 9.7	78.7 ± 10.5	<0.001
AST, IU/L	23.8 ± 18.9	27.0 ± 24.8	<0.001
ALT, IU/L	23.3 ± 22.3	29.1 ± 26.1	<0.001
FBS, mg/dL	90.8 ± 10.7	97.6 ± 12.8	<0.001
eGFR	84.3 ± 47.9	81.7 ± 39.6	<0.001
T-chol, mg/dL	191.6 ± 35.8	202.0 ± 38.2	<0.001
TG, mg/dL	122.4 ± 83.1	157.0 ± 107.4	<0.001
LDL-C, mg/dL	121.2 ± 253.3	121.0 ± 136.2	<0.001
HDL-C, mg/dL	55.7 ± 12.8	53.1 ± 12.5	<0.001

T2DM, type 2 diabetes mellitus; No, number; BMI, body mass index; WC, waist circumference; WHtR, waist height ratio; ABSI, a body shape index; WWI, weight adjusted waist index; VAI, visceral adiposity index; TyG, triglyceride and glucose index; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; FBG, fasting blood glucose; eGFR, estimated glomerular filtration rate; T-chol, total- cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol
Data were presented Mean ± SD or n (%)

Supplementary table 2. Adjusted hazard ratios (HRs) and 95% Confidence interval (95%CI) of NODM across quartiles of body composition indices in total population

	BMI	WC	WHtR	VAI	ABSI	WWI
Q1	1	1	1	1	1	1
Q2	1.14 (1.13-1.15)	1.25 (1.24-1.26)	1.25 (1.23-1.26)	1.18 (1.17-1.19)	1.18 (1.17-1.19)	1.05 (1.04-1.06)
Q3	1.35 (1.34-1.36)	1.51 (1.50-1.53)	1.55 (1.53-1.56)	1.42 (1.40-1.43)	1.42 (1.40-1.43)	1.10 (1.09-1.11)
Q4	1.86 (1.84-1.87)	1.99 (1.97-2.01)	2.03 (2.01-2.05)	1.83 (1.81-1.85)	1.83 (1.81-1.85)	1.13 (1.12-1.14)
P for linear trend	<0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

Adjusted for age, sex, smoking habit, alcohol drinking, physical activity, family history of DM, income percentile, residence area, SBP, DBP, TG, HDL

Supplementary table 3. HRs (95% CI) of NODM based on 1SD increase of body composition indices according to age and sex groups

	Men		Women	
	Crude HR (95% CI)	Adjusted* HR (95% CI)	Crude HR (95% CI)	Adjusted* HR (95% CI)
20-39				
BMI	1.547 (1.540 - 1.554)	1.529 (1.522 - 1.536)	**1.497 (1.486 - 1.508)**	**1.482 (1.471 - 1.493)**
WC	1.531 (1.524 - 1.538)	1.510 (1.502 - 1.517)	1.474 (1.462 - 1.487)	1.458 (1.446 - 1.470)
WHtR	**1.560 (1.553 - 1.568)**	**1.542 (1.534 - 1.549)**	1.491 (1.479 - 1.504)	1.475 (1.463 - 1.487)
VAI	1.316 (1.312 - 1.320)	1.295 (1.290 - 1.299)	1.220 (1.214 - 1.226)	1.217 (1.211 - 1.223)
WWI	1.286 (1.280 - 1.293)	1.282 (1.275 - 1.288)	1.238 (1.226 - 1.250)	1.229 (1.217 - 1.241)
ABSI	1.053 (1.047 - 1.059)	1.046 (1.041 - 1.052)	1.039 (1.027 - 1.050)	1.037 (1.026 - 1.049)
40-59				
BMI	1.318 (1.313 - 1.324)	1.325 (1.319 - 1.330)	1.407 (1.400 - 1.413)	1.397 (1.391 - 1.403)
WC	1.346 (1.341 - 1.352)	1.346 (1.340 - 1.351)	1.441 (1.434 - 1.448)	1.430 (1.423 - 1.437)
WHtR	**1.392 (1.386 - 1.397)**	**1.387 (1.381 - 1.392)**	**1.470 (1.462 - 1.477)**	**1.460 (1.452 - 1.467)**
VAI	1.237 (1.233 - 1.240)	1.221 (1.218 - 1.225)	1.264 (1.260 - 1.268)	1.258 (1.254 - 1.262)
WWI	1.255 (1.249 - 1.260)	1.244 (1.239 - 1.249)	1.312 (1.305 - 1.319)	1.304 (1.297 - 1.311)
ABSI	1.115 (1.110 - 1.120)	1.104 (1.099 - 1.109)	1.156 (1.150 - 1.163)	1.152 (1.146 - 1.158)
60-79				
BMI	1.192 (1.183 - 1.201)	1.204 (1.195 - 1.214)	1.219 (1.210 - 1.228)	1.221 (1.211 - 1.230)
WC	1.218 (1.208 - 1.227)	1.225 (1.215 - 1.234)	**1.232 (1.222 - 1.241)**	**1.232 (1.222 - 1.242)**
WHtR	**1.221 (1.211 - 1.230)**	**1.227 (1.218 - 1.237)**	1.221 (1.211 - 1.230)	1.222 (1.212 - 1.231)
VAI	1.153 (1.146 - 1.160)	1.149 (1.142 - 1.156)	1.163 (1.155 - 1.170)	1.162 (1.155 - 1.170)
WWI	1.138 (1.130 - 1.147)	1.138 (1.129 - 1.147)	1.114 (1.105 - 1.123)	1.114 (1.105 - 1.123)
ABSI	1.077 (1.068 - 1.085)	1.073 (1.065 - 1.082)	1.056 (1.047 - 1.064)	1.054 (1.045 - 1.062)

Adjusted for smoking, alcohol, regular exercise, family history of Diabetes, income, area

HR, hazard ratio; CI, confidence interval; SD, standard deviation; T2DM, type 2 diabetes mellitus; BMI, body mass index; WC, waist circumference; WHtR, waist height ratio; VAI, visceral adiposity index; WWI, weight adjusted waist index; ABSI, A body shape index; DM, diabetes mellitus

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Sex- and Age-Specific Body Composition Indices as Predictors of New-Onset Type 2 Diabetes Mellitus in Koreans: A Nationwide Cohort Study

Short running title: Body composition index and T2DM risk in Korean

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Abstract

Objectives: Hormonal and age-related differences in body composition require tailored approaches for predicting new-onset type 2 diabetes (NODM). Previous studies lacked in-depth stratified analyses. We investigate sex- and age-specific body composition indices associated with NODM.

Design and setting: Retrospective, nationwide, population-based cohort study.

Participants: We analyzed 4,058,891 adults who underwent a health examination in year 2009 and 10-year follow-up data of from the National Health Insurance Service (NHIS).

Outcome measure: NODM risk stratified by sex and age-groups in 20-year intervals according to quartiles or per 1standard-deviation (SD) increase in body mass index (BMI), waist circumference (WC), waist-height ratio (WHtR), visceral adiposity index (VAI), a body shape index (ABSI), and weight-adjusted waist index (WWI).

Results: Among the total subjects, 625,715 individuals (15.4%) developed NODM during median 10-year follow-up. The fourth quartile of WHtR showed the highest hazard ratio (HR) for NODM compared to the first quartile among various indices across the entire population (HR 2.54, 95% CI 2.52–2.57). In men, WHtR consistently exhibited the strongest association with NODM across all age-groups in analysis based on 1-SD increase; ages 20–39 (HR 1.54, 95% CI 1.53–1.55), ages 40–59 (HR 1.39, 95% CI 1.38–1.39), ages 60–79 (HR 1.23, 95% CI 1.22–1.24). In women, the most relevant body composition index for NODM varied by age group; BMI for ages 20–39 (HR 1.48, 95%CI 1.47–1.49), WHtR for ages 40–59 (HR 1.46, 95% CI 1.45–1.47), and WC for ages 60–79 (HR 1.23, 95%CI 1.22–1.24).

Conclusion: WHtR was the strongest predictor of NODM in men across all ages, while in women, the relevant indices varied by age-groups. These findings highlight the need for sex- and age-specific body composition assessments in predicting NODM risk.

Keywords: Type 2 diabetes mellitus; anthropometric index; body composition; body mass index; waist circumference

Strengths and limitation of this study

- The large-scale study using NHIS database represents almost the entire Korean population with 10-year longitudinal follow-up results.
- Sex and age-groups stratified risk of new onset type 2 diabetes mellitus was estimated.
- Due to the lack of laboratory data such as glycated hemoglobin or oral glucose tolerance test results, the severity of diseases could not be evaluated.
- The study focused on the impact of baseline body composition index on long-term outcomes but did not account for changes in body composition during the follow-up period.

1. Introduction

The number of patients diagnosed with type 2 diabetes mellitus (T2DM) has been rapidly growing. In 2021, 540 million patients were diagnosed with T2DM worldwide, which is five-fold the number of diabetes cases in 1980 [1]. Similarly, a Korean epidemiologic study reported that in 2020, 16.7% of adults ≥ 30 years had T2DM, compared to 13.8% in 2018 [2]. Because DM is associated with cerebro-cardiovascular complications and mortality, discovering a screening tool for T2DM is important for early diagnosis. Body composition indices provide simple, rapid, and inexpensive ways to evaluate risks of metabolic disease by simply measuring anthropometric parameters.

Since its development in 1932, body mass index (BMI) has been a cornerstone for measuring obesity [3]. However, in 2007, research from the Framingham Heart study revealed stronger impact of visceral adipose tissue (VAT) on metabolic disease compared to subcutaneous adipose tissue (SAT)[4]. VAT release free fatty acids (FFAs), contributing to insulin resistance, whereas SAT serve as a buffer of FFAs[5]. With the recognition of VAT's significance, alternative body composition indices, such as waist circumference (WC), waist-hip ratio (WHR), and waist-height ratio (WHtR), have been developed to highlight the hazardous metabolic effect of VAT [6]. Later, more complex indices such as a body shape index (ABSI) and visceral adiposity index (VAI) were introduced, showing strong links to cardio-metabolic risk and insulin sensitivity [7 8]. The ABSI is statistically constructed metric designed to capture the metabolic impact of WC independently of height, weight, and BMI, using linear least-square regression [7]. The VAI is developed based on the fact that the harmful effect of visceral fat is related to high triglyceride (TG) and low high-density lipoprotein cholesterol (HDL-chol) level [9]. In lipid metabolism, increased VAT lead

hypertriglyceridemia, which promotes lipoprotein remodeling and accelerates HDL-chol catabolism[5]. By incorporating the detrimental effect of a high TG/HDL-chol ratio along with increased WC, VAI was formulated and has demonstrated its ability to predict metabolic disease in several studies. Furthermore, recognizing the metabolic risks of sarcopenia, researchers developed the weight-adjusted waist index (WWI) to reflect low muscle mass [10]. WWI was created by standardizing WC with body weight. In several studies, WWI has shown a positive association VAT and a negative association with appendicular skeletal muscle mass, making it a distinctive parameter for effectively capturing reduction in muscle mass, unlike other existing body composition[11].

In previous studies, some indices were investigated in terms of new onset T2DM (NODM) development [12]; however, a comprehensive comparison of all six indices, including tailored age- and sex-related risk stratification has not been conducted. However, increasing prevalence of sarcopenia exert significant impact on metabolic risk as people get aged. Not only that, but changes in body composition also differ between the sexes. Menopause causes 15–20% of additional abdominal fat accumulation and decreasing testosterone in men induces muscle mass reduction [13]. Therefore, we hypothesized that different body composition indices would be associated with NODM between a young muscular population and sarcopenic older population, or between men and women. In the present study, body composition indices regarding prediction of NODM were compared in different age and sex groups using 10-year longitudinal national comprehensive cohort data.

Methods

Data source and study population

In the present study, claims data from the National Health Insurance Service (NHIS) database from January 1, 2004 to December 31, 2019 were used. Korea has a universal single-payer national health system and the NHIS maintains national records of all covered inpatient and outpatient visits, procedures, and prescriptions. The International Classification of Disease version 10 (ICD-10) codes were used to identify past medical history and new onset of disease. The study included men and women between 20 and 80 years of age who underwent a health examination between January 1, 2009 and December 31, 2009 and satisfied the following criteria: no history of DM (E10–14), liver disease (K70–77), pancreas disease (K85–87), pancreatectomy (E89.1), or cancer (C00–97) within 5 years or who used a glucocorticoid within 1 year from the date of health checkup at the time of data collection, all of which might affect onset of DM as a secondary cause. Participants with fasting blood glucose ≥ 126 mg/dL at the health examination in 2009, participants with missing and outlier values for height, weight, WC, triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) for the calculation of anthropometric index, and subjects who were deceased at baseline, were excluded**.** Ultimately, a total of 4,058,891patients were included in the analysis. For the examination of body composition indices reflecting age and sex dependent DM risk stratification, we divided the study total population into three groups: young-adult (20-39 years), middle-aged (40-59 years), and elderly (60-79 years). Individuals in their 40s and 50s often experience change in body composition due to childbirth and the perimenopausal period, while those in their 60s and 70s typically face a loss of muscle mass and strength [14]. The detailed study flow is shown in **Supplementary Figure 1**. The Korea University Institutional Review Board approved this study (No. 2022GR0041) which was conducted in accordance with the Declaration of Helsinki of the World Medical Association. We were permitted to use the NHIS data by the NHIS review committee (NHIS-2022-1-704).

The need for informed consent was waived because anonymous and de-identified information was used for analysis.

Definition of body composition index and variables

The characteristics of NHIS databases were presented in previous studies [15]. Among various body composition parameters, six body composition indices were selected for the present study: BMI, WC, WHtR, VAI, ABSI, and WWI, which have been widely studied in large cohorts. Because NHIS has no data on hip circumference, the effect of WHR could not be analyzed in this study. The body composition indices were calculated with the following equations: BMI as weight/height^{2} [3], WHtR as WC/height [4 6], ABSI as $1000 \times WC \times weight^{-2/3} \times height^{5/6}$ [16], VAI as $WC/[39.68 + (1.88 \times BMI)] \times TG/1.03 \times 1.31/HDL$ (for men) and $WC/[36.58 + (1.89 \times BMI)] \times TG/0.81 \times 1.52/HDL$ (for women) [8], and WWI as WC/√weight [17]. Age, sex, residential area, and income percentile were obtained from the insurance eligibility database. Smoking status, alcohol consumption, regular exercise, height, weight, family history of diabetes, TG, and HDL-C were obtained from the health screening examination database. An area with a population > 0.3 million was classified as urban. Alcohol consumption was classified as none, moderate (1–14 cups per week for men, 1–7 cups per week for women), heavy (≥ 15 cups per week for men, ≥ 8 cups per week for women), or unknown. Regular exercise was defined as none, regular (vigorous activity for ≥ 3 days or moderate-intensity activity for ≥ 5 days), irregular (other activities including walking), or unknown.

Study outcomes

The study outcome was the incidence of NODM defined either by searching for ICD-10 codes E11–14, usage of oral hypoglycemic agent (OHA), or a fasting plasma glucose (FPG) level of ≥ 126 mg/dL [18]. The duration of follow-up was defined as the time interval between the health examination date and the date of the study outcome, death, or censoring or the end of the study period (December 31, 2019). We evaluated the relationship between six body composition indices—BMI, WC, WHtR, VAI, ABSI and WWI—and the onset of diabetes mellitus (NODM) over a 10-year period. These indices were compared based on their association with NODM across different 20-year age intervals and between sexes.

Statistical analysis

The baseline characteristics of the study population are presented as mean ± standard deviation (SD) for continuous variables and number (percentage) for categorical variables. The ANOVA and chi-square test were used to compare the characteristics between men and women with different age-groups and between subjects with and without T2DM. Incidence rate of NODM was calculated by dividing the number of subjects diagnosed with NODM with person-years. Cox proportional hazards regression was used to identify association between anthropometric indices and NODM. Calculated hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated based on the quartiles and 1-SD of each body composition index. To account for additional potential confounding factors at the baseline health examination, age, sex, smoking status, alcohol consumption, regular exercise, family history of diabetes, residential area, and income percentile were adjusted (Model 1~5). Additional adjustment with systolic blood pressure, diastolic blood pressure, TG and HDL-C

was presented in supplementary material (Model 6). Not only does the VAI formula contain TG and HDL-C, but also main purpose of our study is to estimate NODM risk by measuring body composition without laboratory test. As a result, we presented result of model 1 through 5 in the main findings. *P*-value < 0.05 was considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Patient and public involvement

Since this study utilized publicly available datasets, there was no direct patient or public involvement in the planning, execution, or analysis steps. Nevertheless, we understand the value of integrating patients and public insights into research. We plan to disseminate our finding to patients and public as valuable information for the T2DM prevention.

Results

Baseline characteristics of study population and 10-year cumulative incidence of NODM

For the 10-year follow-up period, 625,715 subjects were diagnosed with NODM (15.4% of the total population). The mean age of the study population was 41.9 ± 12.2 years and 60.7 % of participants were men. The incidence rate of NODM for the 10-year period was 16.2% in men and 13.3% in women. When age was stratified by two decades, 10-year T2DM incidence in both men and women markedly increased almost 2-fold in the middle-aged group (40–59 years) compared with the young adult group (20–39 years) (men: 14.0% in 20–39 age group, 27.4% in 40–59 age group; women: 10.4% in 20–39 age group, 22.7% in 40–

59 age group; **Figure 1**). In the elderly group, 32.9% of men and 30.7% of women progressed to T2DM during the 10-year follow-up period. The detailed baseline characteristics of men and women with age groups were presented in **Table 1.** In obesity classification based on BMI, percentage of obese men decreases in ages 60-79, while percentage of obese women increases in age 60-79. Comparison of baseline characteristics of patients with or without incidental NODM are shown in **Supplementary table 1**.

Association of the quartiles of body composition indices and NODM incidence across different 20-year age interval and between sexes

Of the various body composition indices, WHtR exhibited the highest HR for the NODM in the fourth quartile group compared with the first quartile in all models of Cox-regression. NODM HR of WHtR in the fully adjusted model was 2.54 (95% CI 2.52–2.57) followed by WC, BMI, VAI, WWI, and ABSI with HRs of 2.54, 2.52, 2.31, 2.19, 1.78, and 1.18, respectively (**Table 2).** When we further adjusted for systolic blood pressure, diastolic blood pressure, triglycerides (TG), and high-density lipoprotein (HDL), which are directly influenced by anthropometric parameter, WHtR still showed the highest HR for NODM among all body composition indices **(Supplementary table 2**).

Subgroup analysis was performed to examine the best body composition indices associated with NODM in different sex and 20-year interval age groups. As shown in **Figure 2A**, in men, WHtR had the highest HR for NODM across all age groups compared with other indices. The impact of body composition indices on NODM was most significant in men aged 20-39, showing a gradual reduction in HR with aging. However, in women, the effect of body composition indices on NODM was greatest in middle-aged group (ages 40–59), with

224 HR value numerically higher than those in both young adult women (ages 20–39) and elderly

Table 1. Baseline Characteristics of patients with or without incident T2DM

	Men (N=2,463,811)				Women (N=1,895,080)			
	Age 20-39	Age 40-59	Age 60-79	*P*	Age 20-39	Age 40-59	Age 60-79	*P*
N	1258327	992621	212863		563530	826450	205100	
BMI, kg/m^2	23.9 ± 3.2	24.0 ± 2.8	23.4 ± 2.8	<0.001	21.4 ± 3.1	23.[illegible].9	24.0 ± 3.1	<0.001
Underweight	35006 (2.8)	18533 (1.9)	7902 (3.7)		72860 (12.9)	210[illegible] (2.5)	5474 (2.7)	
Normal	488605 (38.8)	342039 (34.5)	85976 (40.4)		359414 (63.8)	403[illegible] (48.8)	71525 (34.9)	
Overweight	315404 (25.1)	284633 (28.7)	58937 (27.7)		67955 (12.1)	201[illegible] (24.3)	54453 (26.6)	
Obese	419312 (33.3)	347416 (35.0)	60048 (28.2)		63301 (11.2)	208[illegible] (24.3)	73648 (35.9)	
Income				<0.001				<0.001
Medical aid	1073 (0.1)	698 (0.1)	487 (0.2)		722 (0.1)	15[illegible] (0.2)	738 (0.4)	
≤ 30th	234504 (18.6)	160323 (16.2)	64376 (30.2)		186337 (33.1)	264[illegible] (32.0)	48687 (23.7)	
31st–70th	646329 (51.4)	342703 (34.5)	72448 (34.0)		289033 (51.3)	280[illegible] (33.9)	65071 (31.7)	
> 70th	318804 (25.3)	468547 (47.2)	74038 (34.8)		84574 (15.0)	274[illegible] (33.2)	88603 (43.2)	
Residency area				<0.001				<0.001
Urban	952413 (75.7)	770384 (77.6)	146653 (68.9)		446470 (79.2)	640[illegible] (77.6)	131129 (63.9)	
Rural	305598 (24.3)	221942 (22.4)	66132 (31.1)		116906 (20.8)	185[illegible] (22.4)	73891 (36.0)	
Family history of DM	95941 (7.6)	75935 (7.7)	5822 (2.7)	<0.001	49880 (8.9)	75[illegible] (9.2)	8350 (4.1)	<0.001
Smoking habit				<0.001				<0.001
Never	364532 (29.0)	263588 (26.6)	82287 (38.7)		511139 (90.7)	785[illegible] (95.1)	197053 (96.1)	
Ex-smoker	181767 (14.5)	261163 (26.3)	60755 (28.5)		19931 (3.5)	11[illegible] (1.4)	1911 (0.9)	
Current	704877 (56.0)	462090 (46.6)	68553 (32.2)		28889 (5.1)	22[illegible] (3.7)	4535 (2.2)	
Alcohol intake				<0.001				<0.001
None	314855 (25.0)	283718 (28.6)	94373 (44.3)		298791 (53.0)	606[illegible] (73.4)	181677 (88.6)	
Moderate	572886 (45.5)	402993 (40.6)	70875 (33.3)		172935 (30.7)	151[illegible] (18.3)	14497 (7.1)	
Heavy	342328 (27.2)	282280 928.4)	42639 920.0)		76051 (13.5)	48[illegible] (8.9)	3793 (1.9)	
Exercise				<0.001				<0.001
None	224755 (17.9)	204722 (20.6)	55883 (26.3)		117228 (20.8)	214703 (26.0)	67356 (32.8)	
Irregular	826539 (65.7)	584212 (58.9)	102190 (48.0)		390425 (69.3)	469541 (56.8)	101561 (49.5)	
Regular	195008 (15.5)	195416 (19.7)	53336 (25.1)		50809 (9.0)	136577 (16.5)	34821 (17.0)	
WC, cm	81.5 ± 7.9	83.1 ± 7.2	83.5 ± 7.7	<0.001	70.8 ± 7.5	75.4 ± [illegible].5	80.2 ± 7.9	<0.001

WHtR	0.5 ± 0	0.5 ± 0	0.5 ± 0	<0.001	0.4 ± 0	0.5 ± 0.1	0.5 ± 0.1	<0.001
ABSI	347884.1±17515.9	357304.7±18253.6	369448.7±20420.1	<0.001	337529.8±21711.5	34438[illegible]8±20926.5	363581.9±24347.6	<0.001
WWI	9.7 ± 0.5	10 ± 0.5	10.5 ± 0.6	<0.001	9.5 ± 0.6	1[illegible] ± 0.7	10.8 ± 0.8	<0.001
VAI	431320.6±300187.2	471715.6±311853.9	404461.7±255281.4	<0.001	399669.1±257236.4	5121657±3[illegible]1931.2	630556±343916.3	<0.001
SBP, mmHg	121.9 ± 12.2	124.2 ± 14.3	129.7 ± 16.3	<0.001	111.7 ± 11.3	118[illegible] ± 14.8	128.3 ± 16.5	<0.001
DBP, mmHg	76.4 ± 8.9	78.6 ± 10.0	79.4 ± 10.3	<0.001	70.1 ± 8.4	74.[illegible] ± 9.1	77.9 ± 10.2	<0.001
AST, IU/L	25.4 ± 22.7	26.7 ± 23.2	26.8 ± 15.7	<0.001	19.2 ± 11.2	22.[illegible] ± 14.8	24.8 ± 14.7	<0.001
ALT, IU/L	28.9 ± 28.1	28.2 ± 23.6	23.7 ± 16.9	<0.001	15.2 ± 13.7	19.[illegible] ± 15.9	20.7 ± 16.8	<0.001
FBS, mg/dL	90.5 ± 11.1	94.7 ± 11.7	95.8 ± 11.9	<0.001	87.6 ± 9.9	91.[illegible] ± 9.5	94.2 ± 11.1	<0.001
eGFR	86.8 ± 57.1	81.3 ± 47.8	78.5 ± 34.4	<0.001	90.0 ± 50.0	81.[illegible] ± 47.3	75.8 ± 27.1	<0.001
T-chol, mg/dL	189 ± 34.9	199.7 ± 36.6	194.2 ± 37.3	<0.001	178.2 ± 31.3	197.[illegible] ± 36.4	209.9 ± 38.9	<0.001
TG, mg/dL	139.8 ± 96.6	154.9 ± 101.7	134.5 ± 82.9	<0.001	82.1 ± 47.4	104.[illegible] ± 62.3	132.9 ± 72.9	<0.001
LDL-C,mg/dL	122.0 ± 302.3	117.9 ± 72.2	115.6 ± 60.1	<0.001	125.8 ± 430.0	119.[illegible] ± 64.6	129.5 ± 64.5	<0.001
HDL-C,mg/dL	53.1 ± 11.9	52.3 ± 12.1	52.7 ± 12.6	<0.001	61.8 ± 12.9	58.[illegible] ± 12.8	54.8 ± 12.5	<0.001

Data were presented Mean ± SD or n (%)

T2DM, type 2 diabetes mellitus; No, number; BMI, body mass index; WC, waist circumference; WHtR, waist height ratio; ABSI, a body shape index; WWI, weight adjusted waist index; VAI, visceral adiposity index; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; FBG, fasting blood glucose; eGFR, estimated glomerular filtration rate; T-chol, total- cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol

Table 2. Hazard ratios (HRs) and 95% Confidence interval (95%CI) of NODM across quartiles of body composition indices in total population

	T2DM (N = 625715)	Person year	Incidence rate	Model 1	Model 2	Model 3	Model 4	Model 5
BMI								
Q1 (n=1,005,153)	91,517	9,827,735.2	9.3	1	1	1	1	1
Q2 (n=1,016,249)	128,239	9,778,783.8	13.1	1.41 (1.40-1.42)	1.21 (1.20-1.22)	1.22 (1.21-1.23)	1.22 (1.21-1.23)	1.22 (1.21-1.23)
Q3 (n=1,038,875)	171,369	9,788,956.5	17.5	1.88 (1.87-1.90)	1.52 (1.50-1.53)	1.53 (1.52-1.55)	1.52 (1.51-1.54)	1.54 (1.52-1.55)
Q4 (n=998,614)	234,590	9,031,690.8	26.0	2.80 (2.78-2.82)	2.30 (2.28-2.31)	2.31 (2.29-2.33)	2.29 (2.27-2.31)	2.31 (2.29-2.33)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
WC								
Q1 (n=965,392)	78,371	9,534,939.2	8.2	1	1	1	1	1
Q2 (n=1,100,752)	138,929	10,600,570.5	13.1	1.60 (1.58-1.61)	1.36 (1.35-1.37)	1.35 (1.34-1.36)	1.35 (1.34-1.36)	1.35 (1.34-1.36)
Q3 (n=1,034,301)	176,385	9,698,250.5	18.2	2.22 (2.20-2.24)	1.77 (1.75-1.79)	1.76 (1.74-1.78)	1.75 (1.73-1.76)	1.76 (1.74-1.78)
Q4 (n=958,446)	232,030	8,593,406.1	27.0	3.30 (3.27-3.32)	2.55 (2.53-2.57)	2.52 (2.50-2.54)	2.51 (2.48-2.53)	2.52 (2.50-2.54)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
WHtR								
Q1 (n=1,014,803)	73,264	10,069,987.3	7.3	1	1	1	1	1
Q2 (n=1,015,850)	117,355	9,843,068.3	11.9	1.64 (1.63-1.66)	1.35 (1.34-1.37)	1.35 (1.34-1.36)	1.34 (1.33-1.35)	1.35 (1.33-1.36)
Q3 (n=1,011,915)	171,833	9,499,797.5	18.1	2.49 (2.47-2.51)	1.80 (1.79-1.82)	1.79 (1.78-1.81)	1.78 (1.76-1.80)	1.79 (1.77-1.81)
Q4 (n=1,016,323)	263,263	9,014,313.2	29.2	4.03 (4.00-4.06)	2.58 (2.55-2.60)	2.56 (2.54-2.58)	2.54 (2.52-2.56)	2.54 (2.52-2.57)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
VAI								
Q1 (n=1,014,722)	100,176	9,894,725.8	10.1	1	1	1	1	1
Q2 (n=1,014,723)	125,088	9,780,992.2	12.8	1.26 (1.25-1.27)	1.23 (1.22-1.24)	1.22 (1.21-1.23)	1.22 (1.21-1.23)	1.22 (1.21-1.23)
Q3 (n=1,014,723)	163,206	9,584,646.6	17.0	1.68 (1.67-1.70)	1.56 (1.55-1.57)	1.53 (1.52-1.54)	1.53 (1.51-1.54)	1.53 (1.52-1.54)
Q4 (n=1,014,723)	237,245	9,166,801.7	25.9	2.56 (2.54-2.58)	2.27 (2.25-2.28)	2.20 (2.18-2.21)	2.18 (2.17-2.20)	2.19 (2.17-2.21)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
ABSI								
Q1 (n=1,014,710)	110,242	9,903,776.6	11.1	1	1	1	1	1

Q2 (n=1,014,752)	138,228	9,741,236.9	14.2	1.28 (1.27-1.29)	1.09 (1.08-1.10)	1.08 (1.07-1.09)	1.08 (1.07-1.09)	1.09 (1.08-1.09)
Q3 (n=1,014,964)	166,745	9,559,615.0	17.4	1.57 (1.56-1.58)	1.16 (1.15-1.17)	1.15 (1.14-1.16)	1.15 (1.14-1.16)	1.16 (1.15-1.17)
Q4 (n=1,014,465)	210,500	9,222,537.8	22.8	2.06 (2.04-2.07)	1.20 (1.19-1.21)	1.18 (1.17-1.19)	1.19 (1.18-1.20)	1.18 (1.17-1.19)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
WWI								
Q1 (n=1,011,717)	86,064	9,994,386.9	8.6	1	1	1	1	1
Q2 (n=1,021,449)	126,085	9,868,208.8	12.8	1.49 (1.47-1.50)	1.25 (1.24-1.26)	1.25 (1.23-1.26)	1.24 (1.23-1.25)	1.25 (1.23-1.26)
Q3 (n=1,011,449)	170,662	9,503,139.9	18.0	2.09 (2.07-2.11)	1.51 (1.50-1.52)	1.50 (1.49-1.51)	1.50 (1.48-1.51)	1.50 (1.49-1.51)
Q4 (n=1,014,276)	242,904	9,061,430.7	26.8	3.12 (3.10-3.15)	1.81 (1.79-1.82)	1.79 (1.77-1.80)	1.79 (1.77-1.80)	1.78 (1.76-1.79)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

Model 1: Unadjusted
Model 2: Adjusted for age, sex
Model 3: Adjusted for age, sex, smoking habit, alcohol drinking, physical activity
Model 4: Adjusted for age, sex, smoking habit, alcohol drinking, physical activity, family history of DM
Model 5: Adjusted for age, sex, smoking habit, alcohol drinking, physical activity, family history of DM, income percentile, residence area

women (ages 60-79) (**Figure 2B)**. Similar to men, the WHtR had the highest HR for NODM in women, except in the elderly group.

Association of 1 SD increment of body composition indices with NODM across different 20-year age interval groups and sex groups

In the regression analysis based on quartiles of indices, HRs of NODM were markedly increased in the fourth quartile of indices compared with risk increment observed in the second and third quartiles. To avoid overestimating the association between NODM and the body composition indices, which might occur due to high correlations observed in the fourth quartile, we also evaluated the association between NODM and a 1 standard deviation (SD) increase in each index. The relative risk of NODM with 1 SD increase of body composition indices in each sex and age group is shown in **Figure 3A and 3B**. In men, WHtR had the highest HR across all age groups with 54% increased risk in young adults, 39% in middle-aged, and 23% in the elderly per 1 SD increase, showing sequential decrease in HR values as age increased **(Figure 3A and supplementary table 3)**. Conversely, in women, differential indices showed the highest risk of NODM with 1 SD increase in each age group; BMI had the highest HR in young adults, WHtR in middle-aged subjects, and WC in the elderly. The association of indices related to waist circumference (WC) and waist-to-height ratio (WHtR) remained significant up to middle age but diminishes in older age groups. **(Figure 3B and supplementary table 3)**.

Discussion

The present research included a nationwide cohort database and found that a distinct body composition index adequately predicted the risk of 10-year NODM in different age and sex groups. The incidence of NODM increased 2-fold from the young adult group to the middle-aged group. WHtR was strongly associated with NODM in men across all age groups. In women, BMI in young adult (ages 20–30), WHtR in middle-aged (ages 40–50), and WC in elderly (ages 60–70) showed the strong association with NODM based on 1 SD increase of each index. In men, the influence of body composition indices on NODM was greatest in the young adult group, with a sequential decrease as age increased. In women, the significant effect of body composition indices was maintained in the middle-aged group but showed a decreased impact in the elderly group. Although predictive power of body composition index for NODM was not generally high, we emphasize that consistent application of BMI for assessing metabolic risk in all age and sex groups should be avoided.

Since Bray et al. warned a crisis of diabetes incidence in 2014 [19], the prevalence of T2DM rapidly grew worldwide updating the number of individuals with T2DM every year. In addition to traditional risk factors for T2DM such as obesity, age, ethnicity, and familial history of DM, frequent exposure to highly processed food and sedentary lifestyle warrants periodic screening for T2DM regardless of age. In the Laiteerapong study group, immediate glycemic control after the onset of DM was shown important for reduction of vascular complications and mortality [20]. The legacy effect evidenced in this study emphasizes the significance of early detection and management of DM. BMI has been used as an easy and rapid method to screen DM risk and evaluate the degree of obesity. To compensate for the limitations of BMI in discriminating between visceral and subcutaneous fat, WC, WHtR, and ABSI were suggested [4 6 7]. Laboratory data such as TG and HDL-C were adopted in the VAI

equation [8] and development of WWI was used to discriminate between muscle and fat mass [11].

In several studies, comparison of new indices to BMI for DM screening has been reported. In a Chinese study that included 8,121 subjects 35–60 years of age, WHtR was reported more effective than BMI or WC for T2DM prediction [21]. In the meta-analysis of 31 studies, WHtR was significantly associated with T2DM compared with BMI in both men and women [22]. In another meta-analysis including 22 prospective studies, WHtR and WC showed similar predictability for DM and were superior to BMI [23]. Furthermore, Maryam et al. reported WC predicted T2DM development better than BMI, ABSI, WHtR, and WHR in their prospective study with 9,354 subjects [24]. In a study that included 3,461 Chinese participants, VAI was reported an effective index for DM prediction compared with WC, WHtR, and BMI [25]. Differences in study results might be due to the heterogeneity of the study populations and characteristics. Unlike previous studies, risk stratification was performed in the present study with subjects of different age and sex because they may have different metabolic risks and body composition.

Based on the study results, in women, age had a significant effect on body composition index that is most relevant to incidental DM. Women experience significant changes in hormones and body composition during pregnancy, childbirth, and menopause. Cho et al. showed weight gain in women during perinatal period mostly resulted from visceral fat deposition [26], and in other studies, the number of parity was positively associated with abdominal obesity [27]. Furthermore, in previous research, fat mass volume doubled, and lean mass decreased at the start of menopause with reduction in estrogen level [27]. In several studies, body fat distribution was shown to change from the extremities to the trunk during the perimenopausal period [28]. These undesirable body composition changes are strongly

associated with cardiometabolic disease risks, increasing incidence of DM, dyslipidemia, and cardiovascular disease (CVD) in postmenopausal women [29]. Therefore, the significant increase of DM incidence in women in the 40–59 group compared with the 20–39 group in the present study was likely because women undergo a decrease in estrogen in their mid-to-late 40's and 50's. Regarding the body composition index associated with DM, we demonstrated that every 1SD increase in BMI exhibited the strongest HR for NODM in the young women, however in the middle-aged women, that of WHtR showed the highest HR for NODM. This result may be due to visceral fat accumulation and undesirable body compositional changes after women experience pregnancy and delivery through their 40's and menopause in their 50's.

However, in men, the WHtR had the closest relationship with NODM across all age groups. In numerous literatures, WHtR was shown superior to BMI for DM prediction [23 25]. The reason why WHtR is better than BMI for DM prediction is due to the inclusion of visceral obesity in the WHtR index. Visceral adiposity induces insulin resistance, dysregulation of adipokines, and malfunction of adipocytes, resulting in NODM [30]. However, the reason WHtR is better than WC for NODM prediction remains unknown although several theories have been suggested. A plausible explanation is short stature, which is largely due to genetic factors, might affect visceral obesity, insulin resistance, and vulnerability to metabolic diseases [31]. In addition, because WHtR adjusts for the effect of height on WC, it reflects a different body fat distribution and muscle mass based on individual height [13].

Notably, in the young adult group, BMI of women and WHtR of men had the highest HRs for NODM with 1SD increase, indicating body composition associated with NODM differs between sexes. Women store excess fat first in a metabolically healthy fat region such as subcutaneous fat and lower extremities and then in visceral adipose tissue (VAT), whereas

men predominantly accumulate fat more rapidly as VAT [32]. For women, the importance of VAT starts to appear in the postpartum and perimenopausal period. The present study showed that WHtR was significantly associated with the risk of NODM, especially in young adult men with a sequential decrease with aging; however, in women, the clinically significant effect of WHtR for NODM was obvious around the perimenopausal period. Considering the emerging trend in early-onset DM leading higher incidence of microvascular and macrovascular complications, intervention that reverses or reduces abdominal obesity, especially in young adult men and perimenopausal women, is critical.

The present study had several limitations. Because claims data from NHIS were analyzed, subjects were included and excluded based on ICD-10 codes that clinicians reported to the insurance service. Although we attempted to exclude subjects with secondary causes of DM, including related diseases or medication, some undefined cases may have been inadvertently included or excluded. Due to the absence of data on the dose and duration of glucocorticoid use, we exclude all individuals prescribed glucocorticoid within one year. Also, patients using other medication that could affect development of DM, such as statin, antipsychotics or antiretrovirals, were not excluded. Due to the absence of information on eating habit in our database, we were unable to adjust the effect of diet habit in analysis. Furthermore, due to the lack of laboratory data such as glycated hemoglobin or oral glucose tolerance test results, the severity of diseases could not be evaluated. In addition, any causal relationship could not be evaluated due to the intrinsic restriction of observational studies. Additionally, although we performed receiver operating characteristics (ROC) analysis to compare predictive power of each body composition index, the onset of DM in elderly tend to be multifactorial beyond the effect of body composition, resulting in a decrease in the area under the curve with increasing age. This reduction in predictive power was insufficient to

compare the superiority of the indices, so we did not proceed to pairwise comparison of indices. Finally, because only data of Koreans were included, age- and sex-stratified DM risk should be evaluated in different ethnicities. However, this is the first and most recent large-scale study in which significant body composition indices for NODM were compared using 10-year longitudinal follow-up NHIS database representing almost the entire Korean population. Subjects with probable secondary causes for DM were excluded and multiple variables adjusted that could affect the onset of DM to examine the effect of body composition indices on NODM incidence.

Conclusion

In conclusion, WHtR in men of all age groups, BMI, WHtR, and WC in young adults, middle-aged, and elderly women, respectively, had the strongest association with the 10-year incidence of NODM in Korean population. Applying an age- and sex-specific body composition index is important to appropriately screen for the risk of NODM. Because the incidence of NODM significantly increased in the middle-aged group in both men and women, active surveillance for NODM risk by measuring WC and height is necessary for effective prevention.

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Conflict of interest

The authors declare that they have no competing interests.

Data availability

Study protocol, raw data that support the findings are available from the corresponding author upon reasonable request.

Author contribution

Conceptualization and design: Hye Jin Yoo., Min Jeong Park, Minwoong Kang.

Data acquisition, analysis: Minwoong Kang

Data interpretation: Hye Jin Yoo., Min Jeong Park, Minwoong Kang

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Guarantor- Hye Jin Yoo is the guarantor and takes responsibility for the overall content.

Figure legends

Figure 1. 10-year incidence of T2DM stratified by 10-year age groups in (A) Men and (B) Women

Figure 2. HRs of T2DM across quartiles of body composition indices according to 20-year age group in men (A) and women (B)

HR, hazard ratio; T2DM, type 2 diabetes mellitus; BMI, body mass index; WC, waist circumference; WHtR, waist height ratio

Figure 3. HR of new onset T2DM in fully adjusted model according to 1SD increase of anthropometric indices stratified by 20-year age groups in men (A) and women (B)

HR, hazard ratio; T2DM, type 2 diabetes mellitus; SD, standard deviation; BMI, body mass index; WC, waist circumference; WHtR, waist height ratio; VAI, visceral adiposity index; WWI, weight adjusted waist index; ABSI, A body shape index

Table legends

Table 1. Baseline Characteristics of patients with or without incident T2DM

Table 2. Hazard ratios (HRs) and 95% Confidence interval (95%CI) of T2DM across quartiles of body composition indices in total population

BMI, body mass index; WC, waist circumference; WHtR, waist height ratio; VAI, visceral adiposity index; WWI, weight adjusted waist index; ABSI, A body shape index

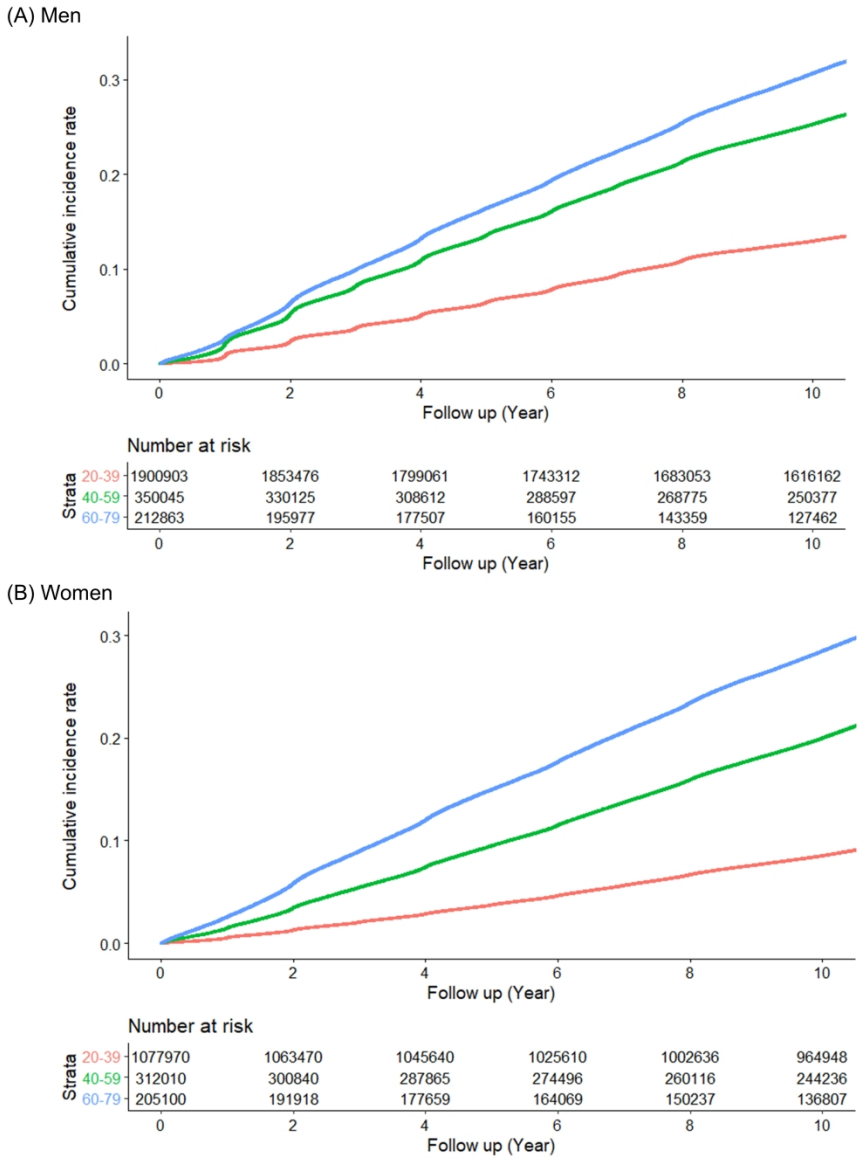

Figure 1. 10-year incidence of T2DM stratified by 10-year age groups in (A) Men and (B) Women

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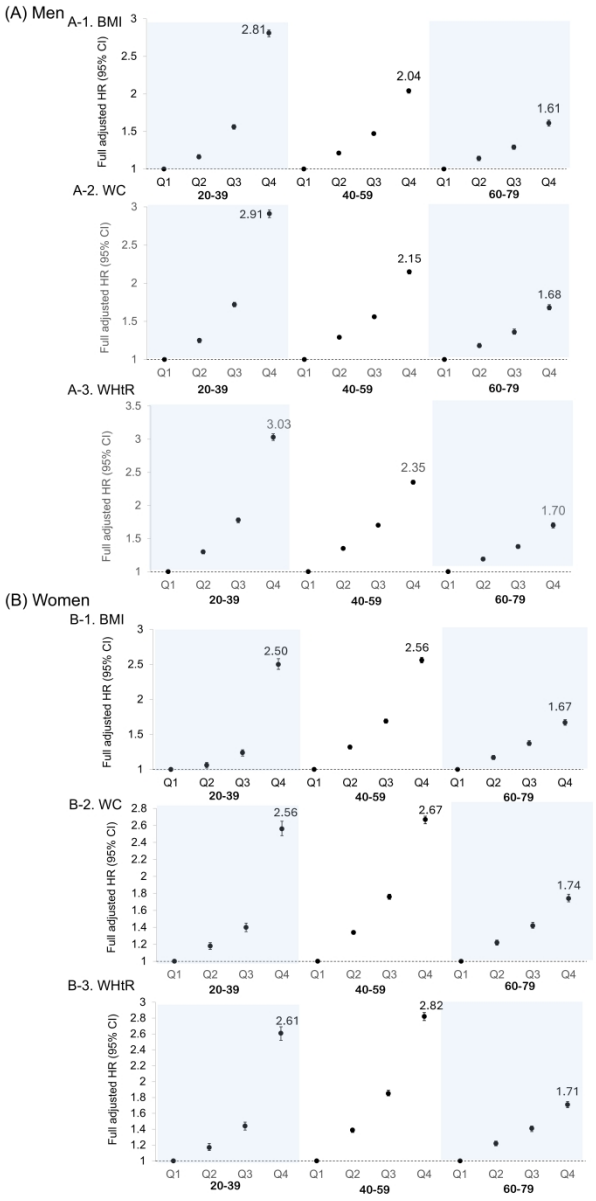


Figure 2. HRs of T2DM across quartiles of body composition indices according to 20-year age group in men (A) and women (B)

308x600mm (300 x 300 DPI)

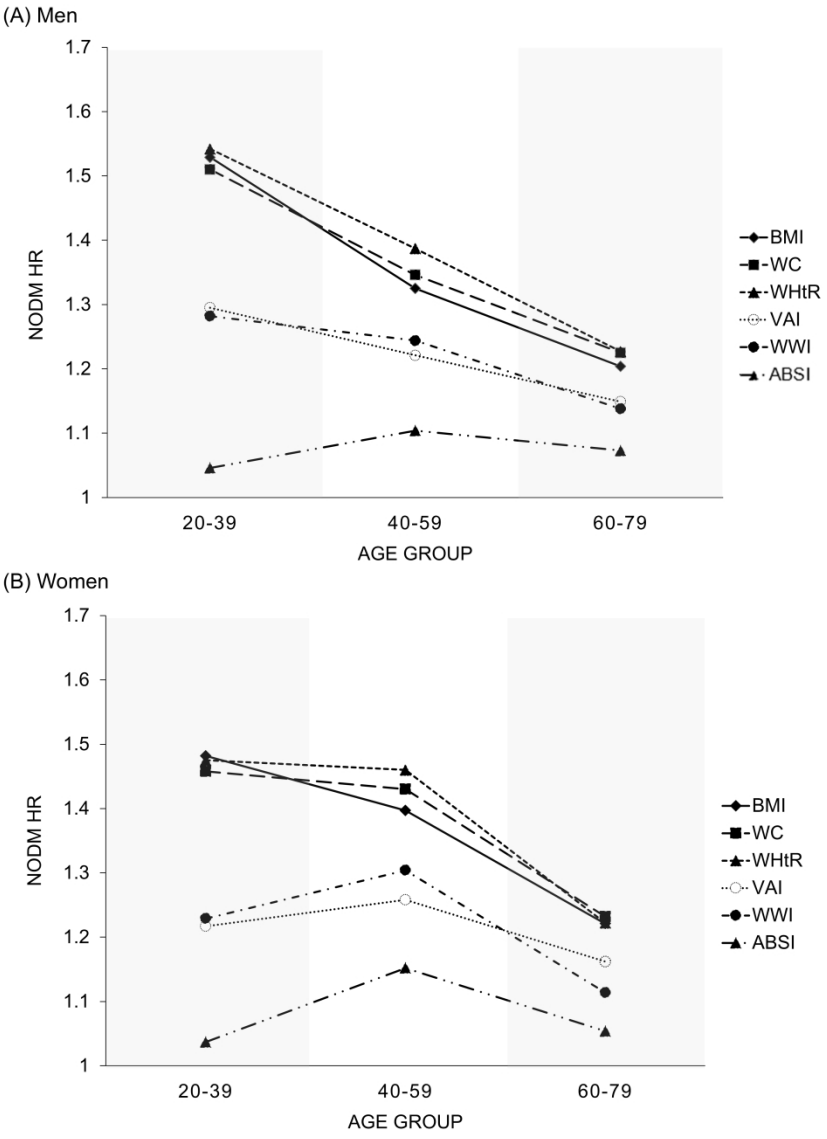


Figure 3. HR of new onset T2DM in fully adjusted model according to 1SD increase of anthropometric indices stratified by 20-year age groups in men (A) and women (B)

308x400mm (300 x 300 DPI)

Table 1. Baseline Characteristics of patients with or without incident T2DM

	Men (N=2,463,811)				Women (N=1,595,080)			
	Age 20-39	Age 40-59	Age 60-79	*p*-value	Age 20-39	Age 40-59	Age 60-79	*p*-value
No. participants	1258327	992621	212863		563530	826450	205100	
BMI, kg/m^2	23.9 ± 3.2	24.0 ± 2.8	23.4 ± 2.8	<0.001	21.4 ± 3.1	23.2 ± 2.9	24.0 ± 3.1	<0.001
Underweight	35006 (2.8)	18533 (1.9)	7902 (3.7)		72860 (12.9)	21004 (2.5)	5474 (2.7)	
Normal	488605 (38.8)	342039 (34.5)	85976 (40.4)		359414 (63.8)	403581 (48.8)	71525 (34.9)	
Overweight	315404 (25.1)	284633 (28.7)	58937 (27.7)		67955 (12.1)	201009 (24.3)	54453 (26.6)	
Obese	419312 (33.3)	347416 (35.0)	60048 (28.2)		63301 (11.2)	200856 (24.3)	73648 (35.9)	
Income percentile				<0.001				<0.001
Medical aid	1073 (0.1)	698 (0.1)	487 (0.2)		722 (0.1)	1696 (0.2)	738 (0.4)	
≤ 30th	234504 (18.6)	160323 (16.2)	64376 (30.2)		186337 (33.1)	264646 (32.0)	48687 (23.7)	
31st–70th	646329 (51.4)	342703 (34.5)	72448 (34.0)		289033 (51.3)	289447 (33.9)	65071 (31.7)	
> 70th	318804 (25.3)	468547 (47.2)	74038 (34.8)		84574 (15.0)	271104 (33.2)	88603 (43.2)	
Unknown	57617 (4.6)	20350 (2.1)	1514 (0.7)		2864 (0.5)	6657 (0.7)	2001 (1.0)	
Residency area				<0.001				<0.001
Urban	952413 (75.7)	770384 (77.6)	146653 (68.9)		446470 (79.2)	649886 (77.6)	131129 (63.9)	
Rural	305598 (24.3)	221942 (22.4)	66132 (31.1)		116906 (20.8)	185208 (22.4)	73891 (36.0)	
Unknown	316 (0)	295 (0)	78 (0)		154 (0)	356 (0)	80 (0)	
Family history of DM	95941 (7.6)	75935 (7.7)	5822 (2.7)	<0.001	49880 (8.9)	72913 (9.2)	8350 (4.1)	<0.001
Smoking status				<0.001				<0.001
Never smoker	364532 (29.0)	263588 (26.6)	82287 (38.7)		511139 (90.7)	785970 (95.1)	197053 (96.1)	
Ex-smoker	181767 (14.5)	261163 (26.3)	60755 (28.5)		19931 (3.5)	11606 (1.4)	1911 (0.9)	
Current	704877 (56.0)	462090 (46.6)	68553 (32.2)		28889 (5.1)	22682 (2.7)	4535 (2.2)	
Unknown	7151 (0.6)	5780 (0.6)	1268 (0.6)		3571 (0.6)	6792 (0.8)	1601 (0.8)	

Heavy drinking				<0.001			<0.001
None	314855 (25.0)	283718 (28.6)	94373 (44.3)		298791 (53.0)	608534 (73.4)	181677 (88.6)
Moderate	572886 (45.5)	402993 (40.6)	70875 (33.3)		172935 (30.7)	151281 (18.3)	14497 (7.1)
Heavy	342328 (27.2)	282280 928.4)	42639 920.0)		76051 (13.5)	48794 (5.9)	3793 (1.9)
Unknown	28258 (2.3)	23630 (2.4)	4976 92.3)		15753 (2.8)	19841 (2.4)	5133 (2.5)
Regular exercise				<0.001			<0.001
None	224755 (17.9)	204722 (20.6)	55883 (26.3)		117228 (20.8)	214703 (26.0)	67356 (32.8)
Irregular	826539 (65.7)	584212 (58.9)	102190 (48.0)		390425 (69.3)	469541 (56.8)	101561 (49.5)
Regular	195008 (15.5)	195416 (19.7)	53336 (25.1)		50809 (9.0)	136577 (16.5)	34821 (17.0)
Unknown	12025 (1.0)	8271 (0.8)	1454 (0.7)		5068 (0.9)	6629 (0.7)	1362 (0.7)
WC, cm	81.5 ± 7.9	83.1 ± 7.2	83.5 ± 7.7	<0.001	70.8 ± 7.5	75.4 ± 7.5	80.2 ± 7.9	<0.001
WHtR	0.5 ± 0	0.5 ± 0	0.5 ± 0	<0.001	0.4 ± 0	0.5 ± 0.1	0.5 ± 0.1	<0.001
ABSI	347884.1 ± 17515.9	357304.7 ± 18253.6	369448.7 ± 20420.1	<0.001	337529.8 ± 21711.5	344381.8 ± 20926.5	363581.9 ± 24347.6	<0.001
WWI	9.7 ± 0.5	10 ± 0.5	10.5 ± 0.6	<0.001	9.5 ± 0.6	10.0 ± 0.7	10.8 ± 0.8	<0.001
VAI	431320.6 ± 300187.2	471715.6 ± 311853.9	404461.7 ± 255281.4	<0.001	399669.1 ± 257236.4	522165.7 ± 301931.2	630556 ± 343916.3	<0.001
SBP, mmHg	121.9 ± 12.2	124.2 ± 14.3	129.7 ± 16.3	<0.001	111.7 ± 11.3	118.6 ± 14.8	128.3 ± 16.5	<0.001
DBP, mmHg	76.4 ± 8.9	78.6 ± 10.0	79.4 ± 10.3	<0.001	70.1 ± 8.4	74.0 ± 10.1	77.9 ± 10.2	<0.001
AST, IU/L	25.4 ± 22.7	26.7 ± 23.2	26.8 ± 15.7	<0.001	19.2 ± 11.2	21.2 ± 16.8	24.8 ± 14.7	<0.001
ALT, IU/L	28.9 ± 28.1	28.2 ± 23.6	23.7 ± 16.9	<0.001	15.2 ± 13.7	19.3 ± 17.9	20.7 ± 16.8	<0.001
FBS, mg/dL	90.5 ± 11.1	94.7 ± 11.7	95.8 ± 11.9	<0.001	87.6 ± 9.9	91.7 ± 10.5	94.2 ± 11.1	<0.001
eGFR	86.8 ± 57.1	81.3 ± 47.8	78.5 ± 34.4	<0.001	90.0 ± 50.0	82.8 ± 27.3	75.8 ± 27.1	<0.001
T-chol, mg/dL	189 ± 34.9	199.7 ± 36.6	194.2 ± 37.3	<0.001	178.2 ± 31.3	187.7 ± 36.4	209.9 ± 38.9	<0.001
TG, mg/dL	139.8 ± 96.6	154.9 ± 101.7	134.5 ± 82.9	<0.001	82.1 ± 47.4	104.7 ± 62.3	132.9 ± 72.9	<0.001
LDL-C, mg/dL	122.0 ± 302.3	117.9 ± 72.2	115.6 ± 60.1	<0.001	125.8 ± 430.0	119.8 ± 84.6	129.5 ± 64.5	<0.001
HDL-C, mg/dL	53.1 ± 11.9	52.3 ± 12.1	52.7 ± 12.6	<0.001	61.8 ± 12.9	55.3 ± 12.8	54.8 ± 12.5	<0.001

Data were presented Mean ± SD or n (%)

T2DM, type 2 diabetes mellitus; No, number; BMI, body mass index; WC, waist circumference; WHtR, waist height ratio; ABSI, a body shape index; WWI, weight adjusted waist index; VAI, visceral adiposity index; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; FBG, fasting blood glucose; eGFR, estimated glomerular filtration rate; T-chol, total- cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol

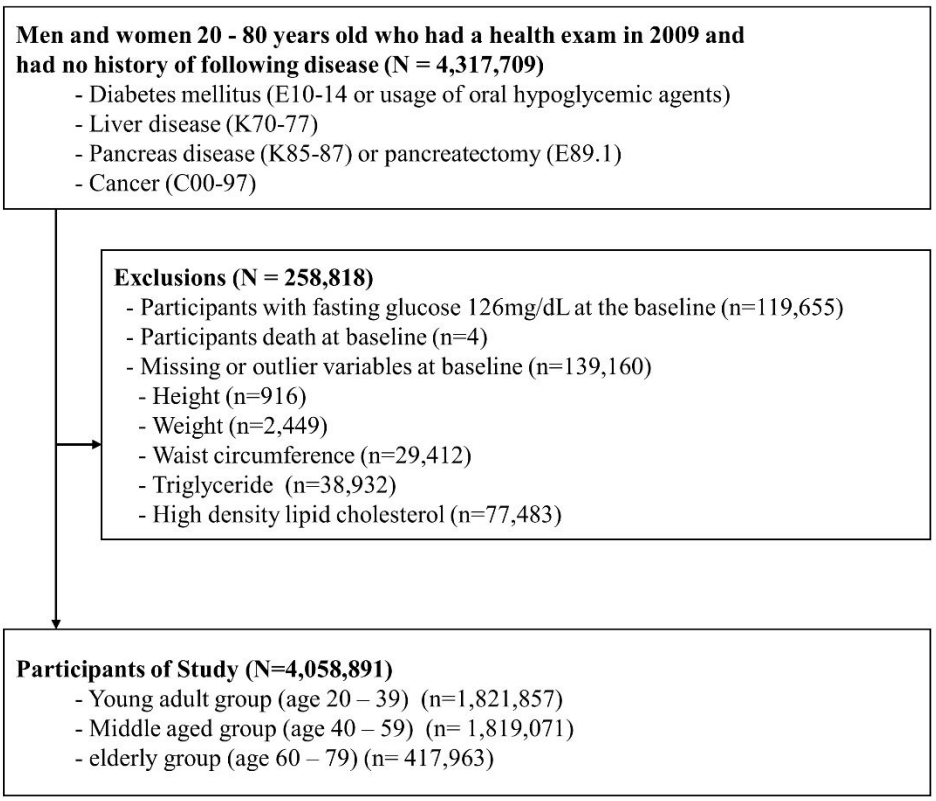
Table 2. Hazard ratios (HRs) and 95% Confidence interval (95%CI) of NODM across quartiles of body composition indices in total population

	T2DM (n) (n=625715)	Person year	Incidence rate	Model 1	Model 2	Model 3	Model 4	Model 5
BMI								
Q1 (n=1,005,153)	91,517	9,827,735.2	9.3	1	1	1	1	1
Q2 (n=1,016,249)	128,239	9,778,783.8	13.1	1.41 (1.40-1.42)	1.21 (1.20-1.22)	1.22 (1.21-1.23)	1.22 (1.21-1.23)	1.22 (1.21-1.23)
Q3 (n=1,038,875)	171,369	9,788,956.5	17.5	1.88 (1.87-1.90)	1.52 (1.50-1.53)	1.53 (1.52-1.55)	1.53 (1.51-1.54)	1.54 (1.52-1.55)
Q4 (n=998,614)	234,590	9,031,690.8	26.0	2.80 (2.78-2.82)	2.30 (2.28-2.31)	2.31 (2.29-2.33)	2.29 (2.27-2.31)	2.31 (2.29-2.33)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
WC								
Q1 (n=965,392)	78,371	9,534,939.2	8.2	1	1	1	1	1
Q2 (n=1,100,752)	138,929	10,600,570.5	13.1	1.60 (1.58-1.61)	1.36 (1.35-1.37)	1.35 (1.34-1.37)	1.35 (1.34-1.36)	1.35 (1.34-1.36)
Q3 (n=1,034,301)	176,385	9,698,250.5	18.2	2.22 (2.20-2.24)	1.77 (1.75-1.79)	1.76 (1.74-1.77)	1.75 (1.73-1.76)	1.76 (1.74-1.78)
Q4 (n=958,446)	232,030	8,593,406.1	27.0	3.30 (3.27-3.32)	2.55 (2.53-2.57)	2.52 (2.50-2.55)	2.51 (2.48-2.53)	2.52 (2.50-2.54)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
WHtR								
Q1 (n=1,014,803)	73,264	10,069,987.3	7.3	1	1	1	1	1
Q2 (n=1,015,850)	117,355	9,843,068.3	11.9	1.64 (1.63-1.66)	1.35 (1.34-1.37)	1.35 (1.34-1.36)	1.34 (1.33-1.35)	1.35 (1.33-1.36)
Q3 (n=1,011,915)	171,833	9,499,797.5	18.1	2.49 (2.47-2.51)	1.80 (1.79-1.82)	1.79 (1.78-1.81)	1.78 (1.76-1.80)	1.79 (1.77-1.81)
Q4 (n=1,016,323)	263,263	9,014,313.2	29.2	4.03 (4.00-4.06)	2.58 (2.55-2.60)	2.56 (2.54-2.58)	2.54 (2.52-2.56)	2.54 (2.52-2.57)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
VAI								
Q1 (n=1,014,722)	100,176	9,894,725.8	10.1	1	1	1	1	1
Q2 (n=1,014,723)	125,088	9,780,992.2	12.8	1.26 (1.25-1.27)	1.23 (1.22-1.24)	1.22 (1.21-1.23)	1.22 (1.21-1.23)	1.22 (1.21-1.23)
Q3 (n=1,014,723)	163,206	9,584,646.6	17.0	1.68 (1.67-1.70)	1.56 (1.55-1.57)	1.53 (1.52-1.54)	1.53 (1.51-1.54)	1.53 (1.52-1.54)
Q4 (n=1,014,723)	237,245	9,166,801.7	25.9	2.56 (2.54-2.58)	2.27 (2.25-2.28)	2.20 (2.18-2.21)	2.18 (2.17-2.20)	2.19 (2.17-2.21)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
ABSI								
Q1 (n=1,014,710)	110,242	9,903,776.6	11.1	1	1	1	1	1
Q2 (n=1,014,752)	138,228	9,741,236.9	14.2	1.28 (1.27-1.29)	1.09 (1.08-1.10)	1.08 (1.07-1.09)	1.08 (1.07-1.09)	1.09 (1.08-1.09)
Q3 (n=1,014,964)	166,745	9,559,615.0	17.4	1.57 (1.56-1.58)	1.16 (1.15-1.17)	1.15 (1.14-1.16)	1.15 (1.14-1.16)	1.16 (1.15-1.17)

Q4 (n=1,014,465)	210,500	9,222,537.8	22.8	2.06 (2.04-2.07)	1.20 (1.19-1.21)	1.18 (1.17-1.19)	1.19 (1.18-1.20)	1.18 (1.17-1.19)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
WWI								
Q1 (n=1,011,717)	86,064	9,994,386.9	8.6	1	1	1	1	1
Q2 (n=1,021,449)	126,085	9,868,208.8	12.8	1.49 (1.47-1.50)	1.25 (1.24-1.26)	1.25 (1.23-1.26)	1.24 (1.23-1.25)	1.25 (1.23-1.26)
Q3 (n=1,011,449)	170,662	9,503,139.9	18.0	2.09 (2.07-2.11)	1.51 (1.50-1.52)	1.50 (1.49-1.51)	1.49 (1.48-1.51)	1.50 (1.49-1.51)
Q4 (n=1,014,276)	242,904	9,061,430.7	26.8	3.12 (3.10-3.15)	1.81 (1.79-1.82)	1.79 (1.77-1.80)	1.78 (1.77-1.80)	1.78 (1.76-1.79)
P for linear trend				< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

Model 1: Unadjusted
Model 2: Adjusted for age, sex
Model 3: Adjusted for age, sex, smoking habit, alcohol drinking, physical activity
Model 4: Adjusted for age, sex, smoking habit, alcohol drinking, physical activity, family history of DM
Model 5: Adjusted for age, sex, smoking habit, alcohol drinking, physical activity, family history of DM, income percentile, residence area

Supplementary Figure 1. Flow diagram for selection of study population



Supplementary table 1. Baseline Characteristics of patients with or without incident NODM

	Overall (N=4,058,891)		
	Non-Diabetes	New onset Diabetes	*P*-value
No. participants	3,433,176	625,715	
Age, years	40.9 ± 12.1	47.9 ± 12.5	<0.001
20-29	707,113 (20.6)	47,752 (7.6)	
30-39	951,882 (27.7)	115,110 (18.4)	
40-49	972,192 (28.3)	184,824 (29.5)	
50-59	507,212 (14.8)	154,843 (24.7)	
60-69	212,964 (6.2)	88,690 (14.2)	
70-79	81,813 (2.4)	34,496 (5.5)	
Sex (n, %)			<0.001
Men	2,058,003 (59.9)	405,808 (64.9)	
Women	1,375,173 (40.1)	219,907 (35.1)	
BMI, kg/m^2	23.2 ± 3.1	24.6 ± 3.3	<0.001
Underweight	147,883 (4.3)	12,896 (2.1)	
Normal	1,559,794 (45.4)	191,346 (30.6)	
Overweight	826,187 (24.1)	156,204 (25.0)	
Obese	899,312 (26.2)	265,269 (42.4)	
Income percentile			<0.001
Medical aid	4,363 (0.1)	951 (0.2)	
≤ 30th	808,739 (23.6)	150,134 (24.0)	
31st–70th	1,444,830 (42.1)	251,201 (40.1)	
> 70th	1,096,557 (31.9)	212,113 (33.9)	
Unknown	78,687 (2.3)	11,316 (1.8)	
Residency area			<0.001
Urban	2,627,635 (76.5)	460,300 (73.6)	
Rural	804,433 (23.4)	165,244 (26.4)	
Unknown	1,108 (0)	171 (0)	
Family history of DM	251,318 (7.3)	60,523 (9.7)	<0.001
Smoking status			<0.001
Never smoker	1,894,045 (55.2)	310,524 (49.6)	
Ex-smoker	443,578 (12.9)	93,555 (15.0)	
Current	1,073,833 (31.3)	217,793 (34.8)	
Unknown	21,720 (0.6)	3,843 (0.6)	
Heavy drinking			<0.001
None	1,500,879 (43.7)	279,069 (44.6)	
Moderate	1,193,151 (34.8)	192,316 (30.7)	
Heavy	656,085 (19.1)	139,800 (22.3)	

Unknown	83,061 (2.4)	14,530 (2.3)	
Regular exercise			<0.001
None	735,567 (21.4)	149,080 (23.8)	
Irregular	211,6047 (61.6)	358,421 (57.3)	
Regular	552,695 (16.1)	113,272 (18.1)	
Unknown	28,867 (0.8)	4,942 (0.8)	
WC, cm	78.6 ± 8.6	82.7 ± 8.8	<0.001
WHtR	0.47 ± 0.05	0.50 ± 0.05	<0.001
ABSI	349,029.1 ± 21,153.0	355,076.7 ± 21,522.2	<0.001
WWI	9.9 ± 0.7	10.2 ± 0.7	<0.001
VAI	443,097.2 ± 284,260.8	565,230.4 ± 373,858.6	<0.001
SBP, mmHg	120.2 ± 14.1	126.0 ± 15.6	<0.001
DBP, mmHg	75.3 ± 9.7	78.7 ± 10.5	<0.001
AST, IU/L	23.8 ± 18.9	27.0 ± 24.8	<0.001
ALT, IU/L	23.3 ± 22.3	29.1 ± 26.1	<0.001
FBS, mg/dL	90.8 ± 10.7	97.6 ± 12.8	<0.001
eGFR	84.3 ± 47.9	81.7 ± 39.6	<0.001
T-chol, mg/dL	191.6 ± 35.8	202.0 ± 38.2	<0.001
TG, mg/dL	122.4 ± 83.1	157.0 ± 107.4	<0.001
LDL-C, mg/dL	121.2 ± 253.3	121.0 ± 136.2	<0.001
HDL-C, mg/dL	55.7 ± 12.8	53.1 ± 12.5	<0.001

T2DM, type 2 diabetes mellitus; No, number; BMI, body mass index; WC, waist circumference; WHtR, waist height ratio; ABSI, a body shape index; WWI, weight adjusted waist index; VAI, visceral adiposity index; TyG, triglyceride and glucose index; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; FBG, fasting blood glucose; eGFR, estimated glomerular filtration rate; T-chol, total- cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol
Data were presented Mean ± SD or n (%)

Supplementary table 2. Adjusted hazard ratios (HRs) and 95% Confidence interval (95%CI) of NODM across quartiles of body composition indices in total population

	BMI	WC	WHtR	VAI	ABSI	WWI
Q1	1	1	1	1	1	1
Q2	1.14 (1.13-1.15)	1.25 (1.24-1.26)	1.25 (1.23-1.26)	1.18 (1.17-1.19)	1.18 (1.17-1.19)	1.05 (1.04-1.06)
Q3	1.35 (1.34-1.36)	1.51 (1.50-1.53)	1.55 (1.53-1.56)	1.42 (1.40-1.43)	1.42 (1.40-1.43)	1.10 (1.09-1.11)
Q4	1.86 (1.84-1.87)	1.99 (1.97-2.01)	2.03 (2.01-2.05)	1.83 (1.81-1.85)	1.83 (1.81-1.85)	1.13 (1.12-1.14)
P for linear trend	<0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

Adjusted for age, sex, smoking habit, alcohol drinking, physical activity, family history of DM, income percentile, residence area, SBP, DBP, TG, HDL

Supplementary table 3. HRs (95% CI) of NODM based on 1SD increase of body composition indices according to age and sex groups

	Men		Women	
	Crude HR (95% CI)	Adjusted* HR (95% CI)	Crude HR (95% CI)	Adjusted* HR (95% CI)
20-39				
BMI	1.547 (1.540 - 1.554)	1.529 (1.522 - 1.536)	**1.497 (1.486 - 1.508)**	**1.482 (1.471 - 1.493)**
WC	1.531 (1.524 - 1.538)	1.510 (1.502 - 1.517)	1.474 (1.462 - 1.487)	1.458 (1.446 - 1.470)
WHtR	**1.560 (1.553 - 1.568)**	**1.542 (1.534 - 1.549)**	1.491 (1.479 - 1.504)	1.475 (1.463 - 1.487)
VAI	1.316 (1.312 - 1.320)	1.295 (1.290 - 1.299)	1.220 (1.214 - 1.226)	1.217 (1.211 - 1.223)
WWI	1.286 (1.280 - 1.293)	1.282 (1.275 - 1.288)	1.238 (1.226 - 1.250)	1.229 (1.217 - 1.241)
ABSI	1.053 (1.047 - 1.059)	1.046 (1.041 - 1.052)	1.039 (1.027 - 1.050)	1.037 (1.026 - 1.049)
40-59				
BMI	1.318 (1.313 - 1.324)	1.325 (1.319 - 1.330)	1.407 (1.400 - 1.413)	1.397 (1.391 - 1.403)
WC	1.346 (1.341 - 1.352)	1.346 (1.340 - 1.351)	1.441 (1.434 - 1.448)	1.430 (1.423 - 1.437)
WHtR	**1.392 (1.386 - 1.397)**	**1.387 (1.381 - 1.392)**	**1.470 (1.462 - 1.477)**	**1.460 (1.452 - 1.467)**
VAI	1.237 (1.233 - 1.240)	1.221 (1.218 - 1.225)	1.264 (1.260 - 1.268)	1.258 (1.254 - 1.262)
WWI	1.255 (1.249 - 1.260)	1.244 (1.239 - 1.249)	1.312 (1.305 - 1.319)	1.304 (1.297 - 1.311)
ABSI	1.115 (1.110 - 1.120)	1.104 (1.099 - 1.109)	1.156 (1.150 - 1.163)	1.152 (1.146 - 1.158)
60-79				
BMI	1.192 (1.183 - 1.201)	1.204 (1.195 - 1.214)	1.219 (1.210 - 1.228)	1.221 (1.211 - 1.230)
WC	1.218 (1.208 - 1.227)	1.225 (1.215 - 1.234)	**1.232 (1.222 - 1.241)**	**1.232 (1.222 - 1.242)**
WHtR	**1.221 (1.211 - 1.230)**	**1.227 (1.218 - 1.237)**	1.221 (1.211 - 1.230)	1.222 (1.212 - 1.231)
VAI	1.153 (1.146 - 1.160)	1.149 (1.142 - 1.156)	1.163 (1.155 - 1.170)	1.162 (1.155 - 1.170)
WWI	1.138 (1.130 - 1.147)	1.138 (1.129 - 1.147)	1.114 (1.105 - 1.123)	1.114 (1.105 - 1.123)
ABSI	1.077 (1.068 - 1.085)	1.073 (1.065 - 1.082)	1.056 (1.047 - 1.064)	1.054 (1.045 - 1.062)

Adjusted for smoking, alcohol, regular exercise, family history of Diabetes, income, area

HR, hazard ratio; CI, confidence interval; SD, standard deviation; T2DM, type 2 diabetes mellitus; BMI, body mass index; WC, waist circumference; WHtR, waist height ratio; VAI, visceral adiposity index; WWI, weight adjusted waist index; ABSI, A body shape index; DM, diabetes mellitus