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# **BMJ Open**

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

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1	Sex- and Age-Specific Body Composition Indices as Predictors of
2	New-Onset Type 2 Diabetes Mellitus in Koreans: A Nationwide
3	Cohort Study
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4 24 5 24	Strengths and limitation of this study
6 7 25	• The large-scale study using NHIS database representing almost the entire Korean
8 9 26	population with 10-year longitudinal follow-up result.
10 11 27 12	• Sex and age-groups stratified risk of new onset type 2 diabetes mellitus was
13 14 28	estimated, which previous studies did not conduct.
15 16 29	• Due to the lack of laboratory data such as glycated hemoglobin or oral glucose
17 18 30 19	tolerance test results, the severity of diseases could not be evaluated.
20 21 31	• Because only data of Koreans were included, external validation was not conducted
22 23 32	with other ethnicities.
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34	Abstract
35	Objectives: Hormonal and age-related differences in body composition require tailored
36	approaches for predicting new-onset type 2 diabetes (NODM). Previous studies lacked in-
37	depth stratified analyses. We investigate sex- and age-specific body composition indices
38	associated with NODM.
39	Design and setting: Retrospective, nationwide, population-based cohort study.
40	Participants: We analyzed 4,058,891 adults who underwent a health examination in year
41	2009 and 10-year follow-up data of from the National Health Insurance Service (NHIS).
42	Outcome measure: NODM risk stratified by sex and age-groups in 20-year intervals
43	according to quartiles or per 1standard-deviation (SD) increase in BMI, WC, WHtR, VAI,
44	ABSI, and WWI
45	Results: Among the total subjects, 625,715 (15.4%) developed NODM during median 10-
46	year follow-up. The fourth quartile of WHtR showed the highest hazard ratio (HR) for
47	NODM compared to the first quartile among various indices across the entire population (HR
48	2.54, 95% CI 2.52–2.57). In men, WHtR consistently exhibited the strongest association with
49	NODM across all age-groups in analysis based on 1-SD increase; ages 20–39 (HR 1.54, 95%
50	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
51	1.22-1.24). In women, different indices exhibited the closest association with NODM; BMI
52	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–
53	1.47), and WC for ages 60–79 (HR 1.23, 95%CI 1.22–1.24).
54	Conclusion: WHtR was the strongest predictor of NODM in men across all ages, while in
55	women, the relevant indices varied by age-groups. These findings highlight the need for sex-
56	and age-specific body composition assessments in predicting NODM risk.
57	Keywords: Type 2 diabetes mellitus; anthropometric index; body composition; body mass

58 index; waist circumference

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# **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<sup>1</sup>. Similarly, in a T2DM epidemiologic study in Korea, 16.7% of adults  $\geq$  30 years had T2DM in 2020 whereas the prevalence of T2DM in 2018 was 13.8%<sup>2</sup>. 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<sup>3</sup>. However, with the discovery of different metabolic risks associated with visceral and subcutaneous fat<sup>4</sup>, alternatives like waist circumference (WC), waist-hip ratio (WHR), and waist-height ratio (WHtR) emerged, highlighting central obesity more effectively <sup>5</sup>. 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 <sup>67</sup>. Recognizing the metabolic risks of sarcopenia, researchers developed the weight-adjusted waist index (WWI) to reflect low muscle mass<sup>8</sup>. 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 <sup>9</sup>. 

In previous studies, these body composition indices were investigated in terms of
new onset T2DM (NODM) prediction <sup>10</sup>; 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

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composition also differ between the sexes. Menopause causes 15–20% of additional
abdominal fat accumulation and decreasing testosterone in men induces muscle mass
reduction <sup>11</sup>. 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.

#### 91 Methods

#### 92 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  $\geq$  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

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(HDL-C) for the calculation of anthropometric index, and subjects who were deceased at baseline, were excluded. Ultimately, a total of 4,058,891 patients 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 <sup>12</sup>. 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 LICY was used for analysis.

#### **Definition of body composition index and variables**

The characteristics of NHIS databases were presented in previous studies <sup>13</sup>. 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<sup>23</sup>, WHtR as WC/height<sup>45</sup>, ABSI as 1000 × WC × weight<sup>-2/3</sup>  $\times$  height<sup>5/6 14</sup>, 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 × BMI)] × TG/0.81 × 1.52/HDL (for women)<sup>7</sup>, and WWI as WC/ $\sqrt{\text{weight}}$ 

<sup>15</sup>. 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 ( $\geq 15$  cups per week for men,  $\geq 8$  cups per week for women), or unknown. Regular exercise was defined as none, regular (vigorous activity for >3 days or moderate-intensity activity for  $\geq$  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  $\geq$  126 mg/dL <sup>16</sup>. 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 

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The baseline characteristics of the study population are presented as mean  $\pm$  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  $41.9 \pm 12.2$  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**.

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# 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)

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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 middleaged, 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

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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<sup>17</sup>, 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<sup>18</sup>. 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 <sup>4.6</sup>. Laboratory data such as TG and HDL-C were adopted in the VAI equation <sup>7</sup> and development of WWI was used to discriminate between muscle and fat mass <sup>9</sup>.

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 <sup>19</sup>. In the meta-analysis of 31 studies, WHtR was significantly associated with T2DM compared with BMI in both men and women <sup>20</sup>. In another meta-analysis including 22 prospective studies, WHtR and WC showed similar predictability for DM and were superior to BMI <sup>21</sup>. Furthermore, Maryam et al. reported WC predicted T2DM development better than BMI, ABSI, WHtR, and WHR in their prospective study with 9,354 subjects <sup>22</sup>. In a study that included 3,461 Chinese participants, VAI was reported an effective index for DM prediction compared with WC, WHtR, and BMI <sup>23</sup>. Differences in study results might be due to the heterogeneity of the

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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 <sup>24</sup>, and in other studies, the number of parity was positively associated with abdominal obesity <sup>25</sup>. Furthermore, in previous research, fat mass volume doubled, and lean mass decreased at the start of menopause with reduction in estrogen level <sup>25</sup>. In several studies, body fat distribution was shown to change from the extremities to the trunk during the perimenopausal period <sup>26</sup>. These undesirable body composition changes are strongly associated with cardiometabolic disease risks, increasing incidence of DM, dyslipidemia, and cardiovascular disease (CVD) in postmenopausal women<sup>27</sup>. 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-tolate 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 <sup>21 23</sup>.

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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 <sup>28</sup>. 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 <sup>29</sup>. In addition, because WHtR adjusts for the effect of height on WC, it reflects a different body fat distribution based on individual height <sup>11</sup>.

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 <sup>30</sup>. 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

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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.

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# 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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# References

- Sun H, Saeedi P, Karuranga S, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract* 2022;183:109119.
- 2 Bae JH, Han KD, Ko SH*, et al.* Diabetes Fact Sheet in Korea 2021. *Diabetes Metab J* 2022;46:417-26.
- 3 Eknoyan G. Adolphe Quetelet (1796-1874)--the average man and indices of obesity. *Nephrol Dial Transplant* 2008;23:47-51.
- 4 Fox CS, Massaro JM, Hoffmann U*, et al.* Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. *Circulation* 2007;116:39-48.
- 5 Price GM, Uauy R, Breeze E, *et al.* Weight, shape, and mortality risk in older persons: elevated waist-hip ratio, not high body mass index, is associated with a greater risk of death. *Am J Clin Nutr* 2006;84:449-60.
- 6 Krakauer NY, Krakauer JC. A new body shape index predicts mortality hazard independently of body mass index. *PLoS One* 2012;7:e39504.
- 7 Amato MC, Giordano C, Galia M, *et al.* Visceral Adiposity Index: a reliable indicator of visceral fat function associated with cardiometabolic risk. *Diabetes Care* 2010;33:920-2.
- 8 Power GA, Dalton BH, Rice CL. Human neuromuscular structure and function in old age: A brief review. *J Sport Health Sci* 2013;2:215-26.
- Park MJ, Hwang SY, Kim NH, et al. A Novel Anthropometric Parameter, Weight-Adjusted
   Waist Index Represents Sarcopenic Obesity in Newly Diagnosed Type 2 Diabetes Mellitus.
   J Obes Metab Syndr 2023;32:130-40.
- 10 Li WC, Chen IC, Chang YC, *et al.* Waist-to-height ratio, waist circumference, and body mass index as indices of cardiometabolic risk among 36,642 Taiwanese adults. *Eur J Nutr* 2013;52:57-65.
- 11 Kodoth V, Scaccia S, Aggarwal B. Adverse Changes in Body Composition During the Menopausal Transition and Relation to Cardiovascular Risk: A Contemporary Review. *Womens Health Rep (New Rochelle)* 2022;3:573-81.
- 12 Chen L, Nelson DR, Zhao Y, *et al.* Relationship between muscle mass and muscle strength, and the impact of comorbidities: a population-based, cross-sectional study of older adults in the United States. *BMC Geriatr* 2013;13:74.
- 13 Chang Bae Chun SYK, Jun Young Lee, Sang Yi Lee. Republic of Korea: health system review 2009. *Health Systems in Transition* 2009;11.
- 14 Christakoudi S, Tsilidis KK, Muller DC, *et al.* A Body Shape Index (ABSI) achieves better mortality risk stratification than alternative indices of abdominal obesity: results from a large European cohort. *Sci Rep* 2020;10:14541.

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15 Park Y, Kim NH, Kwon TY, *et al.* A novel adiposity index as an integrated predictor of cardiometabolic disease morbidity and mortality. *Sci Rep* 2018;8:16753.

- 16 Roh E, Noh E, Hwang SY, *et al.* Increased Risk of Type 2 Diabetes in Patients With Thyroid Cancer After Thyroidectomy: A Nationwide Cohort Study. *J Clin Endocrinol Metab* 2022;107:e1047-e56.
- 17 Bray GA, Popkin BM. Dietary sugar and body weight: have we reached a crisis in the epidemic of obesity and diabetes?: health be damned! Pour on the sugar. *Diabetes Care* 2014;37:950-6.
- 18 Laiteerapong N, Ham SA, Gao Y, et al. The Legacy Effect in Type 2 Diabetes: Impact of Early Glycemic Control on Future Complications (The Diabetes & Aging Study). Diabetes Care 2019;42:416-26.
- 19 Mi SQ, Yin P, Hu N, *et al.* BMI, WC, WHtR, VFI and BFI: which indictor is the most efficient screening index on type 2 diabetes in Chinese community population. *Biomed Environ Sci* 2013;26:485-91.
- 20 Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and metaanalysis. *Obes Rev* 2012;13:275-86.
- 21 Browning LM, Hsieh SD, Ashwell M. A systematic review of waist-to-height ratio as a screening tool for the prediction of cardiovascular disease and diabetes: 0.5 could be a suitable global boundary value. *Nutr Res Rev* 2010;23:247-69.
- 22 Saberi-Karimian M, Mansoori A, Bajgiran MM*, et al.* Data mining approaches for type 2 diabetes mellitus prediction using anthropometric measurements. *J Clin Lab Anal* 2023;37:e24798.
- Chen C, Xu Y, Guo ZR, *et al.* The application of visceral adiposity index in identifying type
  2 diabetes risks based on a prospective cohort in China. *Lipids Health Dis* 2014;13:108.
- 24 Cho GJ, Yoon HJ, Kim EJ, *et al.* Postpartum changes in body composition. *Obesity (Silver Spring)* 2011;19:2425-8.
- 25 Gunderson EP, Sternfeld B, Wellons MF, *et al.* Childbearing may increase visceral adipose tissue independent of overall increase in body fat. *Obesity (Silver Spring)* 2008;16:1078-84.
- 26 Dmitruk A, Czeczelewski J, Czeczelewska E*, et al.* Body composition and fatty tissue distribution in women with various menstrual status. *Rocz Panstw Zakl Hig* 2018;69:95-101.
- 27 Tanaka KI, Kanazawa I, Sugimoto T. Reduced muscle mass and accumulation of visceral fat are independently associated with increased arterial stiffness in postmenopausal women with type 2 diabetes mellitus. *Diabetes Res Clin Pract* 2016;122:141-7.
- Tchernof A, Després JP. Pathophysiology of human visceral obesity: an update. *Physiol Rev* 2013;93:359-404.

- 29 Koch E, Romero T, Romero CX, *et al.* Early life and adult socioeconomic influences on mortality risk: preliminary report of a 'pauper rich' paradox in a Chilean adult cohort. *Ann Epidemiol* 2010;20:487-92.
- 30 Power ML, Schulkin J. Sex differences in fat storage, fat metabolism, and the health risks from obesity: possible evolutionary origins. *Br J Nutr* 2008;99:931-40.

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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.

Data interpretation: H.J.Y., M.J.P., M.K.

Writing - original draft: H.J.Y., M.J.P., M.K.

Writing - review & editing: A.R.J., S.Y.J., E.S., K.M.C., S.H.B.

#### **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

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Table 1. Dasenne Chara			out incluent 12			uding fo	22	
	A = = <b>2</b> 0, 20	Men (N=2,463,811)	A (0.70	<i>p</i> -	W		)) A (0, 70	<i>p</i> -
	Age 20-39	Age 40-59	Age 60-79	value	Age 20-39		Age 60-79	value
No. participants	1258327	992621	212863		563530	ate 02826450	205100	
BMI, kg/m <sup>2</sup>	$23.9 \pm 3.2$	$24.0 \pm 2.8$	$23.4\pm2.8$	< 0.001	$21.4 \pm 3.1$	to n 20.2 ± 2.9	$24.0 \pm 3.1$	< 0.001
Underweight	35006 (2.8)	18533 (1.9)	7902 (3.7)		72860 (12.9)	te 23004 (2.5)	5474 (2.7)	
Normal	488605 (38.8)	342039 (34.5)	85976 (40.4)		359414 (63.8)	a 402 581 (48.8)	71525 (34.9)	
Overweight	315404 (25.1)	284633 (28.7)	58937 (27.7)		67955 (12.1)		54453 (26.6)	
Obese	419312 (33.3)	347416 (35.0)	60048 (28.2)		63301 (11.2)	<b>a a b b s</b> 856 (24.3)	73648 (35.9)	
Income percentile				< 0.001		http Ininir		< 0.001
Medical aid	1073 (0.1)	698 (0.1)	487 (0.2)		722 (0.1)	بق • 96 (0.2)	738 (0.4)	
≤ 30 <sup>th</sup>	234504 (18.6)	160323 (16.2)	64376 (30.2)		186337 (33.1)	26646 (32.0)	48687 (23.7)	
$31^{st} - 70^{th}$	646329 (51.4)	342703 (34.5)	72448 (34.0)		289033 (51.3)	ani 289447 (33.9)	65071 (31.7)	
$> 70^{\text{th}}$	318804 (25.3)	468547 (47.2)	74038 (34.8)		84574 (15.0)	<b>2</b> 7 <b>3</b> 104 (33.2)	88603 (43.2)	
Unknown	57617 (4.6)	20350 (2.1)	1514 (0.7)		2864 (0.5)	and 57 (0.7)	2001 (1.0)	
Residency area				< 0.001		n/ o		< 0.001
Urban	952413 (75.7)	770384 (77.6)	146653 (68.9)		446470 (79.2)	ar 64 <del>0</del> 886 (77.6)	131129 (63.9)	
Rural	305598 (24.3)	221942 (22.4)	66132 (31.1)		116906 (20.8)	<b>189</b> 208 (22.4)	73891 (36.0)	
Unknown	316 (0)	295 (0)	78 (0)		154 (0)	<b>10</b> 356 (0)	80 (0)	
Family history of DM	95941 (7.6)	75935 (7.7)	5822 (2.7)	< 0.001	49880 (8.9)	ogie 78913 (9.2)	8350 (4.1)	< 0.001
Smoking status				< 0.001		at <i>F</i> s.		< 0.001
Never smoker	364532 (29.0)	263588 (26.6)	82287 (38.7)		511139 (90.7)	78 970 (95.1)	197053 (96.1)	
Ex-smoker	181767 (14.5)	261163 (26.3)	60755 (28.5)		19931 (3.5)	1 <u>6</u> 606 (1.4)	1911 (0.9)	
Current	704877 (56.0)	462090 (46.6)	68553 (32.2)		28889 (5.1)	2 <b>9</b> 682 (2.7)	4535 (2.2)	
Unknown	7151 (0.6)	5780 (0.6)	1268 (0.6)		3571 (0.6)	<b>Q</b> <b>Q</b> 192 (0.8)	1601 (0.8)	

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· · · · ·	195416 (19.7)	53336 (25.1)		50809 (9.0)	anc 136577 (16.5)	34821 (17.0)	
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$81.5 \pm 7.9$	83.1 ± 7.2	$83.5 \pm 7.7$	< 0.001	$70.8\pm7.5$	a Ag m B ₱5.4 ± 7.5	$80.2\pm7.9$	
$0.5 \pm 0$	$0.5\pm0$	$0.5 \pm 0$	< 0.001	$0.4 \pm 0$	<b>n</b> .5 ± 0.1	$0.5 \pm 0.1$	
347884.1 ± 17515.9	357304.7 ± 18253.6	$369448.7 \pm 20420.1$	< 0.001	337529.8 ± 21711.5	<b>4</b> 381.8 ± 20926.5	363581.9 ± 24347.6	
$9.7 \pm 0.5$	$10 \pm 0.5$	$10.5 \pm 0.6$	< 0.001	$9.5\pm0.6$	rai = 0.7	$10.8\pm0.8$	
$\begin{array}{r} 431320.6 \pm \\ 300187.2 \end{array}$	471715.6 ± 311853.9	404461.7 ± 255281.4	<0.001	$399669.1 \pm 257236.4$	552165.7± a)01931.2	$630556 \pm 343916.3$	
$121.9\pm12.2$	$124.2 \pm 14.3$	$129.7 \pm 16.3$	< 0.001	$111.7 \pm 11.3$	a 168.6 ± 14.8	$128.3 \pm 16.5$	
$76.4\pm8.9$	$78.6\pm10.0$	$79.4 \pm 10.3$	< 0.001	$70.1 \pm 8.4$	$\frac{1}{10}$ $\frac{74}{9}$ $0 \pm 10.1$	$77.9\pm10.2$	
$25.4 \pm 22.7$	$26.7\pm23.2$	$26.8\pm15.7$	< 0.001	$19.2 \pm 11.2$	ar $29.2 \pm 16.8$	$24.8\pm14.7$	
$28.9\pm28.1$	$28.2\pm23.6$	$23.7\pm16.9$	< 0.001	$15.2 \pm 13.7$	19.3 ± 17.9	$20.7\pm16.8$	
$90.5 \pm 11.1$	$94.7\pm11.7$	$95.8 \pm 11.9$	< 0.001	87.6 ± 9.9 🥌	90.7±10.5	$94.2 \pm 11.1$	
$86.8 \pm 57.1$	$81.3\pm47.8$	$78.5\pm34.4$	< 0.001	$90.0\pm50.0$	<b>Gies</b> 85.8 ± 27.3	$75.8\pm27.1$	
$189 \pm 34.9$	$199.7\pm36.6$	$194.2\pm37.3$	< 0.001	$178.2\pm31.3$	1 <b>9</b> 7.7 ± 36.4	$209.9\pm38.9$	
$139.8\pm96.6$	$154.9\pm101.7$	$134.5\pm82.9$	< 0.001	$82.1 \pm 47.4$	$164.7 \pm 62.3$	$132.9\pm72.9$	
$122.0 \pm 302.3$	$117.9\pm72.2$	$115.6\pm60.1$	< 0.001	$125.8\pm430.0$	$1^{6}_{B}.8 \pm 84.6$	$129.5\pm64.5$	
$53.1 \pm 11.9$	$52.3 \pm 12.1$	$52.7 \pm 12.6$	< 0.001	$61.8\pm12.9$	5 <b>8</b> .3 ± 12.8	$54.8 \pm 12.5$	
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BMJ Open T2DM, type 2 diabetes mellitus; No, number; BMI, body mass index; WC, waist circumference; WHtR, waist height adiusted waist index; WAL viscorel adinasity index; SDP, systelia blood pressure: DDP, diastelia blood pressure: AST, computed an interpretation of the second pressure index; WWI, Lass index; N Ldex; SBP, systolic Ud glucose; eGFR, estima. .poprotein cholesterol T2DM, type 2 diabetes mellitus; No, number; BMI, body mass index; WC, waist circumference; WHR, waist have a strained adjoined to the strained adj weight adjusted waist index; VAI, visceral adiposity index; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase;

	T2DM (n) (n=625715)	Person year	Incidence rate	Model 1	Model 2	Model 3	of Model 4	Model 5
BMI							laro En:	
Q1 (n=1,005,153)	91,517	9,827,735.2	9.3	1	1	1	s reic	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)	2001.21-1.23)	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)	<b>3</b> . <b>3</b> 2 <b>0</b> 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)	<b>∂</b> . <b>2</b> 9 <b>≤</b> 2.27-2.31)	2.31 (2.29-2.33
P for linear trend				< 0.001	< 0.001	< 0.001		< 0.001
WC							dec Prie	
Q1 (n=965,392)	78,371	9,534,939.2	8.2	1	1	1	dat 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)	a) <u>A</u> (1.34-1.36)	1.35 (1.34-1.3
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)	<b>1</b> .73-1.76)	1.76 (1.74-1.73
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)	<b>6</b> 2.51 <b>3</b> 2.48-2.53)	2.52 (2.50-2.54
P for linear trend				< 0.001	< 0.001	< 0.001		< 0.001
WHtR							rain	
Q1 (n=1,014,803)	73,264	10,069,987.3	7.3	1	1	1	n.br	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)	al.34.1.33-1.35)	1.35 (1.33-1.3
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)	<b>G</b> .78 <b>3</b> 1.76-1.80)	1.79 (1.77-1.8
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)	<b>2</b> .54 <b>4</b> 2.52-2.56)	2.54 (2.52-2.5)
P for linear trend				< 0.001	< 0.001	< 0.001	lar <u>4</u> 0.001	< 0.001
VAI							Ine	
Q1 (n=1,014,722)	100,176	9,894,725.8	10.1	1	1	1	<b>10</b> , 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)	<b>a</b> .22 <b>a</b> 1.21-1.23)	1.22 (1.21-1.2)
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)	<b>3</b> .53 <b>3</b> 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	2.19 (2.17-2.2
P for linear trend	1			< 0.001	< 0.001	< 0.001	<b>9</b> 0.001	< 0.001
ABSI							ce I	
Q1 (n=1,014,710)	110,242	9,903,776.6	11.1	1	1	1	<b>Bibi</b> 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 <b>g</b> 1.07-1.09)	1.09 (1.08-1.09
O3 (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 (1.15-1.1

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

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				BM.	J Open		njopen-202 by copyrig		Page 28 of 39
Q4 (n=1,014,465) P for linear trend WWI	210,500	9,222,537.8	22.8	2.06 (2.04-2.07) < 0.001	1.20 (1.19-1.21) < 0.001	1.18 (1.17-1.19) < 0.001	ht, incrt.19561.18-1.20) ft.19560.001 ft.1957	1.18 (1.17-1.19) < 0.001	
O1 (n=1,011,717)	86,064	9,994,386.9	8.6	1	1	1	ος α ς Δ1	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)	<b>в па</b> <b>9.246</b> (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)	el.a0%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)	at 9951.77-1.80)	1.78 (1.76-1.79)	
P for linear trend	,			< 0.001	< 0.001	< 0.001		< 0.001	
							/bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographique ı, Al training, and similar technologies.		







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

338x190mm (300 x 300 DPI)





338x190mm (300 x 300 DPI)

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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

338x330mm (300 x 300 DPI)





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)
40-59

- BMI

-WC

--WWI

ABSI

60-79

**★**-WHtR



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#### Supplementary Figure 1. Flow diagram for selection of study population

### Men and women 20 - 80 years old who had a health exam in 2009 and had no history of following disease (N = 4,317,709)

- Diabetes mellitus (E10-14 or usage of oral hypoglycemic agents)
- Liver disease (K70-77)
- Pancreas disease (K85-87) or pancreatectomy (E89.1)
- Cancer (C00-97)

#### Exclusions (N = 258,818)

- Participants with fasting glucose 126mg/dL at the baseline (n=119,655)
- Participants death at baseline (n=4)
- Missing or outlier variables at baseline (n=139,160)
- Height (n=916)
- Weight (n=2,449)
- Waist circumference (n=29,412)
- Triglyceride (n=38,932)
- High density lipid cholesterol (n=77,483)

#### Participants of Study (N=4,058,891)

- Young adult group (age 20 39) (n=1,821,857)
- Middle aged group (age 40 59) (n= 1,819,071)
- elderly group (age 60 79) (n= 417,963)

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

	Overall (N=	=4,058,891)	
	Non-Diabetes	New onset Diabetes	<i>P</i> -value
No. participants	3,433,176	625,715	
Age, years	$40.9 \pm 12.1$	$47.9 \pm 12.5$	< 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 <sup>2</sup>	$23.2 \pm 3.1$	$24.6 \pm 3.3$	< 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)	

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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	$78.6 \pm 8.6$	$82.7 \pm 8.8$	< 0.001
WHtR	$0.47 \pm 0.05$	$0.50\pm0.05$	< 0.001
ABSI	349,029.1 ± 21,153.0	355,076.7 ± 21,522.2	< 0.001
WWI	$9.9 \pm 0.7$	$10.2 \pm 0.7$	< 0.00
VAI	443,097.2 ± 284,260.8	$565,230.4 \pm 373,858.6$	< 0.001
SBP, mmHg	$120.2 \pm 14.1$	$126.0 \pm 15.6$	< 0.001
DBP, mmHg	75.3 ± 9.7	$78.7\pm10.5$	< 0.001
AST, IU/L	23.8 ± 18.9	$27.0 \pm 24.8$	< 0.001
ALT, IU/L	23.3 ± 22.3	$29.1 \pm 26.1$	< 0.001
FBS, mg/dL	$90.8 \pm 10.7$	$97.6 \pm 12.8$	< 0.001
eGFR	$84.3 \pm 47.9$	$81.7 \pm 39.6$	< 0.001
T-chol, mg/dL	$191.6 \pm 35.8$	$202.0 \pm 38.2$	< 0.001
TG, mg/dL	$122.4 \pm 83.1$	$157.0 \pm 107.4$	< 0.001
LDL-C, mg/dL	$121.2 \pm 253.3$	$121.0 \pm 136.2$	< 0.00
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  $\pm$  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)
<i>P</i> for linear trend	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

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

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	Μ	en	Wor	men	
	Crude	Adjusted*	Crude	Adjusted*	
	HR (95% CI)	HR (95% CI)	HR (95% CI)	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)	

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

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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## **BMJ Open**

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

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Date Submitted by the Author:	25-Jan-2025
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<b>Primary Subject Heading</b> :	Diabetes and endocrinology
Secondary Subject Heading:	Epidemiology, Medical education and training
Keywords:	Body Mass Index, Diabetes Mellitus, Type 2, Preventive Health Services, Obesity

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#### Sex- and Age-Specific Body Composition Indices as Predictors of 1 New-Onset Type 2 Diabetes Mellitus in Koreans: A Nationwide 2 **Cohort Study** 3 Short running title: Body composition index and T2DM risk in Korean 4 5 Min Jeong Park<sup>1\*</sup>, Minwoong Kang<sup>2\*</sup>, Soo Yeon Jang<sup>1</sup>, Ahreum Jang<sup>1</sup>, Eyun Song<sup>1</sup>, Kyung 6 7 Mook Choi<sup>1</sup>, Sei Hyun Baik<sup>1</sup>, Hye Jin Yoo<sup>1</sup> 8 \*These two authors contributed equally to this work 9 10 <sup>1</sup>Division of Endocrinology and Metabolism, Department of Internal Medicine, Korea 11 University College of Medicine, Seoul, Republic of Korea <sup>2</sup> Department of Biomedical Research Center, Korea University Guro Hospital, Seoul, 12 Republic of Korea 13 14 \*Corresponding author: Hye Jin Yoo 15 Division of Endocrinology and Metabolism, Department of Internal Medicine, Korea 16 17 University Guro Hospital, 148, Gurodong-ro, Guro-gu, Seoul 08308, Republic of Korea Tel.: 822-2626-3045, Fax: 822-2626-1096, E-mail: deisy21@korea.ac.kr 18 19 20 Manuscript Word count: 3,370, Abstract word count: 250 21 Number of figures and Tables: Table: 2, Figure: 3 22

1 2		
3 4 5	25	Abstract
6 7	26	Objectives: Hormonal and age-related differences in body composition require tailored
8 9	27	approaches for predicting new-onset type 2 diabetes (NODM). Previous studies lacked in-
10 11	28	depth stratified analyses. We investigate sex- and age-specific body composition indices
12 13 14	29	associated with NODM.
15 16	30	Design and setting: Retrospective, nationwide, population-based cohort study.
17 18	31	Participants: We analyzed 4,058,891 adults who underwent a health examination in year
19 20 21	32	2009 and 10-year follow-up data of from the National Health Insurance Service (NHIS).
22 23	33	Outcome measure: NODM risk stratified by sex and age-groups in 20-year intervals
24 25	34	according to quartiles or per 1standard-deviation (SD) increase in body mass index (BMI),
26 27 28	35	waist circumference (WC), waist-height ratio (WHtR), visceral adiposity index (VAI), a body
28 29 30	36	shape index (ABSI), and weight-adjusted waist index (WWI).
31 32	37	Results: Among the total subjects, 625,715 individuals (15.4%) developed NODM during
33 34 25	38	median 10-year follow-up. The fourth quartile of WHtR showed the highest hazard ratio
35 36 37	39	(HR) for NODM compared to the first quartile among various indices across the entire
38 39	40	population (HR 2.54, 95% CI 2.52-2.57). In men, WHtR consistently exhibited the strongest
40 41	41	association with NODM across all age-groups in analysis based on 1-SD increase; ages 20-
42 43 44	42	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
45 46	43	1.23, 95% CI 1.22–1.24). In women, the most relevant body composition index for NODM
47 48	44	varied by age group; BMI for ages 20-39 (HR 1.48, 95%CI 1.47-1.49), WHtR for ages 40-
49 50	45	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).
51 52 53	46	Conclusion: WHtR was the strongest predictor of NODM in men across all ages, while in
54 55	47	women, the relevant indices varied by age-groups. These findings highlight the need for sex-
56 57	48	and age-specific body composition assessments in predicting NODM risk.
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Keywords: Type 2 diabetes mellitus; anthropometric index; body composition; body mass

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> index; waist circumference 50 51 Strengths and limitation of this study 52 53 The large-scale study using NHIS database represents almost the entire Korean population with 10-year longitudinal follow-up results. 54 Sex and age-groups stratified risk of new onset type 2 diabetes mellitus was 55 • estimated. 56 Due to the lack of laboratory data such as glycated hemoglobin or oral glucose 57 tolerance test results, the severity of diseases could not be evaluated. 58 The study focused on the impact of baseline body composition index on long-term 59 jes 1 outcomes but did not account for changes in body composition during the follow-up 60 61 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<sup>1</sup>. Similarly, a Korean epidemiologic study reported that in 2020, 16.7% of adults $\geq$ 30 years had T2DM, compared to 13.8% in 2018<sup>2</sup>. 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<sup>3</sup>. 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)<sup>4</sup>. VAT release free fatty acids (FFAs), contributing to insulin resistance, whereas SAT serve as a buffer of FFAs<sup>5</sup>. With the recognition of VAT's significance, alternative body composition indices, such as waist circumference (WC), waisthip ratio (WHR), and waist-height ratio (WHtR), have been developed to highlight the hazardous metabolic effect of VAT<sup>6</sup>. 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 <sup>78</sup>. 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 <sup>7</sup>. 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

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86	hypertriglyceridemia, which promotes lipoprotein remodeling and accelerates HDL-chol
87	catabolism <sup>5</sup> . By incorporating the detrimental effect of a high TG/HDL-chol ratio along with
88	increased WC, VAI was formulated and has demonstrated its ability to predict metabolic
89	disease in several studies. Furthermore, recognizing the metabolic risks of sarcopenia,
90	researchers developed the weight-adjusted waist index (WWI) to reflect low muscle mass <sup>10</sup> .
91	WWI was created by standardizing WC with body weight. In several studies, WWI has
92	shown a positive association VAT and a negative association with appendicular skeletal
93	muscle mass, making it a distinctive parameter for effectively capturing reduction in muscle
94	mass, unlike other existing body composition <sup>11</sup> .
95	In previous studies, some indices were investigated in terms of new onset T2DM
96	(NODM) development <sup>12</sup> ; however, a comprehensive comparison of all six indices, including
97	tailored age- and sex-related risk stratification has not been conducted. However, increasing
98	prevalence of sarcopenia exert significant impact on metabolic risk as people get aged. Not
99	only that, but changes in body composition also differ between the sexes. Menopause causes
100	15–20% of additional abdominal fat accumulation and decreasing testosterone in men
101	induces muscle mass reduction <sup>13</sup> . Therefore, we hypothesized that different body
102	composition indices would be associated with NODM between a young muscular population
103	and sarcopenic older population, or between men and women. In the present study, body
104	composition indices regarding prediction of NODM were compared in different age and sex
105	groups using 10-year longitudinal national comprehensive cohort data.
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107	Methods
108	Data source and study population

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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  $\geq$  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 4,058,891 patients 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 <sup>14</sup>. 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). 

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

#### 136 Definition of body composition index and variables

The characteristics of NHIS databases were presented in previous studies <sup>15</sup>. 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<sup>23</sup>, WHtR as WC/height<sup>46</sup>, ABSI as 1000 × WC × weight<sup>-2/3</sup>  $\times$  height<sup>5/6 16</sup>, 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 × BMI)] × TG/0.81 × 1.52/HDL (for women)<sup>8</sup>, and WWI as WC/ $\sqrt{\text{weight}}$ <sup>17</sup>. 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 ( $\geq 15$  cups per week for men,  $\geq 8$  cups per week for women), or unknown. Regular exercise was defined as none, regular (vigorous activity for  $\geq$ 3 days or moderate-intensity activity for  $\geq$  5 days), irregular (other activities including walking), or unknown. 

155	Study	outcomes
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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  $\geq$  126 mg/dL<sup>18</sup>. 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. 

165 Statistical analysis

The baseline characteristics of the study population are presented as mean  $\pm$  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 

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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</li>
were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

184 **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.

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#### 191 **Results**

#### 192 Baseline characteristics of study population and 10-year cumulative incidence of

193 **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–

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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). 

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218Subgroup analysis was performed to examine the best body composition indices219associated with NODM in different sex and 20-year interval age groups. As shown in Figure2202A, in men, WHtR had the highest HR for NODM across all age groups compared with other221indices. The impact of body composition indices on NODM was most significant in men222aged 20-39, showing a gradual reduction in HR with aging. However, in women, the effect of223body composition indices on NODM was greatest in middle-aged group (ages 40–59), with

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4 5	224	HR value numerically higher than those in both young adult women (ages 20-39) and elderly
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Page 13 of 40				В	MJ Open		mjopen-2024-( 1 by copyright,		
2 3 225 4 5	Table 1. Baseli	ine Characteristi	ics of patients with	or without incid	lent T2DN	1	including		
6			Men (N=2,463,811)				Women ( $\mathbf{R} = 1, \mathbf{S} = 5,080$ )		
7		Age 20-39	Age 40-59	Age 60-79	Р	Age 20-39	Ag <b>ka H</b> 0 <b>k</b> 9	Age 60-79	Р
8	Ν	1258327	992621	212863		563530	8 <b>26</b>	205100	
9	BMI, kg/m <sup>2</sup>	$23.9 \pm 3.2$	$24.0 \pm 2.8$	$23.4 \pm 2.8$	< 0.001	$21.4 \pm 3.1$	23 <b>3</b> 23 2 3 2 9	$24.0 \pm 3.1$	< 0.001
10	Underweight	35006 (2.8)	18533 (1.9)	7902 (3.7)		72860 (12.9)	21 🖗 🛱 (🗹.5)	5474 (2.7)	
17	Normal	488605 (38.8)	342039 (34.5)	85976 (40.4)		359414 (63.8)	403.58 <b>E</b> (88.8)	71525 (34.9)	
12	Overweight	315404 (25.1)	284633 (28.7)	58937 (27.7)		67955 (12.1)	2010005(\$4.3)	54453 (26.6)	
14	Obese	419312 (33.3)	347416 (35.0)	60048 (28.2)		63301 (11.2)	2008 5 5 5 ( <b>2</b> 4.3)	73648 (35.9)	
15	Income				< 0.001		and		< 0.001
16	Medical aid	1073 (0.1)	698 (0.1)	487 (0.2)		722 (0.1)	15 <b>86</b> ( <b>G</b> 2)	738 (0.4)	
17	$\leq 30^{th}$	234504 (18.6)	160323 (16.2)	64376 (30.2)		186337 (33.1)	264 🗖 🔁 😫 2.0)	48687 (23.7)	
18	$31^{st} - 70^{th}$	646329 (51.4)	342703 (34.5)	72448 (34.0)		289033 (51.3)	280 <b>4 (3</b> 3.9)	65071 (31.7)	
19	$> 70^{\text{th}}$	318804 (25.3)	468547 (47.2)	74038 (34.8)		84574 (15.0)	274	88603 (43.2)	
20	Residency area				< 0.001		9, × <mark>)</mark>		< 0.001
21	Urban	952413 (75.7)	770384 (77.6)	146653 (68.9)		446470 (79.2)	6408 6 (27.6)	131129 (63.9)	
22	Rural	305598 (24.3)	221942 (22.4)	66132 (31.1)		116906 (20.8)	1852 8 (🙀 2.4)	73891 (36.0)	
23 24	Family history of DM	95941 (7.6)	75935 (7.7)	5822 (2.7)	<0.001	49880 (8.9)	75 8 3 (2)	8350 (4.1)	< 0.001
25	Smoking habit				< 0.001		an		< 0.001
26	Never	364532 (29.0)	263588 (26.6)	82287 (38.7)		511139 (90.7)	785 <b>%</b> 0 ( <b>9</b> 5.1)	197053 (96.1)	
27	Ex-smoker	181767 (14.5)	261163 (26.3)	60755 (28.5)		19931 (3.5)	11 <b>63</b> 6 ( <b>þ</b> .4)	1911 (0.9)	
28	Current	704877 (56.0)	462090 (46.6)	68553 (32.2)		28889 (5.1)	22 <b>6</b> 872 ( <b>2</b> .7)	4535 (2.2)	
29	Alcohol intake				< 0.001		tec		< 0.001
30	None	314855 (25.0)	283718 (28.6)	94373 (44.3)		298791 (53.0)	606.934 (43.4)	181677 (88.6)	
31	Moderate	572886 (45.5)	402993 (40.6)	70875 (33.3)		172935 (30.7)	151281 (J.8.3)	14497 (7.1)	
32	Heavy	342328 (27.2)	282280 928.4)	42639 920.0)		76051 (13.5)	48 <b>@</b> 4 ( <b>\$</b> 9)	3793 (1.9)	
33	Exercise				< 0.001		b at		< 0.001
34	None	224755 (17.9)	204722 (20.6)	55883 (26.3)		117228 (20.8)	214703 (26.0)	67356 (32.8)	
35	Irregular	826539 (65.7)	584212 (58.9)	102190 (48.0)		390425 (69.3)	469541 ( <b>ថ្</b> 6.8)	101561 (49.5)	
36	Regular	195008 (15.5)	195416 (19.7)	53336 (25.1)		50809 (9.0)	136577 ( <b>\$</b> 6.5)	34821 (17.0)	
37	WC, cm	$81.5 \pm 7.9$	$83.1 \pm 7.2$	$83.5 \pm 7.7$	< 0.001	$70.8\pm7.5$	75.4 ± <b><u>6</u>.</b> 5	$80.2 \pm 7.9$	< 0.001
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	WHtR	$0.5 \pm 0$	$0.5 \pm 0$	$0.5 \pm 0$	< 0.001	$0.4 \pm 0$	0. <b>ਵ</b> ± <b>હો</b>	$0.5 \pm 0.1$	< 0.001
	ABSI	347884.1±17515.9	357304.7±18253.6	369448.7±20420.1	< 0.001	337529.8±21711.5	34438 <b>🔤</b> 8± <b>20</b> 926.5	363581.9±24347.6	< 0.001
	WWI	$9.7 \pm 0.5$	$10 \pm 0.5$	$10.5 \pm 0.6$	< 0.001	$9.5 \pm 0.6$	19 ± 0.7	$10.8\pm0.8$	< 0.001
	VAI	431320.6±300187.2	471715.6±311853.9	404461.7±255281.4	< 0.001	399669.1±257236.4	512165 <b>9</b> 7±3 <b>9</b> 1931.2	630556±343916.3	< 0.001
	SBP, mmHg	$121.9 \pm 12.2$	$124.2 \pm 14.3$	$129.7 \pm 16.3$	< 0.001	$111.7 \pm 11.3$	11856 🖬 🖥 4.8	$128.3 \pm 16.5$	< 0.001
	DBP, mmHg	$76.4\pm8.9$	$78.6 \pm 10.0$	$79.4 \pm 10.3$	< 0.001	$70.1 \pm 8.4$	74. <b>8 5 19</b> .1	$77.9 \pm 10.2$	< 0.001
	AST, IU/L	$25.4 \pm 22.7$	$26.7 \pm 23.2$	$26.8 \pm 15.7$	< 0.001	$19.2 \pm 11.2$	22 <b>.0 5</b> .8	$24.8 \pm 14.7$	< 0.001
	ALT, IU/L	$28.9 \pm 28.1$	$28.2 \pm 23.6$	$23.7 \pm 16.9$	< 0.001	$15.2 \pm 13.7$	19. <b>a š š</b> 19.9	$20.7 \pm 16.8$	< 0.001
	FBS, mg/dL	$90.5 \pm 11.1$	$94.7 \pm 11.7$	$95.8 \pm 11.9$	< 0.001	$87.6\pm9.9$	91. <b>2 5 10</b> .5	$94.2 \pm 11.1$	< 0.001
	eGFR	$86.8 \pm 57.1$	$81.3 \pm 47.8$	$78.5 \pm 34.4$	< 0.001	$90.0\pm50.0$	81.8 # 27.3	$75.8 \pm 27.1$	< 0.001
	T-chol, mg/dL	$189 \pm 34.9$	$199.7 \pm 36.6$	$194.2 \pm 37.3$	< 0.001	$178.2 \pm 31.3$	197 <b>ද් දී ද</b> 6.4	$209.9 \pm 38.9$	< 0.001
	TG, mg/dL	$139.8 \pm 96.6$	$154.9 \pm 101.7$	$134.5 \pm 82.9$	< 0.001	$82.1 \pm 47.4$	104 <b>3</b> 7 <b>9</b> 82.3	$132.9 \pm 72.9$	< 0.001
	LDL-C,mg/dL	$122.0 \pm 302.3$	$117.9 \pm 72.2$	$115.6 \pm 60.1$	< 0.001	$125.8 \pm 430.0$	119 <b>2 = <u>\$</u>4</b> .6	$129.5 \pm 64.5$	< 0.001
	HDL-C,mg/dL	$53.1 \pm 11.9$	52.3 ± 12.1	$52.7 \pm 12.6$	< 0.001	$61.8 \pm 12.9$	58 a 5 0.8	$54.8 \pm 12.5$	< 0.001
226	Data were presen				mi				

Data were presented Mean  $\pm$  SD or n (%)

 T2DM, type 2 diabetes mellitus; No, number; BMI, body mass index; WC, waist circumference; WHtR, waist height ratio; ABS, a body shape index; WWI, weight adjusted waist index; VAI, visceral adiposity index; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminarasferase; ALT, alanine aminotransferase; DDT, utastofic blood pressure, AST, asparate annual failure ining, and similar technologies. 13 FBG, fasting blood glucose; eGFR, estimated glomerular filtration rate; T-chol, total- cholesterol; LDL-C, low-density ligopretien cholesterol; HDL-C, high-density lipoprotein cholesterol

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9,031,690.8	26.0	2 90 (2 79 2 92)	1.52 (1.50-1.55)	1.53 (1.52-1.5)	$\Box^{1.52(1.51-1.54)}$	1.54 (1.5
		2.80 (2.78-2.82)	2.30 (2.28-2.31)	2.31 (2.29-2.3)	<b>§</b> 2.29 (2.27-2.31)	2.31 (2.2
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9,534,939.2	8.2	1	1	1 dar (		1
10,600,570.5	13.1	1.60 (1.58-1.61)	1.36 (1.35-1.37)	1.35 (1.34-1.2)	<b>B</b> 1.35 (1.34-1.36)	1.35 (1.3
9,698,250.5	18.2	2.22 (2.20-2.24)	1.77 (1.75-1.79)	1.76 (1.74-1. 🗃 迟	1.75 (1.73-1.76)	1.76 (1.7
8,593,406.1	27.0	3.30 (3.27-3.32)	2.55 (2.53-2.57)	2.52 (2.50-2. <b>5</b> )	2.51 (2.48-2.53)	2.52 (2.5
		< 0.001	< 0.001	< 0.001	< 0.001	< 0.0
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10,069,987.3	7.3	1	1		1	1
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 (1.3
9,499,797.5	18.1	2.49 (2.47-2.51)	1.80 (1.79-1.82)	1.79 (1.78-1.8 <b>4</b> )	<b>6</b> 1.78 (1.76-1.80)	1.79 (1.7
9,014,313.2	29.2	4.03 (4.00-4.06)	2.58 (2.55-2.60)	2.56 (2.54-2.5)	<b>2</b> .54 (2.52-2.56)	2.54 (2.5
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9,894,725.8	10.1	1	1	1 hn	<b>10</b> 1	1
9,780,992.2	12.8	1.26 (1.25-1.27)	1.23 (1.22-1.24)	1.22 (1.21-1.28)	81.22 (1.21-1.23)	1.22 (1.2
9,584,646.6	17.0	1.68 (1.67-1.70)	1.56 (1.55-1.57)	1.53 (1.52-1.🙀)	<b>25</b> 1.53 (1.51-1.54)	1.53 (1.5
9,166,801.7	25.9	2.56 (2.54-2.58)	2.27 (2.25-2.28)	2.20 (2.18-2.21)	<b>2</b> .18 (2.17-2.20)	2.19 (2.1
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# BMJ Open Table 2. Hazard ratios (HRs) and 95% Confidence interval (95%CI) of NODM across quartiles of body composition indices in total

				BMJ Ope	n	d by copy	omiopen-2	
						right, i	2024-09	
O2 (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 (1.07-1.0)	<b>35</b> 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. <b>B</b> )	<b>o</b> 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 g	∞ < 0.001	< 0.001
WWI						ses	arc	
Q1 (n=1,011,717)	86,064	9,994,386.9	8.6	1	1	1 relig	h 201	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) P	5 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 (1.49-1.57)	<b>8</b> 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) 🖉	<b>M</b> 1.79 (1.77-1.80)	1.78 (1.76-1.79)
P for linear trend	,			< 0.001	< 0.001	× 20.001 د 10 × 20	<b>o</b> a < 0.001	< 0.001
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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 245 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).

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**Discussion** 

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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<sup>19</sup>, 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 <sup>20</sup>. 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 <sup>467</sup>. Laboratory data such as TG and HDL-C were adopted in the VAI 

equation <sup>8</sup> and development of WWI was used to discriminate between muscle and fat mass 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 <sup>21</sup>. In the meta-analysis of 31 studies, WHtR was significantly associated with T2DM compared with BMI in both men and women<sup>22</sup>. In another meta-analysis including 22 prospective studies, WHtR and WC showed similar predictability for DM and were superior to BMI<sup>23</sup>. Furthermore, Maryam et al. reported WC predicted T2DM development better than BMI, ABSI, WHtR, and WHR in their prospective study with 9,354 subjects <sup>24</sup>. In a study that included 3,461 Chinese participants, VAI was reported an effective index for DM prediction compared with WC, WHtR, and BMI<sup>25</sup>. 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 <sup>26</sup>, and in other studies, the number of parity was positively associated with abdominal obesity <sup>27</sup>. Furthermore, in previous research, fat mass volume doubled, and

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lean mass decreased at the start of menopause with reduction in estrogen level <sup>27</sup>. In several
studies, body fat distribution was shown to change from the extremities to the trunk during

the perimenopausal period <sup>28</sup>. These undesirable body composition changes are strongly

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associated with cardiometabolic disease risks, increasing incidence of DM, dyslipidemia, and 310 cardiovascular disease (CVD) in postmenopausal women<sup>29</sup>. Therefore, the significant 311 increase of DM incidence in women in the 40–59 group compared with the 20–39 group in 312 the present study was likely because women undergo a decrease in estrogen in their mid-to-313 314 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 315 young women, however in the middle-aged women, that of WHtR showed the highest HR for 316 NODM. This result may be due to visceral fat accumulation and undesirable body 317 compositional changes after women experience pregnancy and delivery through their 40's 318 and menopause in their 50's. 319 However, in men, the WHtR had the closest relationship with NODM across all age 320 groups. In numerous literatures, WHtR was shown superior to BMI for DM prediction <sup>23 25</sup>. 321 The reason why WHtR is better than BMI for DM prediction is due to the inclusion of 322 visceral obesity in the WHtR index. Visceral adiposity induces insulin resistance, 323 dysregulation of adipokines, and malfunction of adipocytes, resulting in NODM <sup>30</sup>. However, 324 the reason WHtR is better than WC for NODM prediction remains unknown although several 325 theories have been suggested. A plausible explanation is short stature, which is largely due to 326 genetic factors, might affect visceral obesity, insulin resistance, and vulnerability to 327 metabolic diseases <sup>31</sup>. In addition, because WHtR adjusts for the effect of height on WC, it 328 329 reflects a different body fat distribution and muscle mass based on individual height <sup>13</sup>. Notably, in the young adult group, BMI of women and WHtR of men had the highest 330 HRs for NODM with 1SD increase, indicating body composition associated with NODM 331 differs between sexes. Women store excess fat first in a metabolically healthy fat region such 332 as subcutaneous fat and lower extremities and then in visceral adipose tissue (VAT), whereas 333 19

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men predominantly accumulate fat more rapidly as VAT <sup>32</sup>. 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 

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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. 

#### 367 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.

1 2			
3 4 5	376	Refe	erences
6 7	377	1.	Sun H, Saeedi P, Karuranga S <i>, et al.</i> IDF Diabetes Atlas: Global, regional and country-level
8	378		diabetes prevalence estimates for 2021 and projections for 2045. <i>Diabetes Res Clin Pract</i>
9 10	379		2022;183:109119.
11	380	2.	Bae JH, Han KD, Ko SH <i>, et al.</i> Diabetes Fact Sheet in Korea 2021. <i>Diabetes Metab J</i>
12 12	381		2022;46:417-26.
14	382	3.	Eknoyan G. Adolphe Quetelet (1796-1874)the average man and indices of obesity.
15 16	383		Nephrol Dial Transplant 2008;23:47-51.
10	384	4.	Fox CS, Massaro JM, Hoffmann U, et al. Abdominal visceral and subcutaneous adipose
18	385		tissue compartments: association with metabolic risk factors in the Framingham Heart
19 20	386		Study. <i>Circulation</i> 2007;116:39-48.
21	387	5.	Shah RV, Murthy VL, Abbasi SA, et al. Visceral adiposity and the risk of metabolic
22 23	388		syndrome across body mass index: the MESA Study. JACC Cardiovasc Imaging
24	389		2014;7:1221-35.
25 26	390	6.	Price GM, Uauy R, Breeze E, et al. Weight, shape, and mortality risk in older persons:
27	391		elevated waist-hip ratio, not high body mass index, is associated with a greater risk of
28 29	392		death. Am J Clin Nutr 2006;84:449-60.
30	393	7.	Krakauer NY, Krakauer JC. A new body shape index predicts mortality hazard
31 22	394		independently of body mass index. <i>PLoS One</i> 2012;7:e39504.
32 33	395	8.	Amato MC, Giordano C, Galia M, et al. Visceral Adiposity Index: a reliable indicator of
34 25	396		visceral fat function associated with cardiometabolic risk. <i>Diabetes Care</i> 2010;33:920-2.
35 36	397	9.	Chauhan A, Singhal A, Goyal P. TG/HDL Ratio: A marker for insulin resistance and
37	398		atherosclerosis in prediabetics or not? J Family Med Prim Care 2021;10:3700-5.
38 39	399	10.	Power GA, Dalton BH, Rice CL. Human neuromuscular structure and function in old age: A
40	400		brief review. J Sport Health Sci 2013;2:215-26.
41 42	401	11.	Park MJ, Hwang SY, Kim NH <i>, et al.</i> A Novel Anthropometric Parameter, Weight-Adjusted
43	402		Waist Index Represents Sarcopenic Obesity in Newly Diagnosed Type 2 Diabetes Mellitus.
44 45	403		J Obes Metab Syndr 2023;32:130-40.
45 46	404	12.	Li WC, Chen IC, Chang YC, et al. Waist-to-height ratio, waist circumference, and body
47	405		mass index as indices of cardiometabolic risk among 36,642 Taiwanese adults. Eur J Nutr
48 49	406		2013;52:57-65.
50	407	13.	Kodoth V, Scaccia S, Aggarwal B. Adverse Changes in Body Composition During the
51 52	408		Menopausal Transition and Relation to Cardiovascular Risk: A Contemporary Review.
53	409		Womens Health Rep (New Rochelle) 2022;3:573-81.
54 55	410	14.	Chen L, Nelson DR, Zhao Y, et al. Relationship between muscle mass and muscle strength,
56	411		and the impact of comorbidities: a population-based, cross-sectional study of older adults
57 58	412		in the United States. <i>BMC Geriatr</i> 2013;13:74.
59 60			22

Page 24 of 40

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3			
4 5	413	15.	Chang Bae Chun SYK, Jun Young Lee, Sang Yi Lee. Republic of Korea: health system
6	414		review 2009. Health Systems in Transition 2009;11.
7 8	415	16.	Christakoudi S, Tsilidis KK, Muller DC, et al. A Body Shape Index (ABSI) achieves better
9	416		mortality risk stratification than alternative indices of abdominal obesity: results from a
10 11	417		large European cohort. <i>Sci Rep</i> 2020;10:14541.
12	418	17.	Park Y, Kim NH, Kwon TY, et al. A novel adiposity index as an integrated predictor of
13	419		cardiometabolic disease morbidity and mortality. Sci Rep 2018;8:16753.
14 15	420	18.	Roh E, Noh E, Hwang SY, et al. Increased Risk of Type 2 Diabetes in Patients With Thyroid
16	421		Cancer After Thyroidectomy: A Nationwide Cohort Study. J Clin Endocrinol Metab
17 18	422		2022;107:e1047-e56.
19	423	19.	Bray GA, Popkin BM. Dietary sugar and body weight: have we reached a crisis in the
20 21	424		epidemic of obesity and diabetes?: health be damned! Pour on the sugar. <i>Diabetes Care</i>
22	425		2014;37:950-6.
23 24	426	20.	Laiteerapong N, Ham SA, Gao Y <i>, et al.</i> The Legacy Effect in Type 2 Diabetes: Impact of
2 <del>4</del> 25	427		Early Glycemic Control on Future Complications (The Diabetes & Aging Study). Diabetes
26 27	428		Care 2019;42:416-26.
27 28	429	21.	Mi SQ, Yin P, Hu N, et al. BMI, WC, WHtR, VFI and BFI: which indictor is the most efficient
29	430		screening index on type 2 diabetes in Chinese community population. Biomed Environ Sci
30 31	431		2013;26:485-91.
32	432	22.	Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist
33 34	433		circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-
35	434		analysis. <i>Obes Rev</i> 2012;13:275-86.
36 37	435	23.	Browning LM, Hsieh SD, Ashwell M. A systematic review of waist-to-height ratio as a
38	436		screening tool for the prediction of cardiovascular disease and diabetes: $0.5$ could be a
39 40	437		suitable global boundary value. <i>Nutr Res Rev</i> 2010;23:247-69.
40 41	438	24.	Saberi-Karimian M, Mansoori A, Bajgiran MM <i>, et al.</i> Data mining approaches for type 2
42	439		diabetes mellitus prediction using anthropometric measurements. J Clin Lab Anal
43 44	440		2023;37:e24798.
45	441	25.	Chen C, Xu Y, Guo ZR, et al. The application of visceral adiposity index in identifying type
46 47	442		2 diabetes risks based on a prospective cohort in China. <i>Lipids Health Dis</i> 2014;13:108.
48	443	26.	Cho GJ, Yoon HJ, Kim EJ, et al. Postpartum changes in body composition. Obesity (Silver
49 50	444		<i>Spring)</i> 2011;19:2425-8.
51	445	27.	Gunderson EP, Sternfeld B, Wellons MF, et al. Childbearing may increase visceral adipose
52	446		tissue independent of overall increase in body fat. Obesity (Silver Spring) 2008;16:1078-84.
53 54	447	28.	Dmitruk A, Czeczelewski J, Czeczelewska E, et al. Body composition and fatty tissue
55	448		distribution in women with various menstrual status. Rocz Panstw Zakl Hig 2018;69:95-
56 57	449		101.
58			
59 60			23

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4 5 6	450 451	29. Tanaka KI, Kanazawa I, Sugimoto T. Reduced muscle mass and accumulation of visceral fat
7	451	with type 2 diabetes mellitus. <i>Diabetes Res Clin Pract</i> 2016;122:141-7
8 9	453	30. Tchernof A, Després JP. Pathophysiology of human visceral obesity: an update. <i>Physiol Rev</i>
10 11	454	2013;93:359-404.
12	455	31. Koch E, Romero T, Romero CX, et al. Early life and adult socioeconomic influences on
13 14	456	mortality risk: preliminary report of a 'pauper rich' paradox in a Chilean adult cohort. Ann
15	457	<i>Epidemiol</i> 2010;20:487-92.
16 17	458	32. Power ML, Schulkin J. Sex differences in fat storage, fat metabolism, and the health risks
18	459	from obesity: possible evolutionary origins. <i>Br J Nutr</i> 2008;99:931-40.
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51 52 53	474	The authors declare that they have no competing interests.
54	475	
55 56 57	476	Data availability
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3 4 5	477	Study protocol, raw data that support the findings are available from the corresponding author upon
6 7	478	reasonable request.
8 9	479	
10 11 12	480	Author contribution
13 14 15	481	Conceptualization and design: Hye Jin Yoo., Min Jeong Park, Minwoong Kang.
16 17 18	482	Data acquisition, analysis: Minwoong Kang
19 20 21	483	Data interpretation: Hye Jin Yoo., Min Jeong Park, Minwoong Kang
22 23	484	Writing - original draft: Hye Jin Yoo., Min Jeong Park, Minwoong Kang
24 25 26	485	Writing - review & editing: Ahreum Jang., Soo Yeon Jang., Eyun Song, Kyung Mook Choi, Sei Hyun
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29 30 31	487	Guarantor- Hye Jin Yoo is the guarantor and takes responsibility for the overall content.
32 33	488	Figure legends
34 35 36	489	Figure 1. 10-year incidence of T2DM stratified by 10-year age groups in (A) Men and
37 38	490	(B) Women
39 40	491	
41 42 43	492	Figure 2. HRs of T2DM across quartiles of body composition indices according to 20-year
44 45	493	age group in men (A) and women (B)
46 47 48	494 495	HR, hazard ratio; T2DM, type 2 diabetes mellitus; BMI, body mass index; WC, waist circumference; WHtR, waist height
40 49	496	ratio
50 51	497	
52 53	498	Figure 3. HR of new onset T2DM in fully adjusted model according to 1SD increase of
54 55 56 57	499	anthropometric indices stratified by 20-year age groups in men (A) and women (B)
58 59 60		25

2 3		
4	500	HR, hazard ratio; T2DM, type 2 diabetes mellitus; SD, standard deviation; BMI, body mass index; WC, waist
5	501	circumference; WHtR, waist height ratio; VAI, visceral adiposity index; WWI, weight adjusted waist index; ABSI, A body
6 7	502	shape index
8	503	
9 10	505	
10 11 12	504	Table legends
14 15 16	505	Table 1. Baseline Characteristics of patients with or without incident T2DM
16 17 18	506	Table 2. Hazard ratios (HRs) and 95% Confidence interval (95%CI) of T2DM across
19 20	507	quartiles of body composition indices in total population
21 22	508	BMI, body mass index; WC, waist circumference; WHtR, waist height ratio; VAI, visceral adiposity index; WWI, weight
22 23	509	adjusted waist index; ABSI, A body shape index
24 25 26 27 28 29 30 31 23 34 35 37 38 30 41 42 43 45 46 47 48 950 51 52 53 54 55 56 57 58 960		







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308x400mm (300 x 300 DPI)

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Table 1. Baseline Characteristics of patients with or without incident T2DM									
		Men (N=2,463,811)			Women 2 N=1,595,080)				
	Age 20-39	Age 40-59	Age 60-79	<i>p</i> -value	Age 20-39	s Enge s Age 40-59	Age 60-79	<i>p</i> - value	
No. participants	1258327	992621	212863		563530	eigne 2826450	205100		
BMI, kg/m <sup>2</sup>	$23.9 \pm 3.2$	$24.0 \pm 2.8$	$23.4 \pm 2.8$	< 0.001	$21.4 \pm 3.1$	ed to 10.2 ± 2.9	$24.0 \pm 3.1$	< 0.00	
Underweight	35006 (2.8)	18533 (1.9)	7902 (3.7)		72860 (12.9)	te 23 004 (2.5)	5474 (2.7)		
Normal	488605 (38.8)	342039 (34.5)	85976 (40.4)		359414 (63.8)	ag a 02 581 (48.8)	71525 (34.9)		
Overweight	315404 (25.1)	284633 (28.7)	58937 (27.7)		67955 (12.1)	$a_{1} = 0$	54453 (26.6)		
Obese	419312 (33.3)	347416 (35.0)	60048 (28.2)		63301 (11.2)	ata 2008856 (24.3)	73648 (35.9)		
Income percentile				< 0.001		ninii		< 0.00	
Medical aid	1073 (0.1)	698 (0.1)	487 (0.2)		722 (0.1)	<b>9</b> 96 (0.2)	738 (0.4)		
≤ 30 <sup>th</sup>	234504 (18.6)	160323 (16.2)	64376 (30.2)		186337 (33.1)	<b>2</b> <b>1</b> <b>2</b> <b>6</b> <b>4</b> 6 (32.0)	48687 (23.7)		
$31^{st}-70^{th}$	646329 (51.4)	342703 (34.5)	72448 (34.0)		289033 (51.3)	ani 289447 (33.9)	65071 (31.7)		
$> 70^{\text{th}}$	318804 (25.3)	468547 (47.2)	74038 (34.8)		84574 (15.0)	27 <b>2</b> 104 (33.2)	88603 (43.2)		
Unknown	57617 (4.6)	20350 (2.1)	1514 (0.7)		2864 (0.5)	and \$657 (0.7)	2001 (1.0)		
Residency area				< 0.001		simi		< 0.00	
Urban	952413 (75.7)	770384 (77.6)	146653 (68.9)		446470 (79.2)	ar 640 886 (77.6)	131129 (63.9)		
Rural	305598 (24.3)	221942 (22.4)	66132 (31.1)		116906 (20.8)	189208 (22.4)	73891 (36.0)		
Unknown	316 (0)	295 (0)	78 (0)		154 (0)	<b>0</b> ,356 (0)	80 (0)		
Family history of DM	95941 (7.6)	75935 (7.7)	5822 (2.7)	< 0.001	49880 (8.9)	<b>ŭ</b> 789913 (9.2)	8350 (4.1)	< 0.00	
Smoking status				< 0.001		s. at A		< 0.00	
Never smoker	364532 (29.0)	263588 (26.6)	82287 (38.7)		511139 (90.7)	78 <b>9</b> 970 (95.1)	197053 (96.1)		
Ex-smoker	181767 (14.5)	261163 (26.3)	60755 (28.5)		19931 (3.5)	19606 (1.4)	1911 (0.9)		
Current	704877 (56.0)	462090 (46.6)	68553 (32.2)		28889 (5.1)	20682 (2.7)	4535 (2.2)		
Unknown	7151 (0.6)	5780 (0.6)	1268 (0.6)		3571 (0.6)	<b>6</b> 192 (0.8)	1601 (0.8)		

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Heavy drinking None						-20) yrig		
Heavy drinking None						24-( jht,		
None				< 0.001		093598 incluc		
	314855 (25.0)	283718 (28.6)	94373 (44.3)		298791 (53.0)	60 <b>9</b> 534 (73.4)	181677 (88.6)	
Moderate	572886 (45.5)	402993 (40.6)	70875 (33.3)		172935 (30.7)	<b>ថ្មី</b> 15 <b>व</b> 281 (18.3)	14497 (7.1)	
Heavy	342328 (27.2)	282280 928.4)	42639 920.0)		76051 (13.5)	us <u>5</u> ,94 (5.9)	3793 (1.9)	
Unknown	28258 (2.3)	23630 (2.4)	4976 92.3)		15753 (2.8)	s sei 12841 (2.4)	5133 (2.5)	
Regular exercise				< 0.001		025. Inem		
None	224755 (17.9)	204722 (20.6)	55883 (26.3)		117228 (20.8)	ີ່ອີ້ສູ່ໄອ້703 (26.0)	67356 (32.8)	
Irregular	826539 (65.7)	584212 (58.9)	102190 (48.0)		390425 (69.3)	<b>5</b> 41 (56.8)	101561 (49.5)	
Regular	195008 (15.5)	195416 (19.7)	53336 (25.1)		50809 (9.0)	and 1345577 (16.5)	34821 (17.0)	
Unknown	12025 (1.0)	8271 (0.8)	1454 (0.7)		5068 (0.9)	dat (0.7)	1362 (0.7)	
WC, cm	$81.5\pm7.9$	83.1 ± 7.2	$83.5 \pm 7.7$	< 0.001	$70.8\pm7.5$	a B ₱5.4 ± 7.5	$80.2\pm7.9$	
WHtR	$0.5\pm0$	$0.5 \pm 0$	$0.5 \pm 0$	< 0.001	$0.4 \pm 0$	<b>5</b> ±0.1	$0.5 \pm 0.1$	
ABSI	347884.1 ± 17515.9	357304.7 ± 18253.6	$369448.7 \pm 20420.1$	< 0.001	337529.8 ± 21711.5	<b>9 4 3 4 3 4 3 8 1</b> .8 ± <b>3 0 9 26</b> .5	363581.9 ± 24347.6	
WWI	$9.7\pm0.5$	$10 \pm 0.5$	$10.5 \pm 0.6$	< 0.001	$9.5\pm0.6$	$\frac{1}{20}0 \pm 0.7$	$10.8\pm0.8$	
VAI	431320.6 ± 300187.2	471715.6 ± 311853.9	404461.7 ± 255281.4	<0.001	399669.1 ± 257236.4	a 201931.2	$630556 \pm 343916.3$	
SBP, mmHg	$121.9 \pm 12.2$	$124.2 \pm 14.3$	$129.7\pm16.3$	<0.001	$111.7 \pm 11.3$	nd $168.6 \pm 14.8$	$128.3\pm16.5$	
DBP, mmHg	$76.4\pm8.9$	$78.6\pm10.0$	$79.4\pm10.3$	< 0.001	$70.1 \pm 8.4$	$74.0 \pm 10.1$	$77.9\pm10.2$	
AST, IU/L	$25.4 \pm 22.7$	$26.7\pm23.2$	$26.8 \pm 15.7$	< 0.001	$19.2 \pm 11.2$	$29.2 \pm 16.8$	$24.8\pm14.7$	
ALT, IU/L	$28.9\pm28.1$	$28.2 \pm 23.6$	$23.7 \pm 16.9$	< 0.001	$15.2 \pm 13.7$	19.3 ± 17.9	$20.7\pm16.8$	
FBS, mg/dL	$90.5 \pm 11.1$	$94.7 \pm 11.7$	$95.8 \pm 11.9$	< 0.001	87.6 ± 9.9	90.7±10.5	$94.2 \pm 11.1$	
eGFR	$86.8 \pm 57.1$	$81.3\pm47.8$	$78.5\pm34.4$	< 0.001	$90.0\pm50.0$	<b>gie</b> 83.8 ± 27.3	$75.8\pm27.1$	
T-chol, mg/dL	$189 \pm 34.9$	$199.7 \pm 36.6$	$194.2\pm37.3$	< 0.001	$178.2\pm31.3$	1 <b>9</b> 7.7 ± 36.4	$209.9\pm38.9$	
TG, mg/dL	$139.8 \pm 96.6$	$154.9\pm101.7$	$134.5\pm82.9$	< 0.001	$82.1\pm47.4$	1 <b>9</b> 4.7 ± 62.3	$132.9\pm72.9$	
LDL-C, mg/dL	$122.0\pm302.3$	$117.9 \pm 72.2$	$115.6\pm60.1$	< 0.001	$125.8\pm430.0$	$1 \frac{6}{10}.8 \pm 84.6$	$129.5\pm64.5$	
HDL-C, mg/dL	$53.1 \pm 11.9$	$52.3\pm12.1$	$52.7 \pm 12.6$	< 0.001	$61.8\pm12.9$	5 <b>8</b> .3 ± 12.8	$54.8 \pm 12.5$	
Data were presented Mea	$n \pm SD \text{ or } n (\%)$					ogra		
						phic		

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BMJ Open T2DM, type 2 diabetes mellitus; No, number; BMI, body mass index; WC, waist circumference; WHtR, waist height adiusted waist index; WAL viscorel adinasity index; SDP, systelia blood pressure: DDP, diastelia blood pressure: AST, computed an interpretation of the second pressure index; WWI, Less index; W Less; SBP, systolic , Jopprotein cholesterol The second secon weight adjusted waist index; VAI, visceral adiposity index; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase;

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del

population								
	T2DM (n) (n=625715)	Person year	Incidence rate	Model 1	Model 2	Model 3	of Monodel 4	Model 5
BMI							laro En:	
Q1 (n=1,005,153)	91,517	9,827,735.2	9.3	1	1	1	seic seic	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)	2001.21-1.23)	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)	<b>6</b> . <b>8</b> 2 <b>0</b> (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)	<b>∂</b> . <b>2</b> 9 <b>₹</b> 2.27-2.31)	2.31 (2.29-2.33)
P for linear trend				< 0.001	< 0.001	< 0.001		< 0.001
WC							ndec erie	
Q1 (n=965,392)	78,371	9,534,939.2	8.2	1	1	1	d fro dat	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)	<b>a b 1</b> .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)	<b>1</b> .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)	<b>2</b> .51 <b>2</b> .48-2.53)	2.52 (2.50-2.54)
P for linear trend				< 0.001	< 0.001	< 0.001		< 0.001
WHtR							rair	
Q1 (n=1,014,803)	73,264	10,069,987.3	7.3	1	1	1	n.b 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)	al.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)	<b>d</b> .78 <b>2</b> 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)	<b>1</b> .54 <b>0</b> 2.52-2.56)	2.54 (2.52-2.57)
P for linear trend				< 0.001	< 0.001	< 0.001	ar ≤0.001	< 0.001
VAI							Ine	
Q1 (n=1,014,722)	100,176	9,894,725.8	10.1	1	1	1	<b>10</b> , 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)	<b>a</b> .22 <b>%</b> 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)	<b>9</b> .53 <b>6</b> 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	1			< 0.001	< 0.001	< 0.001	<b>g</b> <b>9</b> 0.001	< 0.001
ABSI							Се	
Q1 (n=1,014,710)	110,242	9,903,776.6	11.1	1	1	1	<b>Bib</b> 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 <b>8</b> 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)	1.158.1.14-1.16)	1.16 (1.15-1.17)
							<u> </u>	

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

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1 2 3 4 5	Q4 (n=1,014,465) P for linear trend	210,500	9,222,537.8	22.8	2.06 (2.04-2.07) < 0.001	1.20 (1.19-1.21) < 0.001	1.18 (1.17-1.19) < 0.001	arright, inct.1958.1.18-1.20)	1.18 (1.17-1.19) < 0.001	
6	WWI							18 1 foi		
7	Q1 (n=1,011,717)	86,064	9,994,386.9	8.6	1	1	1	u Ba	1	
8	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)	<b>9 2 4 4 1</b> .23-1.25)	1.25 (1.23-1.26)	
9	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)	<u>මූ ස</u> ී (කි. 48-1.51)	1.50 (1.49-1.51)	
10	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)	a 49:01.77-1.80)	1.78 (1.76-1.79)	
11	P for linear trend				< 0.001	< 0.001	< 0.001		< 0.001	
13 14 15 16 17	Model 1: Unadjusted Model 2: Adjusted for age, sex Model 3: Adjusted for age, sex, smoking habit, alcohol drinking, physical activity, family history of DM 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 Model 5: 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 Model 5: 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 Model 5: 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 Model 5: 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 Model 5: 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 Model 5: 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 Model 5: 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 Model 5: 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, f									
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#### Supplementary Figure 1. Flow diagram for selection of study population

### Men and women 20 - 80 years old who had a health exam in 2009 and had no history of following disease (N = 4,317,709)

- Diabetes mellitus (E10-14 or usage of oral hypoglycemic agents)
  - Liver disease (K70-77)
  - Pancreas disease (K85-87) or pancreatectomy (E89.1)
  - Cancer (C00-97)

#### Exclusions (N = 258,818)

- Participants with fasting glucose 126mg/dL at the baseline (n=119,655)
- Participants death at baseline (n=4)
- Missing or outlier variables at baseline (n=139,160)
  - Height (n=916)
- Weight (n=2,449)
- Waist circumference (n=29,412)
- Triglyceride (n=38,932)High density lipid cholesterol (n=77,483)
- And An A A A

#### Participants of Study (N=4,058,891)

- Young adult group (age 20 39) (n=1,821,857)
- Middle aged group (age 40 59) (n= 1,819,071)
- elderly group (age 60 79) (n=417,963)

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31st-70th

Unknown Residency area

> 70th

Urban

Rural

Unknown

Smoking status

Ex-smoker

Current

Unknown

Heavy drinking

Moderate

None

Heavy

Never smoker

Family history of DM

1 2

	Overall (N=	4,058,891)		
	Non-Diabetes	New onset Diabetes	<i>P</i> -value	
No. participants	3,433,176	625,715		
Age, years	$40.9 \pm 12.1$	$47.9 \pm 12.5$	< 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 <sup>2</sup>	$23.2 \pm 3.1$	$24.6\pm3.3$	< 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	

4,363 (0.1)

808,739 (23.6)

1,444,830 (42.1)

1,096,557 (31.9)

78,687 (2.3)

2,627,635 (76.5)

804,433 (23.4)

1,108 (0)

251,318 (7.3)

1,894,045 (55.2)

443,578 (12.9)

1,073,833 (31.3)

21,720 (0.6)

1,500,879 (43.7)

1,193,151 (34.8)

656,085 (19.1)

951 (0.2)

150,134 (24.0)

251,201 (40.1)

212,113 (33.9)

11,316 (1.8)

460,300 (73.6)

165,244 (26.4)

171 (0)

60,523 (9.7)

310,524 (49.6)

93,555 (15.0)

217,793 (34.8)

3,843 (0.6)

279,069 (44.6)

192,316 (30.7)

139,800 (22.3)

< 0.001

< 0.001

< 0.001

< 0.001

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

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2				
5 4	Unknown	83,061 (2.4)	14,530 (2.3)	
5 6	Regular exercise			< 0.001
7	None	735 567 (21.4)	149 080 (23 8)	
8	Irregular	211 6047 (61 6)	358 421 (57 3)	
9	niegulai	211,0047 (01.0)	556,421 (57.5)	
10	Regular	552,695 (16.1)	113,272 (18.1)	
11	Unknown	28,867 (0.8)	4,942 (0.8)	
12	WC, cm	$78.6 \pm 8.6$	$82.7 \pm 8.8$	< 0.001
14	WHtR	$0.47\pm0.05$	$0.50 \pm 0.05$	< 0.001
15	ABSI	$349,029.1 \pm 21,153.0$	355,076.7 ± 21,522.2	< 0.001
10	WWI	$9.9 \pm 0.7$	$10.2 \pm 0.7$	< 0.001
18	VAI	$443.097.2 \pm 284.260.8$	$565.230.4 \pm 373.858.6$	< 0.001
19 20	SBP. mmHg	$120.2 \pm 14.1$	$126.0 \pm 15.6$	< 0.001
20 21	DBP mmHg	$75.3 \pm 9.7$	$78.7 \pm 10.5$	< 0.001
22		$238 \pm 189$	$27.0 \pm 24.8$	<0.001
23		23.0 ± 10.9	$27.0 \pm 24.0$	-0.001
24	ALT, IU/L	$23.3 \pm 22.3$	$29.1 \pm 26.1$	<0.001
25	FBS, mg/dL	$90.8 \pm 10.7$	$97.6 \pm 12.8$	< 0.001
26	eGFR	$84.3 \pm 47.9$	$81.7 \pm 39.6$	< 0.001
27 28	T-chol. mg/dL	$191.6 \pm 35.8$	$202.0 \pm 38.2$	< 0.001
29	TG mg/dL	122 4 + 83 1	$157.0 \pm 107.4$	<0.001
30		122.1 = 05.1		-0.001
31	LDL-C, mg/dL	$121.2 \pm 253.3$	$121.0 \pm 136.2$	< 0.001
32	HDL-C, mg/dL	55.7 ± 12.8	53.1 ± 12.5	< 0.001
33	$T_{2} D M ( -2 1' 1 )$	11'4 NT 1 DN/T 1 1	$\cdot$ 1 WO $\cdot$ $\cdot$ C	WILLIN

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  $\pm$  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)
<i>P</i> 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

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

	М	en	Women			
	Crude	Adjusted*	Crude	Adjusted*		
	HR (95% CI)	HR (95% CI)	HR (95% CI)	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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