Fluctuations in Waist Circumference Increase the Risk of Diabetes in 61,587 Older Adults: 4 Years' Chort Study

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Research

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Abstract

Purpose: To evaluate the effect of fluctuations in waist circumference (WC), weight, body mass index (BMI) on diabetes incidence in older adults.

Patients and methods: We examined a prospective cohort of 61,587 older adults (age, 60-96 years) who did not have diabetes at study initiation. Data on weight, BMI, and WC were collected and participants were followed-up until 31 December 2019 . The main endpoint was new-onset diabetes. A Cox regression model was used to estimate the risk of diabetes (hazard ratios [HRs] and confidence intervals [CI]) in these participants.

Results: During a mean followed-up of 3.6 years, individuals being overweight (HR [95% CI] 1.87 [1.62-2.17]), obesity (1.41 [1.26-1.59]), abdominal obesity (1.42 [1.28-1.58]), and obesity plus abdominal obesity at baseline (1.93 [1.66-2.25]) had higher risk of diabetes onset. Compared with older adults who "remained normal WC", who "remained abdominally obese" (HR=1.66), "became abdominally obese"(HR=1.58) and "achieved normal WC" (HR=1.36) were also significantly associated with diabetes onset,as well as increase in WC >3 cm or >5% compared with baseline level . Weight gain or loss >6 kg or weight gain >5%; increase or decrease in BMI >2 kg/m2 or an increase in BMI >10% were associated with a higher diabetes risk. Diabetes risk reduced by 19% in overweight older adults who exercised daily.

Conclusion: For old adults, waist circumference, BMI and healthy weight maintenance reduce diabetes risk. The findings may provide evidence for developing guidelines of proper weight and waist circumference control for older adults.

Introduction

Diabetes is a chronic non-communicable disease, and its prevalence is rapidly increasing globally. Diabetes causes various health issues and contributes to a huge economic burden due to its serious long-term complications. The prevalence of diabetes in Chinese adults was 12.8%, suggesting that diabetes is a serious public health concern in China.[1]

The prevalence of overweight and obesity in Chinese adults tripled from 11.7–29.2% between 1991 and 2009.[2] Overweight, obesity, and abdominal obesity are strong risk factors for diabetes in all age groups. In a 23-year-long prospective study of British men, increased body mass index(BMI) accounted for 26% of the increased incidence of type 2 diabetes(T2DM), suggesting a strong link between obesity and diabetes risk.[3]

Little is known about how the fluctuations in waist circumference (WC) and body weight changes affect diabetes risk in older adults. In older adults, a decline in organ function and changes in body composition can cause serious complications, resulting in higher morbidity and mortality. The risk of diabetes in older adults may therefore differ from that in young and middle-aged populations. China, with its increasingly ageing population, has a diabetes prevalence of 20.4% among older adults.[4] Thus, a better understanding of the association between diabetes incidence and WC, weight, BMI, and the changes in these parameters in older adults is necessary to develop better individualised weight management strategies for older adults.

In this study, we aimed to examine the effect of WC, weight, BMI, and the changes in these parameters as well as the effect of physical activity on diabetes incidence in older individuals.

Material And Methods

Study population and examinations

Participants in our study were recruited in 2015.1-2015.12 from among older adults aged 60 years and above living in Tianjin Binhai New Area, a new industrialised coastal special zone located in north-eastern China that has relatively good economic conditions and is urbanised. The participants were local residents from 37 different neighbourhood committees who underwent annual physical examinations (funded by the Government of Binhai, New Area; free of charge for local residents aged 60 years or older) at nearby community health service centres. Physical examinations included the following anthropometric measurements: weight, height, WC, systolic blood pressure (SBP), and diastolic blood pressure (DBP). Laboratory tests evaluated white blood cell (WBC) and platelet (PLT) counts and haemoglobin (Hgb), total cholesterol (TC), triglyceride (TG), fasting blood glucose (FBG), alanine transaminase (ALT), aspartate transaminase (AST), total bilirubin (TBIL), serum creatinine(Scr), and blood urea nitrogen (BUN) levels. A face-to-face interview was conducted to collect information on sociodemographic characteristics. All physical examination data were recorded in a unified online database.

In total, 162,826 people underwent physical examination in 2015; 79,389 of them without severe cardiovascular disease, cerebrovascular disease, hepatic or renal dysfunction, and malignant tumours were included in our study. We excluded participants with diabetes and those who had self-reported using hypoglycaemic drugs before the study (n = 17625). Therefore, 61,764 individuals were included and followed-up until they were diagnosed with diabetes or until the end of 2018. During the follow-up period, 177 participants who did not undergo annual physical examinations were also excluded. Finally, 61,587 participants were included in the final cohort analysis (median follow-up: 3.6 years, range: 0.3-4.0 years). Informed consent was obtained from all participants, and the study protocol was approved by the Institutional Review Board of Tianjin Medical University Metabolic Diseases Hospital.

Assessment of BMI and WC

Body weight, height, and BMI were measured according to standard protocol. WC was measured as the horizontal girth of the waist through the midpoint between the anterior superior spine and the lower margin of the 12th rib. According to baseline BMI, individuals were categorised as underweight (< 18.5 kg/m^2), normal weight (18.5–23.9 kg/m^2), overweight (24-27.9 kg/m^2), and obese (≥ 28 kg/m^2). According to baseline WC, individuals were categorised as having normal WC (< 85 cm in women or < 90 cm in men) or abdominal obesity (≥ 85 cm in women or ≥ 90 cm in men). The cut-offs were based on the Guidelines for the Prevention and Control of Overweight and Obesity in Chinese Adults. Based on changes in BMI from baseline to the final examination, individuals were classified into four groups: “remained underweight or maintained normal weight” (BMI maintained at < 24 kg/m^2), “became obese or overweight” (BMI changed from < 24 kg/m^2 to ≥ 24 kg/m^2), “became normal or underweight” (BMI changed from ≥ 24 kg/m^2 to < 24 kg/m^2) and “remained obese or overweight” (BMI maintained at ≥ 24 kg/m^2). Based on changes in WC status, participants were classified as “retained normal WC”, “became abdominally obese”, “achieved normal WC”, and “remained abdominally obese”. The variation in weight, BMI, and WC during follow-up was defined as the difference between the values at baseline in 2015 and at diabetes diagnosis or at the final examination in 2018. The percentage change in weight, BMI, and WC during follow-up was defined as the variation divided by the corresponding baseline value × 100. We combined the underweight and normal weight groups in certain analyses because the number of individuals with newly diagnosed diabetes in these groups was low.

Assessment of diabetes

Glucose levels were measured using fasting serum samples (blood samples collected after overnight fasting for at least 8 hours) obtained during the annual physical examinations and using separate FBG tests performed every 3–6 months. A standard 75-g glucose tolerance test was also administered if the preliminary FBG level was higher than 6.1 mmol/L to further examine the 2-hour postprandial plasma glucose value. The presence of diabetes was determined according to the criteria formulated by the World Health Organization(WHO) expert committee on diabetes in 1999 .

Other Covariates

Data on age, sex, smoking habits (never, past smoker, or current smoker), alcohol consumption (never, less than once a week, more than once a week, or everyday), dietary preference (vegetarian diet, animal-based diet, or balanced diet), frequency of physical activity (never, less than once a week, more than once a week, or everyday), and medication history (use of hypoglycaemic agents, anti-hypertensive drugs, statins, and psychotropic drugs) were collected from the initial face-to-face interview. Blood pressure was measured twice on the right arm after at least five minutes of resting, and the average of the two values was recorded. The presence of hypertension was determined based on an SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg, or the use of anti-hypertensive drugs.

Statistical analysis

Continuous variables are described as mean values ± standard deviation (mean ± SD) and categorical variables as numbers and percentages (%). Participants were categorised according to baseline BMI and WC levels; changes in BMI and WC status; variations in weight, BMI, and WC; and the frequency of physical activity. Sex- (male, female) and age-specific (age < 75 years old; age ≥ 75 years old) subgroup analyses were also performed. Time at risk was calculated as the interval in days from the date of the initial examination in 2015 to the date of diabetes diagnosis or the date of the final examination in 2018. Cox proportional hazards regression models were used to estimate the hazard ratios (HRs) and 95%

confidence intervals (95% CIs) for new-onset diabetes, using values in individuals with normal BMI and WC; those with stable weight, BMI, and WC; and those who did not exercise regularly as the reference. The regression models were adjusted for confounders, including baseline age, ALT and TBIL levels, alcohol consumption, and statin use. All statistical analyses were performed using SPSS version 22.0. All P-values were based on 2-sided tests, and $P < 0.05$ was considered statistically significant.

Results

During a median follow-up of 3.6 years, among the 61,587 older individuals without diabetes at baseline, 1,414 new-onset cases of diabetes were identified (6.4/1000 person-years); the annual incidence of diabetes was 0.76%.

Compared with older individuals without diabetes, those diagnosed with diabetes were younger; had a higher prevalence of hypertension; used statins more frequently; had a higher baseline BMI, WC, and TG, FBG, ALT, and AST level; had lower TBIL levels; and had a lower frequency of smoking and daily drinking ($P < 0.05$)(Table 1).

Table 1
Characteristics of patients with newly diagnosed diabetes, and hazard ratios (HRs) for diabetes in older individuals (2015–2018) calculated using univariate and multivariate analysis

	New-onset diabetes		**Univariate analysis**		**Multivariate analysis**
	No	**Yes**	**HR (95% CI)**	**P value**	**HR (95% CI)**
Number	60173 (97.7%)	1414 (2.3%)			
Sex					
Men (%)	26573 (97.7%)	638 (2.3%)	1.00	0.428	
Women (%)	33600 (97.7%)	776 (2.3%)	0.96 (0.86–1.06)		
Age (years)	67.68 ± 6.09	66.98 ± 5.90	0.98 (0.97–0.99)	< 0.001	
60–70	40415 (97.6%)	1013 (2.4%)	1.00	0.002	1.00*
71–80	16749 (98.0%)	344 (2.0%)	0.83 (0.73–0.93)		0.82 (0.72–0.92)
>80	3009 (98.1%)	57 (1.9%)	0.76 (0.58-1.00)		0.75 0.58–0.99)
Hypertension					
No (%)	26811 (97.9%)	577 (2.1%)	1.00	0.008	
Yes (%)	33362 (97.6%)	837 (2.4%)	1.15 (1.04–1.28)		
SBP (mmHg)	127.47 ± 13.51	127.44 ± 12.56	1.00 (0.99-1.00)	0.641	
<120	16261 (97.8%)	359 (2.2%)	1.00	0.016	
120–139	36026 (97.6%)	896 (2.4%)	1.11 (0.98–1.25)		
≥140	7886 (98.0%)	159 (2.0%)	0.88 (0.73–1.06)		

*P < 0.01, **P < 0.05.

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cells; Hgb, haemoglobin; PLT, platelet; TC, total cholesterol; TG, triglyceride; FBG, fasting blood glucose; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin; Scr, serum creatinine; BUN, blood urea nitrogen.

	New-onset diabetes		Univariate analysis		Multivariate analysis
	No Yes HR (95% CI)			P value HR (95% CI)	
DBP (mmHg)	78.71 ± 7.63	78.51 ± 7.05	1.00 (0.99-1.00)	0.202	
<80	28102 (97.7%)	667 (2.3%)	1.00	0.026	
80–89	26782 (97.6%)	649 (2.4%)	1.01 (0.91–1.12)		
≥90	5289 (98.2%)	98 (1.8%)	0.76 (0.61–0.94)		
BMI (kg/m²)	24.66 ± 3.08	25.56 ± 3.19	1.09 (1.07–1.11)	< 0.001	
<18.5	811 (99.1%)	7 (0.9%)	0.48 (0.23-1.00)	< 0.001	0.48 (0.23–1.02)
18.5–23.9	26577 (98.2%)	479 (1.8%)	1.00		1.00 *
24-27.9	24622 (97.5%)	641 (2.5%)	1.43 (1.27–1.61)		1.28 (1.14–1.45)
≥28	8163 (96.6%)	287 (3.4%)	1.91 (1.65–2.21)		1.48 (1.28–1.72)
WC (cm)	84.94 ± 8.54	87.01 ± 9.15	1.03 (1.02–1.03)	< 0.001	
<85 (Women)/ <90 (Men)	37389 (98.0%)	748 (2.0%)	1.00	< 0.001	
≥85 (Women)/ ≥90 (Men)	22784 (97.2%)	666 (2.8%)	1.44 (1.30–1.60)		
TC (mmol/L)	5.24 ± 1.12	5.24 ± 1.32	0.99 (0.95–1.04)	0.993	
<5.2	30436 (97.6%)	746 (2.4%)	1.00	0.083	
≥5.2	29737 (97.8%)	668 (2.2%)	0.91 (0.82–1.01)		

*P < 0.01, **P < 0.05.

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cells; Hgb, haemoglobin; PLT, platelet; TC, total cholesterol; TG, triglyceride; FBG, fasting blood glucose; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin; Scr, serum creatinine; BUN, blood urea nitrogen.

	New-onset diabetes		Univariate analysis		Multivariate analysis
	No	Yes	HR (95% CI)	P value	HR (95% CI)
TG (mmol/L)	1.54 ± 0.95	1.72 ± 1.07	1.12 (1.09–1.16)	< 0.001	
< 1.7	43392 (97.9%)	929 (2.1%)	1.00	< 0.001	
≥ 1.7	16781 (97.2%)	485 (2.8%)	1.33 (1.19–1.48)		
FBG (mmol/L)	5.35 ± 0.91	5.96 ± 1.35	1.08 (1.07–1.09)	< 0.001	
<6.1	52939 (98.3%)	911 (1.7%)	1.00	< 0.001	1.00 *
6.1–6.9	5819 (95.2%)	294 (4.8%)	2.82 (2.47–3.22)		2.75 (2.40–3.14)
≥ 7.0	1415 (87.1%)	209 (12.9%)	7.85 (6.75–9.13)		7.34 (6.29–8.56)
ALT (U/L)	21.72 ± 14.67	24.74 ± 14.71	1.01 (1.00-1.01)	< 0.001	
<40	56788 (97.8%)	1266 (2.2%)	1.00	< 0.001	1.00 *
≥40	3385 (95.8%)	148 (4.2%)	1.90 (1.60–2.25)		1.42 (1.20–1.70)
AST (U/L)	23.62 ± 12.17	24.67 ± 11.11	1.00 (1.00-1.01)	0.003	
<45	58603 (97.8%)	1348 (2.2%)	1.00	< 0.001	
≥45	1570 (96.0%)	66 (4.0%)	1.76 (1.38–2.26)		
TBIL (µmol/L)	13.91 ± 6.02	13.49 ± 5.74	0.99 (0.98-1.00)	0.007	
<20	53499 (97.7%)	1286 (2.3%)	1.00	0.008	1.00 *

*P < 0.01, **P < 0.05.

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cells; Hgb, haemoglobin; PLT, platelet; TC, total cholesterol; TG, triglyceride; FBG, fasting blood glucose; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin; Scr, serum creatinine; BUN, blood urea nitrogen.

	New-onset diabetes		Univariate analysis		Multivariate analysis
	No Yes HR (95% CI)			P value HR (95% CI)	
≥20	6674 (98.1%)	128 (1.9%)	0.78 (0.65–0.94)		0.70 (0.58–0.84)
Scr (μmol/L)	75.60 ± 22.05	75.89 ± 19.40	1.00 (1.00-1.01)	0.705	
<106	56698 (97.7%)	1332 (2.3%)	1.00	0.976	
≥106	3475 (97.7%)	82 (2.3%)	1.00 (0.80–1.25)		
BUN (mmol/L)	5.66 ± 2.00	5.59 ± 1.89	0.98 (0.96–1.01)	0.236	
<7.1	51425 (97.6%)	1243 (2.4%)	1.00	0.007	
≥7.1	8748 (98.1%)	171 (1.9%)	0.80 (0.68–0.94)		
Hgb (g/L)	138.76 ± 15.11	139.32 ± 16.04	1.00 (1.00-1.01)	0.268	
<110 (Women)/ <120 (Men)	1663 (97.7%)	39 (2.3%)	1.02 (0.74–1.41)	0.888	
≥110 (Women)/ 120 (Men)	58510 (97.7%)	1375 (2.3%)	1.00		
WBC (*10^{12}/L)	6.02 ± 3.96	6.21 ± 3.56	1.01 (1.00-1.02)	0.073	
<4.0	3464 (98.7%)	45 (1.3%)	0.54 (0.40–0.72)	< 0.001	
4.0-9.9	55856 (97.6%)	1349 (2.4%)	1.00		
≥10	853 (97.7%)	20 (2.3%)	0.98 (0.63–1.53)		
PLT (*10^{12}/L)	209.57 ± 55.85	209.24 ± 53.14	1.00 (1.00–1.00)	0.747	

*P < 0.01, **P < 0.05.

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cells; Hgb, haemoglobin; PLT, platelet; TC, total cholesterol; TG, triglyceride; FBG, fasting blood glucose; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin; Scr, serum creatinine; BUN, blood urea nitrogen.

	New-onset diabetes		Univariate analysis		Multivariate analysis
	No	Yes	HR (95% CI)	P value	HR (95% CI)
<100	56174 (97.7%)	1328 (2.3%)	1.55 (1.06–2.27)	0.007	
100–299	726 (96.4%)	27 (3.6%)	1.00		
≥300	3273 (98.2%)	59 (1.8%)	0.76 (0.58–0.98)		
Smoking status					
Never	45412 (75.5%)	1132 (80.1%)	1.00	< 0.001	
Past	2816 (4.7%)	58 (4.1%)	0.82 (0.63–1.06)		
Current	11945 (19.9%)	224 (15.8%)	0.74 (0.64–0.85)		
Alcohol consumption					
Never	50475 (83.9%)	1242 (87.8%)	1.00	0.001	1.00 *
Less than once a week	4363 (7.3%)	77 (5.4%)	0.71 (0.57–0.90)		0.67 (0.53–0.84)
More than once a week	1507 (2.5%)	30 (2.1%)	0.80 (0.56–1.15)		0.70 (0.49–1.01)
Everyday	3828 (6.4%)	65 (4.6%)	0.69 (0.54–0.88)		0.66 (0.51–0.85)
Diet					
Animal-based	732 (1.2%)	16 (1.1%)	1.00	0.828	
Balanced	57227 (95.1%)	1349 (95.4%)	1.08 (0.66–1.78)		
Vegetarian diet	2214 (3.7%)	49 (3.5%)	1.00 (0.57–1.76)		

*P < 0.01, **P < 0.05.

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cells; Hgb, haemoglobin; PLT, platelet; TC, total cholesterol; TG, triglyceride; FBG, fasting blood glucose; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin; Scr, serum creatinine; BUN, blood urea nitrogen.

	New-onset diabetes		Univariate analysis		Multivariate analysis
	No Yes HR (95% CI)			P value HR (95% CI)	
Physical activity					
Never	12706 (21.1%)	307 (21.7%)	1.00	0.676	
Less than once a week	3193 (5.3%)	82 (5.8%)	1.06 (0.83–1.35)		
More than once a week	13467 (22.4%)	304 (21.5%)	0.93 (0.79–1.09)		
Everyday	30807 (51.2%)	721 (51.0%)	0.98 (0.85–1.12)		
History of drug use					
Statins					
No (%)	59856 (97.7%)	1401 (2.3%)	1.00	0.046	1.00**
Yes (%)	317 (96.1%)	13 (3.9%)	1.74 (1.01–3.01)		1.85 (1.07–3.20)
Psychotropics					
No (%)	60018 (97.7%)	1410 (2.3%)	1.00	0.752	
Yes (%)	155 (97.5%)	4 (2.5%)	1.17 (0.44–3.13)		
*P < 0.01, **P < 0.05.					
BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cells; Hgb, haemoglobin; PLT, platelet; TC, total cholesterol; TG, triglyceride; FBG, fasting blood glucose; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin; Scr, serum creatinine; BUN, blood urea nitrogen.					

In the univariate regression analysis, individuals being overweight or obesity in BMI, abdominal obesity in WC, with hyperlipemia, use of statins, with impaired glucose regulation or abnormal liver function were significantly associated with diabetes onset. Individuals with higher levels of TBIL and individuals with habit of smoking and drinking more frequently had a lower diabetes risk. The multivariate regression analysis showed that the increase in BMI, FBG and ALT levels, and the use of statins were independent risk factors for diabetes (Table 1). The risk of diabetes in overweight or obese individuals was 1.28- and 1.48-times higher, respectively, than that in individuals with normal weight at baseline. Compared with older individuals with normal FBG levels at baseline, those with FBG levels of 6.1-7.0 mmol/L or higher than 7.0 mmol/L had a 1.75- and 6.34-times higher risk of diabetes, respectively. Compared with older individuals with ALT levels less than 40 U/L, those with ALT levels of 40 U/L and higher had a 42% higher risk of diabetes. Older individuals using statins had an 85% higher risk of diabetes than those not using statins.

When the complete study population was examined,baseline BMI and WC levels were associated with the incidence of diabetes. Obese older men with normal WC had the highest risk of diabetes(Table 2), followed by obese older men with abdominal obesity, overweight older men with abdominal obesity, and older men with normal weight and WC. Similarly, obese older women with abdominal obesity had the highest risk of diabetes, followed by overweight older women with abdominal obesity and older women with normal weight and WC. Among older adults aged less than 75 years, obese individuals with abdominal obesity had the highest risk of diabetes, followed by obese individuals with normal WC and overweight individuals with abdominal obesity. Among older adults aged 75 years and older, overweight people with normal WC had the highest risk of diabetes, followed by overweight people with abdominal obesity.

Table 2
Hazard ratios (HRs) for diabetes according to baseline body mass index (BMI) and waist circumference (WC) values in older individuals (2015–2018).

	Normal WC			Abdominal obesity		
BMI (kg/m^2)	< 24	24-27.9	≥ 28	< 24	24-27.9	≥ 28
Number	24806	12556	775	3068	12707	7675
New cases of diabetes (%)	433 (1.7%)	293 (2.3%)	22 (2.8%)	53 (1.7%)	348 (2.7%)	265 (3.5%)
No. per 1000 person-years	4.9	6.6	8.0	4.9	7.7	9.7
HR (95% CI)*△	1.00	1.33 (1.15–1.54)	1.60 (1.05–2.46)	0.99 (0.74–1.31)	1.53 (1.33–1.77)	1.93 (1.66–2.25)
Men						
Number	11184	6405	366	1047	5145	3064
New cases of diabetes (%)	204 (1.8%)	16 (2.5%)	15 (4.1%)	14 (1.3%)	144 (2.8%)	99 (3.2%)
No. per 1000 person-years	5.2	7.1	11.5	3.8	8.1	9.0
HR (95% CI)*△	1.00	1.38 (1.13–1.70)	2.24 (1.32–3.78)	0.75 (0.44–1.29)	1.54 (1.24–1.91)	1.76 (1.38–2.24)
Women						
Number	13622	6151	409	2021	7562	4611
New cases of diabetes (%)	229 (1.7%)	131 (2.1%)	7 (1.7%)	39 (1.9%)	204 (2.7%)	166 (3.6%)
No. per 1000 person-years	4.7	5.8	4.8	5.4	7.5	10.1
HR (95% CI)*△	1.00	1.24 (1.00-1.54)	0.99 (0.47–2.10)	1.16 (0.82–1.62)	1.57 (1.30–1.90)	2.10 (1.72–2.56)
Age < 75 years						

* $P < 0.001$, ** $P < 0.05$, CI, confidence interval

△The HRs were adjusted for confounders including baseline age, ALT and TBIL levels, alcohol consumption, and statin use.

	Normal WC			Abdominal obesity		
Number	20390	10866	673	2448	10827	6758
New cases of diabetes (%)	377 (1.8%)	253 (2.3%)	21 (3.1%)	44 (1.8%)	310 (2.9%)	247 (3.7%)
No. per 1000 person-years	5.2	6.5	8.8	5.1	8.1	10.2
HR (95% CI)*△	1.00	1.26 (1.08–1.48)	1.68 (1.08–2.61)	0.96 (0.71–1.32)	1.52 (1.31–1.77)	1.95 (1.66–2.29)
Age ≥ 75 years						
Number	4416	1690	102	620	1880	917
New cases of diabetes (%)	56 (1.3%)	40 (2.4%)	1 (1.0%)	9 (1.5%)	38 (2.0%)	18 (2.0%)
No. per 1000 person-years	3.6	6.7	2.7	4.1	5.7	5.5
HR(95% CI)△**	1.00	1.92 (1.28–2.89)	0.80 (0.11–5.77)	1.13 (0.56–2.28)	1.60 (1.06–2.41)	1.57 (0.92–2.67)
* P < 0.001, ** P < 0.05, CI, confidence interval						
△The HRs were adjusted for confounders including baseline age, ALT and TBIL levels, alcohol consumption, and statin use.						

Compared with older adults who “remained underweight or maintained normal weight”, older adults who “became overweight or obese” (HR = 1.96), who “remained overweight or obese”(HR = 1.88), “became underweight or achieved normal weight” (HR = 1.72) were significantly associated with diabetes onset. Compared with older adults who “remained normal WC”, older adults who “remained abdominally obese” (HR = 1.66), who “became abdominally obese”(HR = 1.58), “achieved normal WC” (HR = 1.36) were also significantly associated with diabetes onset.(Table 3).

Table 3

Hazard ratios (HRs) for diabetes according to body mass index (BMI) and waist circumference (WC) status in older individuals (2015–2018)

	Remained normal/ underweight	**Normal/underweight to overweight/obese**	**Overweight/obese to normal/underweight**	**Remained overweight/obese**
Number	22133 (35.9%)	5741 (9.3%)	4110 (6.7%)	29603 (48.1%)
New cases of diabetes (%)	322 (1.5%)	164 (2.9%)	103 (2.5%)	825 (2.8%)
No. per 1000 person-years	4.1	8.1	7.5	7.8
HR (95% CI)*△	1.00	1.96 (1.62–2.37)	1.72 (1.38–2.15)	1.88 (1.65–2.14)
	Retained normal waist circumference	**Normal waist circumference to abdominal obesity**	**Abdominal obesity to normal waist circumference**	**Remained abdominally obese**
Number	30030 (48.8%)	8107 (13.2%)	5086 (8.2%)	18382 (29.8%)
No. new cases of diabetes (%)	524 (1.7%)	224 (2.8%)	121 (2.4%)	545 (3.0%)
No. per 1000 person-years	4.9	7.8	6.7	8.4
HR (95% CI)*△	1.00	1.58 (1.36–1.85)	1.36 (1.11–1.65)	1.66 (1.48–1.88)

* $P < 0.001$, CI, confidence interval

△The HRs were adjusted for confounders including baseline age, ALT and TBIL levels, alcohol consumption, and statin use.

During the follow-up period, weight remained unchanged in 24.9% of the older adults; however, 38.1% of them lost weight and 37.0% gained weight. The risk of diabetes was significantly higher in older adults who gained or lost > 6 kg of weight or showed a 5–10% or higher increase in weight relative to baseline than in those with unchanged weight. The BMI of 20.2% of the older adults remained unchanged during follow-up, whereas 36.5% of them showed increased BMI and 43.3% showed decreased BMI. The risk of diabetes was significantly higher in the older adults with a BMI increase or decrease of > 2 kg/m^2 or a BMI increase of > 10% relative to baseline than in those with unchanged BMI (Table 4).

Table 4
Hazard ratios (HRs) for diabetes according to weight, body mass index (BMI), and waist circumference (WC) variation in older individuals (2015–2018).

Weight change (kg)	**<-6**	**-6 to -3**	**-3 to 0**	**0**	**0 to 3**	**3 to 6**	**>6**
Number	3694	6062	13730	15313	13365	5417	4006
New-onset diabetes (%)	122 (3.3%)	134 (2.2%)	283 (2.1%)	348 (2.3%)	239 (1.8%)	129 (2.4%)	159 (4.0%)
New-onset diabetes/1000 person-years	9.7	6.2	5.8	6.5	5.0	6.7	11.4
HR (95% CI)*△	1.48 (1.21–1.83)	0.98 (0.81–1.20)	0.91 (0.77–1.06)	1.00	0.79 (0.67–0.93)	1.05 (0.86–1.29)	1.77 (1.47–2.14)
Weight change (%)	**<-10%**	**-10% to -5%**	**-5% to 0**	**0**	**0 to 5%**	**5–10%**	**>10%**
Number	3103	5348	10054	19206	10100	6796	6980
New-onset diabetes (%)	67 (2.2%)	130 (2.4%)	233 (2.3%)	393 (2.0%)	217 (2.1%)	167 (2.5%)	207 (3.0%)
New-onset diabetes/1000 person-years	6.1	6.8	6.5	5.8	6.0	6.9	8.4
HR (95% CI)*△	1.08 (0.83–1.40)	1.19 (0.97–1.45)	1.14 (0.97–1.34)	1.00	1.06 (0.90–1.25)	1.21 (1.01–1.45)	1.48 (1.25–1.75)
BMI change (kg/m^2)	**<-2**	**-2 to -1**	**-1 to 0**	**0**	**0 to 1**	**1 to 2**	**>2**
Number	4655	6613	11206	12422	11869	7453	7369
New-onset diabetes (%)	142 (3.1%)	145 (2.2%)	226 (2.0%)	288 (2.3%)	228 (1.9%)	139 (1.9%)	246 (3.3%)
New-onset diabetes/1000 person-years	8.6	6.1	5.6	6.5	5.4	5.2	9.5
HR (95% CI)*△	1.32 (1.08–1.62)	0.95 (0.78–1.16)	0.87 (0.73–1.04)	1.00	0.83 (0.70–0.99)	0.80 (0.65–0.98)	1.45 (1.22–1.72)

*P < 0.01, CI, confidence interval

△The HRs were adjusted for confounders including baseline age, ALT and TBIL levels, alcohol consumption, and statin use.

Weight change (kg)	<-6	-6 to -3	-3 to 0	0	0 to 3	3 to 6	>6
BMI change (%)	**<-10%**	**-10% to -5%**	**-5% to 0**	**0**	**0 to 5%**	**5–10%**	**>10%**
Number	2917	6073	13543	12422	13782	7045	5805
New-onset diabetes (%)	84 (2.9%)	150 (2.5%)	281 (2.1%)	288 (2.3%)	258 (1.9%)	156 (2.2%)	197 (3.4%)
New-onset diabetes/1000 person-years	8.1	6.9	5.8	6.5	5.2	6.2	9.7
HR (95% CI)*△	1.27 (0.99–1.62)	1.07 (0.88–1.30)	0.90 (0.76–1.06)	1.00	0.81 (0.68–0.95)	0.96 (0.79–1.16)	1.48 (1.23–1.77)
WC change (cm)	**<-6**	**-6 to -3**	**-3 to 0**	**0**	**0 to 3**	**3 to 6**	**>6**
Number	5451	5027	8027	19206	8242	6272	9362
New-onset diabetes (%)	129 (2.4%)	121 (2.4%)	180 (2.2%)	393 (2.0%)	167 (2.0%)	159 (2.5%)	265 (2.8%)
New-onset diabetes/1000 person-years	6.6	6.7	6.4	5.8	5.7	7.1	8.0
HR (95% CI)*△	1.17 (0.96–1.43)	1.17 (0.96–1.44)	1.10 (0.92–1.31)	1.00	1.00 (0.83–1.19)	1.25 (1.04–1.50)	1.41 (1.20–1.65)
WC change (%)	**<-10%**	**-10% to -5%**	**-5% to 0**	**0**	**0 to 5%**	**5–10%**	**>10%**
Number	3103	5348	10054	19206	10100	6796	6980
New-onset diabetes (%)	67 (2.2%)	130 (2.4%)	233 (2.3%)	393 (2.0%)	217 (2.1%)	167 (2.5%)	207 (3.0%)
New-onset diabetes/1000 person-years	6.1	6.8	6.6	5.8	6.0	6.9	8.4
HR (95% CI)*△	1.08 (0.83–1.40)	1.19 (0.97–1.45)	1.14 (0.97–1.34)	1.00	1.06 (0.90–1.25)	1.21 (1.01–1.45)	1.48 (1.25–1.75)

*P < 0.01, CI, confidence interval

△The HRs were adjusted for confounders including baseline age, ALT and TBIL levels, alcohol consumption, and statin use.

During the follow-up period, the WC in 37.2% of the older adults remained unchanged, although it increased in 30.0% of them and decreased in 38.3%. The risk of diabetes was significantly higher among older adults who showed WC increases of 3–6 cm or more and among those with WC increases of 5–10% or more relative to baseline than among those with unchanged WC (Table 4).

Our final analysis involved the assessment of new-onset diabetes risk according to the frequency of physical activity at different baseline BMI levels (Table 5). We found that a higher frequency of physical activity was associated with a lower risk of new-onset diabetes. Interestingly, the risk of diabetes in overweight older adults who exercised daily was 19% lower than normal BMI people who did not exercise regularly.

Table 5
Hazard ratios (HRs) for diabetes according to baseline body mass index (BMI) and frequency of physical exercise in older individuals (2015–2018).

	Never	Less than once a week	More than once a week	Everyday
Number				
BMI < 24 kg/m^2	6315	1477	6279	13803
24 kg/m^2 ≤ BMI < 28 kg/m^2	4972	1352	5569	13370
BMI ≥ 28 kg/m^2	1726	446	1923	4355
No. of new cases of diabetes (%)				
BMI < 24 kg/m^2	105 (1.7%)	24 (1.6%)	101 (1.6%)	256 (1.9%)
24 kg/m^2 ≤ BMI < 28 kg/m^2	146 (2.9%)	42 (3.1%)	141 (2.5%)	312 (2.3%)
BMI ≥ 28 kg/m^2	56 (3.2%)	16 (3.6%)	62 (3.2%)	153 (3.5%)
No. per 1000 person-years				
BMI < 24 kg/m^2	4.7	3.8	4.6	5.2
24 kg/m^2 ≤ BMI < 28 kg/m^2	8.2	8.7	7.1	6.6
BMI ≥ 28 kg/m^2	9.1	10.1	9.0	9.9
HR (95% CI)$^{\triangle}$				
BMI < 24 kg/m^2	1.00	0.98 (0.63–1.53)	0.98 (0.74–1.29)	1.16 (0.92–1.45)
24 kg/m^2 ≤ BMI < 28 kg/m^2	1.00	1.08 (0.77–1.52)	0.88 (0.69–1.11)	0.81 (0.67–0.99)
BMI ≥ 28 kg/m^2	1.00	0.76 (0.48–1.21)	0.48 (0.18–1.28)	0.67 (0.38–1.16)

CI, confidence interval

$^{\triangle}$The HRs were adjusted for confounders including baseline age, ALT and TBIL levels, alcohol consumption, and statin use.

Discussion

Metabolic disorders, including obesity and high blood glucose and serum lipid levels, can significantly increase the risk of diabetes. A cohort study involving 51405 Korean men[5] showed that individuals who developed T2DM were likely to have a higher BMI, FBG and serum lipid levels, which is consistent with our findings. Similar conclusions were drawn in the meta-analysis by Lotta et al,[6] who showed that compared with healthy individuals, metabolically unhealthy individuals had a higher risk of T2DM, irrespective of BMI category.

While, in the univariate regression analysis, individuals with the habit of smoking and drinking more frequently had a lower diabetes risk. Maybe it was because individuals without the habits of smoking and drinking gave up smoking and drinking after they were combined with multiple chronic diseases and they were also more susceptible to be suffered from diabetes in the future.

Our study showed that older adults with higher BMI at baseline had a higher risk of developing diabetes. Overweight at baseline was a strong predictor of diabetes risk, independent of weight gain. The relative risk (RR) of diabetes for people with BMI 30.0-34.9 kg/m^2 or ≥ 35 kg/m^2 was up to 20.1- or 38.8-times higher than that among those with BMI < 23 kg/m^2.[7] In a retrospective cohort study of 1257 parous women,[8] initial BMI and BMI after 28–48 years of follow-up were found to be strongly associated with diabetes risk, which increased with weight gain.

Among overweight or obese older adults, the risk of diabetes was higher in abdominally obese individuals than in those with normal WC, and obese older adults with abdominal obesity had the highest risk. The WC mainly reflects visceral fat content. The increase in body fat percentage is associated with a higher risk of diabetes, even in those with normal weight or underweight.[9] National Diabetes and Metabolic Disease Survey[10] showed that compared with people with normal weight and WC, people with obese, obesity and combination of the two had 1.88-, 1.12-, and 2.19-times higher odds of diabetes, respectively. This could be because an increase in WC results in the release of more free fatty acids from adipose tissue, causing lipid toxicity in beta cells, which in turn leads to a further decline in islet cell secretion.

The increase in WC (> 3 cm or > 5%) was also associated with an increased risk of diabetes, so increase in WC may be a predictor of T2DM. Moreover, the American Health Professionals Study[11]showed that 20% of the risk of diabetes could be attributed to an increase of > 2.5 cm in WC. The diabetes risk in people with a WC increase of 14.6 cm or more increased by 70% during a 4-year follow-up period.

The risk of new-onset diabetes in obese older adults with abdominal obesity was higher in women than in men. The proportion of older adults with central obesity is higher among women, and that the risk of diabetes is higher among adults with central obesity than among those with low BMI and WC[10]. While women generally have a higher percentage of fat, including total fat mass, subcutaneous thigh fat, and subcutaneous abdominal fat, they are more sensitive to the negative effects of excess fat accumulation. Increasing levels of visceral fat were associated with an approximately 3-fold increase in diabetes risk in women, while the risk in men increased by a modest 20%[12]. The central distribution of adipose tissue had a greater influence on the incidence of non-insulin-dependent diabetes in women than in men and may contribute to an increased risk of diabetes[13]. Together, these findings suggest that abdominal obesity may be a stronger risk factor for diabetes among women.

In our age-dependent subgroup analysis, the RR of diabetes in obese or abdominally obese adults aged 75 years and older was lower than that in those aged less than 75 years. According to a cross-sectional survey of Tianjin residents in 2017, the incidence of diabetes is the highest in people aged 75 years (0.75%) and then rapidly declines with age (0.4% in people aged 85 years). However, in our study, this trend only appeared in obese or abdominally obese older adults. The effect of overweight and obesity on the incidence of diabetes gradually weakens with increasing age. Further, older adults may not be as easily affected by a slight increase in risk owing to weight gain as younger people. Considering the close connection between obesity and several life-threatening conditions such as cardiovascular disease and stroke[14], older obese people may be more likely to have a combination of these diseases and thus experience early death. The survivors may not be as susceptible to such disorders, including diabetes, which could explain the low incidence of diabetes in adults aged over 75 years.

Weight gain and large weight fluctuations were independent risk factors of diabetes, regardless of baseline BMI levels[15], and this risk was positively correlated with the extent of weight gain[16,17].The diabetes risk was higher among those who became obese, remained obese, or achieved a normal BMI than among those who remained non-obese. 9.1% of diabetes cases could be avoided if obese individuals became non-obese[18] Some studies on weight loss through lifestyle interventions, such as the Da Qing study from China and the Diabetes Prevention Program, a 43% and 34% decrease in diabetes risk, respectively, was observed in individuals with prediabetes after long-term follow-up[19,20]. But when we analysed how the variation in weight and BMI and a high increase or decrease in weight or BMI affects the risk of new-onset diabetes, a U-shaped curve was found. Older adults who became obese or overweight had the highest risk of diabetes, followed by those who remained overweight or obese and those who achieved normal weight or became underweight, the corresponding risk of diabetes also increased in older adults with high weight loss (> 6 kg during follow-up). The possible reason is that the individuals were older adults in our study. During weight loss, older adults may lose proportionately more muscle mass than younger individuals. This loss of skeletal muscle and the increased proportion of fat may contribute to increased insulin resistance, which may weaken the benefit derived from the weight loss. And weight change across adulthood increased all cause and cause specific mortality.[21]

Physical activity is important for diabetes prevention. Physical activity can effectively reduce the risk of diabetes[22–25]and an appropriate increase in energy consumption can effectively regulate postprandial insulin secretion and improve the glucose metabolism status.[26] This effect can persist for up to 10 years. However, the target population that can gain the most benefits from regular exercise is yet to be identified. The effect of moderate- or high-intensity exercise on diabetes prevention is more obvious in obese people.[27,28] People with normal weight can benefit more from exercise or gain the same benefits as obese people, and prediabetes.[29] In our study, daily exercise can reduce the risk of diabetes by 19% for overweight older adults, but the risk of diabetes did not show a significant decline for people with normal weight who exercised daily. This may be because people with normal body weight already had a low risk of diabetes. Moreover, the body fat content in people with normal weight was lower, and hence a further significant decline in body weight and fat would be challenging.

Our study has some strengths. It was the first large-scale prospective cohort study on the effect of obesity indicators and their changes on the incidence of diabetes in older adults from urban areas of northern China. Our study included over 60000 individuals, and the data were maintained in an updated database, which ensured the accuracy and integrity of this large amount of data. Moreover, subgroup analyses were performed according to sex, age, and baseline BMI levels, and confounders were adjusted for to minimise their influence. Furthermore, the participants enrolled in our study were community residents, and not inpatients, and our cohort was thus well-representative of the general older adult population.

Nevertheless, our study also had several limitations. First, the follow-up was only 4 years, and the long-time effect of changes in weight, BMI and WC did not appear, and next we will prolong the follow-up time. Second, our participants were from a coastal city in northern China; hence, our data may not be generalisable to individuals of other ethnicities and those living in other areas.

Conclusion

our study demonstrated that obesity, overweight, and abdominal obesity at baseline and the increase or decrease in body weight, BMI, and WC during follow-up are associated with an increased risk of diabetes in older adults. Daily exercise can reduce the risk of diabetes, and it has greater benefit in overweight older adults. The findings may provide evidence for developing guidelines of proper weight control for older adults.

Abbreviations

BMI:body mass index, T2DM:type 2 diabetes, WC:waist circumferecne, SBP:systolic blood pressure, DBP:diastolic blood pressure, WBC:white blood cell, PLT:platelet, Hgb:haemoglobin, TC:total cholesterol, TG:triglyceride, FBG:fasting blood glucose, ALT:alanine transaminase, AST:aspartate transaminase,TBIL:total bilirubin, Scr:serum creatinine, BUN:blood urea nitrogen, WHO:World Health Organization, HRs:hazard ratios, 95% CIs:95% confidence intervals, RR:relative risk.

Declarations

Ethics approval and consent to participate

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Participants provided written informed consent and the study protocol was approved by the Institutional Review Board of Tianjin Medical University Metabolic Diseases Hospital.

Consent for publication

Not applicable

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Author Contributions

Linna Wu and Hongyan Liu contributed equally to this work. LW and HoL were responsible for the whole test process and writing the article. Zhuang Cui and Xiaowen Gong were responsible for the statistical analysis. Fang Hou, Yourui Zhang , Hao Liu, Chunlan Lu were responsible for collecting data, and Pei Yu were responsible for designing the research.

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References

1. Li Y, Teng D, Shi X, et al. Prevalence of diabetes recorded in mainland China using 2018 diagnostic criteria from the American Diabetes Association: national cross sectional study. BMJ. 2020 Apr;28:369:m997.

2. Gordon-Larsen P, Wang H, Popkin BM. Overweight dynamics in Chinese children and adults. Obes Rev. 2014;15(Suppl 1):37–48.
3. Sarah L, Hardoon RW, Morris MC, Thomas, et al. Is the recent rise in type 2 diabetes incidence from 1984 to 2007 explained by the trend in increasing BMI?: evidence from a prospective study of British men. Diabetes Care. 2010;33:1494–6.
4. Yang WY, Lu JM, Weng JP, et al. Prevalence of diabetes among men and women in China. N Engl J Med. 2010;362:1090–101.
5. Kim ES, Jeong JS, Han K, et al. Impact of weight changes on the incidence of diabetes mellitus: a Korean nationwide cohort study. Sci Rep. 2018;8(1):3735.
6. Luca A, Lotta A, Abbasi, Stephen J, Sharp, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: A systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177–87.
7. Amy R, Weinstein, Howard D, Sesso IM, Lee,et al. Relationship of physical activity vs body mass index with type 2 diabetes in women. JAMA. 2014;292(10):1188–94.
8. Dawson SI, Smith WCS, Watson MS, et al. A cohort study of reproductive risk factors, weight and weight change and the development of diabetes mellitus. Diabetes Obes Metab. 2013;5(4):244–50.
9. Javier Gómez-Ambrosi. Silva C, Juan C, Galofré, et al. Body adiposity and type 2 diabetes: increased risk with a high body fat percentage even having a normal BMI. Obesity (Silver Spring) 2011; 19(7):1439–44.
10. Hou X, Lu J, Weng J, et al. Impact of waist circumference and body mass index on risk of cardiometabolic disorder and cardiovascular disease in Chinese adults: a national diabetes and metabolic disorders survey. PLoS One. 2013;8(3):e57319. doi:10.1371/journal.pone.0057319.
11. Wang PKoh-Banerjee,Y, Frank B, Hu, et al. Changes in body weight and body fat distribution as risk factors for clinical diabetes in US men. Am J Epidemiol. 2004;159(12):1150–9.
12. Kanaya AM, Harris T, Goodpaster BH, et al. Adipocytokines attenuate the association between visceral adiposity and diabetes in older adults. Diabetes Care. 2004;27(6):1375–80.
13. Haffner SM, Mitchell BD, Hazuda HP,et al. Greater influence of central distribution of adipose tissue on incidence of non-insulin-dependent diabetes in women than men. Am J Clin Nutr. 1991;53(5):1312–7.
14. Jiang CQ, Xu L, Zhang WS, et al. Adiposity and mortality in older Chinese: an 11-year follow-up of the Guangzhou Biobank Cohort. StudySci Rep. 2020;10(1):1924.
15. Sundell MKataja-Tuomola,J, Männistö S, et al. Short-term weight change and fluctuation as risk factors for type 2 diabetes in Finnish male smokers. Eur J Epidemiol. 2010;25(5):333–9.
16. Monique AM, Jacobs-van der Bruggen A, Spijkerman, Pieter HM, van Baal, et al. Weight change and incident diabetes: addressing an unresolved issue. Am J Epidemiol. 2010;172(3):263–70.
17. Song BM, Kim HC, Kim DJ, et al. Aminotransferase levels, body mass index, and the risk of diabetes: a prospective cohort study. Ann Epidemiol. 2018;28(10):675–80.e6.

18. Andrew Stokes, Jason M, Collins, Bethany F, Grant, et al. Obesity progression between young adulthood and midlife and incident diabetes: a retrospective cohort study of U.S. adults. Diabetes Care. 2018;41(5):1025–31.
19. Li G, Zhang P, Wang J, et al. Cardiovascular mortality, all-cause mortality, and diabetes incidence after lifestyle intervention for people with impaired glucose tolerance in the Da Qing Diabetes Prevention Study: a 23-year follow-up study. Lancet Diabetes Endocrinol. 2014;2(6):474–80.
20. Knowler WC, Fowler SE, Hamman RF, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet. 2009;374(9702):1677–86.
21. Chen Chen Y, Ye Y, Zhang, et al. Weight change across adulthood in relation to all cause and cause specific mortality: prospective cohort study. BMJ 2019 Oct 16;367:l5584.
22. Lindström J, Ilanne-Parikka P, Peltonen M, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. Lancet. 2006;368:1673–9.
23. Li G, Zhang P, Wang J, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. The Lancet. 2008;371:1783–9.
24. Jeon CY, Lokken RP, Hu FB, van Dam RM. Physical activity of moderate intensity and risk of type 2 diabetes: a systematic review. Diabetes Care. 2007;30:744–52.
25. Liu H, Wang L, Zhang S, et al. One-year weight losses in the Tianjin Gestational Diabetes Mellitus Prevention Programme: A randomized clinical trial. Diabetes Obes Metab. 2018;20:1246–55.
26. Hansen ALS, Carstensen B, Helge JW, et al. Combined heart rate- and accelerometer- assessed physical activity energy expenditure and associations with glucose homeostasis markers in a population at high risk of developing diabetes: the ADDITION-PRO study. Diabetes Care. 2013;36:3062–9.
27. Chae JS, Kang R, Kwak JH, et al. Supervised exercise program, BMI, and risk of type 2 diabetes in subjects with normal or impaired fasting glucose. Diabetes Care. 2012;35:1680–5.
28. Qin L, Corpeleijn E, Jiang C, et al. Physical activity, adiposity, and diabetes risk in middle- aged and older Chinese population: the Guangzhou Biobank Cohort Study. Diabetes Care. 2010;33:2342–8.
29. Sampson M, Clark A, Bachmann M, et al. Lifestyle Intervention With or Without Lay Volunteers to Prevent Type 2 Diabetes in People With Impaired Fasting Glucose and/or Nondiabetic Hyperglycemia: A Randomized Clinical Trial.JAMA Intern Med. 2020 Nov 2; e205938.