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Diabetes in the suburbs of Beijing: epidemiology and risk factors: a retrospective cohort study

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1. Diabetes in the suburbs of Beijing: epidemiology and risk

2 factors: a retrospective cohort study

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4 5	25	Abstract
6 7	26	Objective We aimed to detect the incidence and risk factors of type 2 diabetes
8 9	27	mellitus (T2DM) development in the suburbs of Beijing.
10 11	28	Design Cohort study with record linkage to incidence data.
12 13	29	Setting We performed a 5-year follow-up study in a randomly selected suburban
14 15	30	population including 1,114 subjects aged≥18 years living in the suburbs of Beijing.
16 17	31	Participants 118 subjects with T2DM in baseline according to the 1999 WHO
18 19	32	criteria were excluded, and 895 subjects attended the follow-up assessment in 2012.
20 21	33	The non-diabetic subjects at baseline were classified into two groups: normal glucose
22 23	34	tolerance (NGT) group (n=673) and impaired glucose regulation (IGR) group(n=222),
23 24 25	35	the incidence and risk factors of diabetes development in each group were
25 26 27	36	investigated.
28	37	Outcome measures a structured questionnaire of sociodemographic characteristics,
29 30	38	height, weight, waist circumference, hip circumference and blood pressure, oral
31 32	39	glucose tolerance test, serum lipid levels.
33 34 35	40	Results Out of the 895 non-diabetic subjects, 67 developed diabetes with 29 in NGT
36 37	41	group and 38 in IGR group respectively after 5-year follow-up, giving a overall 5-year
38 39	42	cumulative incidence of diabetes of 13%. The incidence of diabetes was 15.5 cases
40 41	43	per 1000 person-years, while 8.9 cases per 1000 person-years in NGT group and 35.7
42 43	44	cases per 1000 person-years in IGR group (P<0.01, RR=4.03, 95%CI:2.58-9.29).
44 45	45	Binary logistic regression analysis showed that the risk factors of diabetes
46 47	46	development included FPG in NGT group, while gender, WHR, FPG and DBP in IGR
48 49	47	group.
50 51	48	Conclusions: During a mean follow-up of 5.0 years, the incidence of T2DM in the
52 53	49	suburbs of Beijing was 15.5 per 1000 person-years. Early prevention of diabetes
54 55	50	should focus on IGR subjects. Elevated FPG predicted diabetes development for both
56 57	51	NGT and IGR subjects. Female, overweight/obesity and DBP were risk factors for
58 59	52	diabetes development in IGR subjects.
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Strengths and limitations of this study			
\triangleright	Provide new data on the incidence of T2DM in the Beijing area.		
	The increase in the FPG level is a strong predictor of diabetes		
	development.		
	A cohort selected by multiple stage sampling at baseline.		
	A relatively long follow-up period.		
	The limitation is that many variables assessed as risk factors were not		
	updated regularly and the data were collected only at the baseline		
	investigation and at the end of the study.		

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67	Introduction
68	Diabetes mellitus is a clinical syndrome characterized by disordered
69	glycometabolism. The lack and/or insufficiency of insulin induces metabolic disorders
70	related to saccharides, lipids, proteins, water and electrolytes, resulting in
71	hyperglycemia as the main clinical feature. Long-term hyperglycemia leads to
72	macrovascular and microvascular complications, which may result in disability and
73	death. ^{1,2} Diabetes is increasingly prevalent, affecting 451 million (8.4%) adults
74	worldwide, and these figures are expected to increase to 693 million (9.9%) by 2045. ³
75	Type 2 diabetes mellitus (T2DM) accounts for over 90% of diabetes cases. Diabetes,
76	as a leading cause of death, ^{1,3,4} is becoming a public issue and placing a heavy burden
77	on the health care system. ⁵ In 2017, approximately 5 million deaths of adults
78	worldwide were attributed to diabetes, and the global healthcare expenditure
79	associated with people with diabetes was estimated to be \$850 billion. ³
80	As T2DM is usually asymptomatic, it can remain undiagnosed for many years.
81	Almost half of all people (49.7%) living with diabetes were undiagnosed in 2017. ³
82	Accordingly, screening for prediabetes/T2DM and preventing the evolution of
83	diabetes in individuals with risk factors are essential. Currently, it is believed that the
84	risk factors related to the development of T2DM may include age, body mass index
85	(BMI), body fat distribution, family history of diabetes, history of cardiovascular
86	disease (CVD), history of gestational diabetes mellitus (GDM), race/ethnicity, diet,
87	physical inactivity, hypertension, dyslipidemia and prediabetes. ^{4,6-14} Some studies
88	demonstrated that birth weight, ^{15,16} income, ¹⁷ socioeconomic status, ^{18,19} working
89	hours, ^{19,20} occupation ²¹ and genetic factors ²²⁻²⁴ might also contribute to the
90	development of T2DM.
91	Along with the process of urbanization, the aging of the population, changes in
92	lifestyle, and the increasing prevalence of obesity and overweight, the prevalence of
93	diabetes in China has increased over the past three decades. The prevalence of

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diabetes in China was 0.67% in 1980,²⁵ 2.12% in 1995,²⁶ 5.5% in 2001,²⁷ 9.7% in 2008,²⁸ 9.7% in 2010²⁹ and 10.4% in 2013.³⁰ As the capital, there is limited information regarding the incidence of diabetes and prediabetes in Beijing. Certain studies have suggested that there might be different diabetic risk patterns in Asian populations.³¹⁻³⁴ The objective of this study is to determine the incidence of and risk factors for T2DM in the suburbs of Beijing. **Materials and Methods** Study population The study population was residents living in the suburbs (Huairou, Pinggu and Hepingli) of Beijing. Individuals aged 18 years or older who were willing to participate and provided informed consent were eligible to participate in the study. Pregnant women were excluded from the study. We performed a 5-year perspective cohort study. Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research. The baseline survey occurred from June 2007 to September 2008 by a random sampling method with a follow-up examination from May to July 2012. All subjects were asked to undergo a personal interview, physical examination and blood test. Subjects with T2DM at baseline were excluded, and the nondiabetic subjects at baseline were divided into the normal glucose tolerance (NGT) group and the impaired glucose regulation (IGR) group. We analyzed the incidence and risk factors of diabetes development in each group. Diabetes mellitus was defined according to the 1990 WHO criteria or the self-reported prior diagnosis of diabetes with current medication use. IGR was determined if the subjects had a fasting plasma glucose (FPG) level of 6.1-6.9 mmol/L and/or a 2-hour plasma glucose level of 7.8-11.0 mmol/L. **Data collection**

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Sociodemographic characteristics—Data were collected with a structured questionnaire via a face-to-face interview to assess general information (gender, age, nationality, education status, occupation, per capita income), personal history (smoking history, alcohol history, physical activity, dietary habits), family history (diabetes mellitus, hypertension, hyperlipidemia, myocardial infarction, stroke, obesity), and history of current illness (diabetes, hypertension, hyperlipidemia, and cardiovascular, cerebrovascular diseases, kidney diseases). Subjects who were diagnosed with T2DM between recruitment and the end of follow-up were asked to report the date of diagnosis.

Anthropometric measurements — Subjects were examined for height, weight, waist circumference (WC), hip circumference (HC) and blood pressure. All subjects were asked to take off their shoes, socks, hats and coats, stand erectly and look straight forward with their arms relaxed and their heels together. Height was measured in centimeters using a height bar, and weight was measured in kilograms using a digital weighing scale. The WC was the circumference of the waist at the horizontal line of the umbilicus measured in centimeters using a measuring tape, and the HC was the circumference of hips at the horizontal line of the anterior superior spine measured in centimeters using a measuring tape. BMI was calculated as weight in kilograms divided by the square of height in meters (kg/m^2) , while the waist-to-hip ratio (WHR) was calculated as WC (cm) divided by HC (cm). The blood pressure values used were an average of three measurements, which were taken 2 min apart using a mercury sphygmomanometer. The subjects were asked to stop smoking and consuming alcohol the day before the examination and to sit quietly in a chair for at least 5 min in the half-hour before the measurement with their arms bare and placed at the chest level. Laboratory examination — Venous blood samples after 8-14 hours of fasting were obtained from subjects for the measurement of FPG, total cholesterol (TC), triglycerides (TGs), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C). Venous blood samples, after a 75 g oral glucose

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load, were obtained to measure 2-hour plasma glucose (PG2h). Subjects were instructed to maintain normal physical activity without dietary limit (the intake of saccharides should be no less than 150 g per day) before proceeding with the oral glucose tolerance test. **Statistical analysis** The differences in continuous and categorical variables between the NGT group and IGR group were examined using the t test and the χ^2 test statistic, respectively. Kaplan-Meier survival estimates were used to calculate the 5-year cumulative incidence of T2DM. The log-rank test was used to compare the survival curves. The Mantel-Haenszel χ^2 test of trends was used to analyze the ordinal data. Binary logistic regression analyses were used to estimate the odds ratio and 95% confidence interval for the development of diabetes. All analyses were performed using SPSS statistical software version 17.0, and a P value<0.05 was considered statistically significant. **Results** Characteristics of the study population at baseline A total of 1,114 residents participated in the study, and 1,014 subjects completed the follow-up, with an overall response rate of 91.0%. After eliminating 118 subjects who were diagnosed with diabetes at baseline and one subject with severe data deficiency, 895 subjects (308 men and 587 women) with a mean age of 48.1 ± 11.9 years were included in the analysis, with 673 in the NGT group and 222 in the IGR group. The baseline characteristics of the 895 subjects in the study are shown in Table 1. Continuous variables are expressed as the mean±standard deviation (sd) and were examined using the t test, while categorical variables are expressed as percentages and were examined using the χ^2 test. There was no significant difference between the NGT group and the IGR group in gender, height, family history of T2DM, smoking history, alcohol history, exercise time, diastolic blood pressure (DBP) or HDL-C. The differences between the two groups in age, weight, BMI, WC, WHR, systolic blood

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3 4	176	pressure (SBP), FPG, PG2h, TGs, TC, LDL-C and duration of follow-up was
5 6	177	statistically significant.
7 8	178	Incidence of T2DM
9 10	179	During the follow-up, T2DM developed in 67 subjects, 29 in the NGT group and 38
11 12	180	in the IGR group, resulting in T2DM onset rates of 15.45, 8.86 and 35.67 per 1,000
13 14	181	person-years in the total study population, the NGT group and the IGR group,
15 16	182	respectively (Table 2). The difference in the incidence of T2DM between the NGT
17 18	183	group and the IGR group was statistically significant (χ^2 =37.38, P<0.01, RR=4.03,
19 20	184	95% CI: 2.58-9.29).
21 22	185	The 5-year cumulative incidence of T2DM was 13%, with 10% in the NGT group and
23 24	186	20% in the IGR group. The mean follow-up duration was 5.008 years (SE=0.013,
25 26	187	95% CI: 4.982-5.033), with 5.003 years (SE=0.012, 95% CI: 5.010-5.056) in the NGT
27 28 29	188	group and 4.933 years (SE=0.038, 95% CI: 4.859-5.007) in the IGR group. Using the
29 30 31	189	log-rank test, we found that the cumulative incidence of T2DM in the IGR group was
32 33	190	significantly higher than that in the NGT group (χ^2 =36.905, P<0.0001). The results
34 35	191	of the Kaplan-Meier survival analyses are shown in Figure 1.
36 37	192	Analyses of the risk factors for diabetes development
38 39	193	The results of binary logistic regression analyses for the development of T2DM in the
40 41	194	NGT and IGR groups are shown in Table 3. FPG contributed to the development of
42 43	195	T2DM in the NGT group, and the OR was 6.111 (1.379, 27.070; P=0.017). Gender,
44 45	196	WHR, DBP, and FPB contributed to the development of T2DM in the IGR group, and
46 47	197	the ORs were 7.293 (1.074, 49.549, P=0.042), 2.874E8 (8.386, 9.847E15; P=0.028),
48 49	198	1.068 (1.009, 1.130; P=0.024) and 7.243 (2.314, 22.673; P=0.001), respectively. The
50 51	199	increase in exercise time slightly decreased the risk of T2DM in the IGR group, with
52 53	200	an OR of 0.923 (0.847, 1.005; P=0.066).
54 55	201	Discussion
56 57	202	The prevalence of diabetes mellitus has been increasing markedly in recent decades.
58 59	203	Among adults aged from 20-79 years in 2017, there were an estimated 425 million

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204	cases of diabetes ³ . However, the astonishing prevalence may be partly attributable to
205	the increase in population and the prolongation of the life-span. ³⁵ Accordingly, we
206	studied the growing trend of T2DM by investigating the cumulative incidence of
207	T2DM. Our results showed that 15.45 new cases of diabetes per 1,000 people-years
208	were diagnosed during the five-year observation period (2007-2012). This marked
209	trend is consistent with diabetes incidence rates worldwide, such as those described in
210	the ATTICA study in Greece (12.9 cases per 1,000 person-years from 2002 to 2012) ³⁶
211	and those described in a study conducted in Mexico (12.7 cases per 1,000 person-
212	years from 1990 to 2008). ³⁷ The incidence rate found in our study is lower than that in
213	a study of Pima Indians (23.5 cases per 1,000 person-years during 1991 to 2003) ³⁸ and
214	in a study conducted in northern Spain (95.2 cases per 1,000 person-years during
215	1998 to 2005) ³⁹ and is higher than that observed in a study conducted in Iran (10.6
216	cases per 1000 person-years from 1999 to 2011) ⁴⁰ and in the SUPREME-DM project
217	in the USA (11.5 cases per 1000 person-years from 2006 to 2011). ⁴¹ The T2DM
218	incidence in the suburbs of Beijing is higher than that identified in the investigation
219	conducted by Wang C et al in a Chinese population in 2010 (9.5 cases per 1000
220	person-years in men and 9.2 in women). ⁴² This difference may partly be due to the
221	relatively higher standard of living in the suburbs of Beijing.
222	The development of diabetes is based on the interaction between genes and lifestyle
223	and environmental factors.43,44 Compared with the NGT group that had an incidence
224	of 8.86 cases per 1,000 person-years, the IGR group (35.67 cases per 1,000 person-
225	years) had a higher incidence rate (RR=4.03, 95% CI: 2.58-9.29, P<0.01). In our
226	study, the development of diabetes was mainly the consequence of elevated FPG in
227	the NGT group. Diabetes development was mainly associated with sex (female),
228	abnormal WHR, elevated DBP and elevated FPG in the IGR group. The increase in
229	the FPG level was a strong predictor of diabetes development in both the NGT group
230	and the IGR group, with 6.111- and 7.243-times increased risk per unit increase,
231	respectively.

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3 4	232	In our study, the WHR measurement was found to predict diabetes risk. Some studies
5 6	233	have declared that WHR, as an obesity indicator, was superior to BMI and WC. 45,46 A
7 8	234	meta-analysis demonstrated that either BMI or WC (WHR) predicted or was
9 10	235	independently associated with type 2 diabetes, regardless of the controversial findings
11 12	236	regarding which one was better. ⁴⁷
13 14	237	Age and family history of diabetes were widely believed to be risk factors for diabetes
15 16	238	development. ^{4,6-14} However, we found only an increasing trend of diabetes
17 18	239	development in the elderly population and in subjects with a family history of
19 20	240	diabetes ($P > 0.05$). This finding might be related to the short period of follow-up and
21 22	241	the subjects' unawareness of their family history of diabetes.
23 24 25	242	There is evidence that T2DM can be prevented in high-risk individuals by a lifestyle
25 26 27	243	program of regular exercise.48,49 Surprisingly, our study found that exercise did not
27 28 29	244	exert a beneficial effect on diabetes incidence, a finding similar to that of the
30 31	245	ATTICA study. ^{36,50} However, we did find a decreasing trend in diabetes incidence
32 33	246	with increasing exercise time. The increase in exercise time slightly decreased the risk
34 35	247	of T2DM in the IGR group, with an OR of 0.923 (0.847, 1.005; P=0.066).
36 37	248	The strengths of our study are that the study was based on a cohort selected by
38 39	249	multiple stage sampling at baseline with a relatively long follow-up period. The
40 41	250	limitation is that many variables assessed as risk factors were not updated regularly,
42 43	251	which might have changed during the follow-up period, and the data were collected
44 45	252	only at the baseline investigation and at the end of the study.
46 47	253	Conclusions
48 49	254	During a mean follow-up of 5.0 years, the incidence of T2DM in the suburbs of
50 51	255	Beijing was 15.45 cases per 1000 person-years, which was relatively higher than the
52 53	256	incidence in many other areas worldwide. Compared with the NGT subjects, the IGR
54 55	257	subjects were more susceptible to T2DM. To prevent diabetes development, all
56 57	258	subjects should pay special attention to elevated FPG. In addition, sex, WHR, and
58 59 60	259	DBP were predictors of T2DM in IGR subjects.

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260	The findings in this study provide new data on the incidence of T2DM in the Beijing
261	area. The predictors of T2DM reported in the present study may be conducive to

262 formulating a protocol for diabetes prevention.

263 Authors' contributions

264	Conceptualization,	B.Z.; Data	curation,	H.Z.;	Formal	analysis,	H.Z.;	Investigation,
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- L.X. and X.Z.; Methodology, B.Z.; Project administration, L.X., X.Z. and B.Z.;
- 266 Writing original draft, L.X. and X.Z.; Writing review & editing, B.Z.. All authors
- read and approved the final manuscript, as well as the submission of this work. B.Z.
- supervised and managed the data. B.Z. is the guarantor of this work.

270 **Conflicts of interest**

- 271 The authors declare that they have no conflicts of interest.
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- technology support program (2009BAI80B04).
- 277 Ethics approval
 - 278 Ethical approval was gained from Ethics Committee of Clinical Trials of
- 279 Drugs/Devices in China-Japan Friendship Hospital (2011-049).

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Variable at baseline	NGT group	IGR group	t or χ^2 , <i>P</i>
	(n=673)	(n=222)	value
Gender (%male)	34.9	32.9	0.306, 0.625
Age (years)	46.75±11.57	52.01±12.03	-5.813, 0.000
Height (cm)	161.85±7.94	161.18±7.83	1.092, 0.275
Weight (kg)	64.32±10.75	67.49±11.05	-3.777, 0.000
BMI (kg/m ²)	24.52±3.40	25.93±3.50	-5.332, 0.000
WC (cm)	83.04±9.75	86.82±9.20	-5.075, 0.000
WHR	0.87 ± 0.07	0.89±0.06	-3.495, 0.000
SBP (mmHg)	119.71±18.37	125.18±20.13	-3.582, 0.000
DBP (mmHg)	78.02±11.21	79.75±12.66	-1.843, 0.066
FPG (mmol/L)	5.25±0.42	5.82±0.61	-15.875,
			0.000
PG2h (mmol/L)	5.90±1.01	8.29±1.52	-26.692,
			0.000
TGs (mmol/L)	1.42±1.17	1.61 ± 1.08	-2.165, 0.031
TC (mmol/L)	4.56±0.92	4.84±0.95	-3.865, 0.000
HDL-C (mmol/L)	1.35±0.34	1.34±0.36	0.464, 0.643
LDL-C (mmol/L)	2.77±0.77	3.08±0.81	-4.648, 0.000
Exercise duration	5.85±11.81	5.59±8.06	0.305, 0.761
(hours)			
FH of T2DM (%)	15.5	21.4	3.722, 0.068
Smoking history (%)	22.4	20.7	0.286, 0.641
Alcohol history (%)	27.9	28.8	0.076, 0.796
Years of follow-up	4.85±0.32	4.79±0.56	2.081, 0.038
(year)			

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BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; SBP, 282

283 systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose;

PG2h, 2-hour plasma glucose; TC, total cholesterol; TGs, triglycerides; HDL-C, high-284

285 density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FH,

family history. Exercise duration is expressed as hours per week. 286

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1 2

<text>

	Cases of diabetes	Follow-up (person-	Incidence (per 1,000
		years)	person-years)
NGT group	29	3,271.5	8.86
IGR group	38	1,065.3	35.67
Total	67	4,336.8	15.45

to occurrence of the terms of term

288 Table 2. The incidence of T2DM during the follow-up

	NGT group		IGR group	
	OR (95% CI)	P value	OR (95% CI)	Р
				valı
Sex	0.375 (0.067, 2.103)	0.265	7.293 (1.074, 49.549)	0.0
Age (years)	1.013 (0.962, 1.068)	0.615	1.019 (0.964, 1.077)	0.4
Weight (kg)	1.044 (0.927, 1.175)	0.478	1.056 (0.929, 1.200)	0.4
BMI (kg/m ²)	0.934 (0.653, 1.336)	0.710	0.971 (0.661, 1.427)	0.8
WC (cm)	1.073 (0.936, 1.230)	0.311	0.904 (0.748, 1.092)	0.2
WHR	0.006 (0.000,	0.473	2.874E8 (8.386,	0.0
	7058.081)		9.847E15)	
SBP (mmHg)	1.013 (0.976, 1.052)	0.492	0.992 (0.958, 1.026)	0.6
DBP (mmHg)	0.955 (0.890, 1.024)	0.198	1.068 (1.009, 1.130)	0.0
FPG (mmol/L)	6.111 (1.379, 27.070)	0.017	7.243 (2.314, 22.673)	0.0
TC (mmol/L)	2.719 (0.917, 8.067)	0.071	0.814 (0.141, 4.699)	0.8
TGs (mmol/L)	0.996 (0.589, 1.684)	0.989	0.926 (0.491, 1.749)	0.8
HDL-C (mmol/L)	2.536 (0.519, 12.395)	0.250	0.622 (0.071, 5.460)	0.6
LDL-C (mmol/L)	0.604 (0.206, 1.769)	0.358	1.070 (0.181, 6.321)	0.9
Exercise duration	1.013 (0.947, 1.084)	0.707	0.923 (0.847, 1.005)	0.0
(hours)				
FH of T2DM	1.868 (0.492, 7.090)	0.358	2.062 (0.656, 6.478)	0.2
Smoking history	0.766 (0.186, 3.162)	0.713	1.591 (0.346, 7.317)	0.5
e ,		0.624	1.685 (0.458, 6.203)	

Table 3. Multivariate logistic regression model for the development of T2DM

 295 LDL-C, low-density lipoprotein cholesterol; FH, family history. Gender was defined

as male (n=1) or female (n=2), FH of T2DM was defined as no (n=1) or yes (n=2),

Page 17 of 23

3 4	297	smoking history was defined as no (n=1) or yes (n=2), and alcohol history was
5 6	298	defined as no (n=1) or yes (n=2). Exercise duration was expressed as hours per week.
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302	Figure	legend	

303 Figure 1. Cumulative incidence of T2DM in the NGT group and the IGR group (log-

tor peer teries only

304 rank test: χ^2 =36.905, P<0.0001)

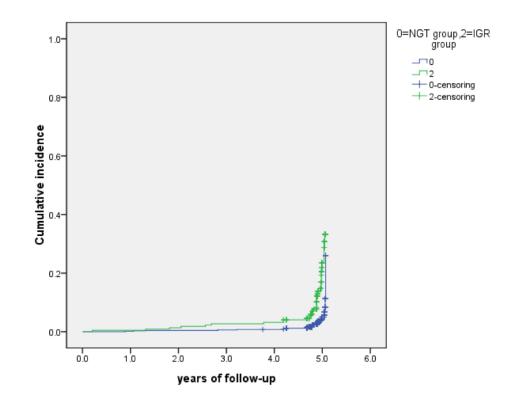
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4	310	References
5 6	311	1. Mortality GBD, Causes of Death C. Global, regional, and national age-sex specific all-cause and
7	312	cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global
8	313	Burden of Disease Study 2013. Lancet 2015;385:117-171.
9 10	314	2. Wong E, Backholer K, Gearon E, et al. Diabetes and risk of physical disability in adults: a
11	315	systematic review and meta-analysis. Lancet Diabetes Endocrinol 2013;1:106-114.
12	316	3. Cho NH, Shaw JE, Karuranga S, et al. IDF Diabetes Atlas: Global estimates of diabetes
13 14	317	prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract 2018;138:271-281.
15	318	4. Mc Donald Posso AJ, Bradshaw Meza RA, Mendoza Morales EA, et al. Diabetes in Panama:
16	319	Epidemiology, Risk Factors, and Clinical Management. Ann Glob Health 2015;81:754-764.
17 18	320	5. Bommer C, Sagalova V, Heesemann E, et al. Global Economic Burden of Diabetes in Adults:
19	321	Projections From 2015 to 2030. Diabetes Care 2018;41:963-970.
20	322	6. Weber MB, Oza-Frank R, Staimez LR, et al. Type 2 diabetes in Asians: prevalence, risk factors,
21 22	323	and effectiveness of behavioral intervention at individual and population levels. Annu Rev Nutr
23	324	2012;32:417-439.
24	325	7. Perez CM, Soto-Salgado M, Suarez E, et al. High Prevalence of Diabetes and Prediabetes and
25 26	326	Their Coexistence with Cardiovascular Risk Factors in a Hispanic Community. J Immigr Minor Health
27	327	2015;17:1002-1009.
28	328	8. Aljoudi AS, Taha AZ. Knowledge of diabetes risk factors and preventive measures among
29 30	329	attendees of a primary care center in eastern Saudi Arabia. Ann Saudi Med 2009;29:15-19.
31	330	9. American Diabetes A. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in
32 33	331	Diabetes-2018. Diabetes Care 2018;41:S13-S27.
34	332	10. Fletcher B, Gulanick M, Lamendola C. Risk factors for type 2 diabetes mellitus. J Cardiovasc
35	333	Nurs 2002;16:17-23.
36 37	334	11. Karter AJ, Schillinger D, Adams AS, et al. Elevated rates of diabetes in Pacific Islanders and
38	335	Asian subgroups: The Diabetes Study of Northern California (DISTANCE). Diabetes Care
39	336	2013;36:574-579.
40 41	337	12. Harjo TC, Perez A, Lopez V, et al. Prevalence of diabetes and cardiovascular risk factors among
42	338	California Native American adults compared to other ethnicities: the 2005 California Health Interview
43	339	Survey. Metab Syndr Relat Disord 2011;9:49-54.
44 45	340	13. Akter S, Rahman MM, Abe SK, et al. Prevalence of diabetes and prediabetes and their risk factors
46	341	among Bangladeshi adults: a nationwide survey. Bull World Health Organ 2014;92:204-213, 213A.
47	342	14. Amarasinghe S, Balakumar S, Arasaratnam V. Prevalence and risk factors of diabetes mellitus
48 49	343	among adults in Jaffna District. Ceylon Med J 2015;60:107-110.
50	344	15. Pettitt DJ, Jovanovic L. Low birth weight as a risk factor for gestational diabetes, diabetes, and
51	345	impaired glucose tolerance during pregnancy. <i>Diabetes Care</i> 2007;30 Suppl 2:S147-149.
52 53	346	16. Harder T, Rodekamp E, Schellong K, et al. Birth weight and subsequent risk of type 2 diabetes: a
54	347	meta-analysis. Am J Epidemiol 2007;165:849-857.
55	348	17. Barker L, Crespo R, Gerzoff RB, et al. Residence in a distressed county in Appalachia as a risk
56 57	349	factor for diabetes, Behavioral Risk Factor Surveillance System, 2006-2007. <i>Prev Chronic Dis</i>
58	350	2010;7:A104.
59 60	200	
60		

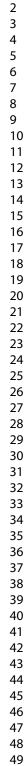
3	351	18. Espelt A, Arriola L, Borrell C, et al. Socioeconomic position and type 2 diabetes mellitus in
4 5	352	Europe 1999-2009: a panorama of inequalities. <i>Curr Diabetes Rev</i> 2011;7:148-158.
6	353	19. Kivimaki M, Virtanen M, Kawachi I, et al. Long working hours, socioeconomic status, and the
7	354	risk of incident type 2 diabetes: a meta-analysis of published and unpublished data from 222 120
8 9	355	individuals. <i>Lancet Diabetes Endocrinol</i> 2015;3:27-34.
9 10	356	20. Bannai A, Yoshioka E, Saijo Y, et al. The Risk of Developing Diabetes in Association With Long
11	357	Working Hours Differs by Shift Work Schedules. <i>J Epidemiol</i> 2016;26:481-487.
12 13	358	21. Honda T, Kuwahara K, Nakagawa T, et al. Leisure-time, occupational, and commuting physical
14	359	activity and risk of type 2 diabetes in Japanese workers: a cohort study. <i>BMC Public Health</i>
15	360	2015;15:1004.
16 17	361	2015,15,1004.22. Ma RC, Hu C, Tam CH, et al. Genome-wide association study in a Chinese population identifies a
18		
19	362	susceptibility locus for type 2 diabetes at 7q32 near PAX4. <i>Diabetologia</i> 2013;56:1291-1305.
20	363	23. Grarup N, Sandholt CH, Hansen T, et al. Genetic susceptibility to type 2 diabetes and obesity:
21 22	364	from genome-wide association studies to rare variants and beyond. <i>Diabetologia</i> 2014;57:1528-1541.
23	365	24. Florez JC, Jablonski KA, Bayley N, et al. TCF7L2 polymorphisms and progression to diabetes in
24	366	the Diabetes Prevention Program. N Engl J Med 2006;355:241-250.
25 26	367	25. Gruop NDrC. A mass survey of diabetes mellitus in a population of 300,000 in 14 provinces and
27	368	municipalities in China (author's transl). Zhonghua Nei Ke Za Zhi 1981;20:678-683.
28	369	26. Pan XR, Yang WY, Li GW, et al. Prevalence of diabetes and its risk factors in China, 1994.
29 30	370	National Diabetes Prevention and Control Cooperative Group. Diabetes Care 1997;20:1664-1669.
31	371	27. Chan JC, Malik V, Jia W, et al. Diabetes in Asia: epidemiology, risk factors, and
32	372	pathophysiology. <i>JAMA</i> 2009;301:2129-2140.
33 34	373	28. Yang W, Lu J, Weng J, et al. Prevalence of diabetes among men and women in China. <i>N Engl J</i>
34 35	374	Med 2010;362:1090-1101.
36	375	29. Xu Y, Wang L, He J, et al. Prevalence and control of diabetes in Chinese adults. JAMA
37	376	2013;310:948-959.
38 39	377	30. Wang L, Gao P, Zhang M, et al. Prevalence and Ethnic Pattern of Diabetes and Prediabetes in
40	378	China in 2013. JAMA 2017;317:2515-2523.
41	379	31. Narayan KM, Aviles-Santa L, Oza-Frank R, et al. Report of a National Heart, Lung, And Blood
42 43	380	Institute Workshop: heterogeneity in cardiometabolic risk in Asian Americans In the U.S.
44	381	Opportunities for research. J Am Coll Cardiol 2010;55:966-973.
45	382	32. Oza-Frank R, Ali MK, Vaccarino V, et al. Asian Americans: diabetes prevalence across U.S. and
46 47	383	World Health Organization weight classifications. <i>Diabetes Care</i> 2009;32:1644-1646.
48	384	33. Ma RC, Chan JC. Type 2 diabetes in East Asians: similarities and differences with populations in
49	385	Europe and the United States. Ann N Y Acad Sci 2013;1281:64-91.
50 51	386	34. Gujral UP, Pradeepa R, Weber MB, et al. Type 2 diabetes in South Asians: similarities and
52	387	differences with white Caucasian and other populations. <i>Ann N Y Acad Sci</i> 2013;1281:51-63.
53	388	35. Gulland A. Global life expectancy has risen, reports WHO. <i>BMJ</i> 2014;348:g3369.
54 55	389	 36. Koloverou E, Panagiotakos DB, Pitsavos C, et al. 10-year incidence of diabetes and associated
55 56		
57	390	risk factors in Greece: the ATTICA study (2002-2012). Rev Diabet Stud 2014;11:181-189.
58 50		
59 60		

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3 4	391	37. Gonzalez-Villalpando C, Davila-Cervantes CA, Zamora-Macorra M, et al. Incidence of type 2
4 5	392	diabetes in Mexico: results of the Mexico City Diabetes Study after 18 years of follow-up. Salud
6	393	<i>Publica Mex</i> 2014;56:11-17.
7	394	38. Pavkov ME, Hanson RL, Knowler WC, et al. Changing patterns of type 2 diabetes incidence
8 9	395	among Pima Indians. Diabetes Care 2007;30:1758-1763.
10	396	39. Valdes S, Botas P, Delgado E, et al. Population-based incidence of type 2 diabetes in northern
11 12	397	Spain: the Asturias Study. Diabetes Care 2007;30:2258-2263.
13	398	40. Derakhshan A, Sardarinia M, Khalili D, et al. Sex specific incidence rates of type 2 diabetes and
14	399	its risk factors over 9 years of follow-up: Tehran Lipid and Glucose Study. PLoS One 2014;9:e102563.
15 16	400	41. Nichols GA, Schroeder EB, Karter AJ, et al. Trends in diabetes incidence among 7 million
17	401	insured adults, 2006-2011: the SUPREME-DM project. Am J Epidemiol 2015;181:32-39.
18	402	42. Wang C, Li J, Xue H, et al. Type 2 diabetes mellitus incidence in Chinese: contributions of
19 20	403	overweight and obesity. Diabetes Res Clin Pract 2015;107:424-432.
21	404	43. Murea M, Ma L, Freedman BI. Genetic and environmental factors associated with type 2 diabetes
22	405	and diabetic vascular complications. Rev Diabet Stud 2012;9:6-22.
23 24	406	44. InterAct C, Langenberg C, Sharp S, et al. Design and cohort description of the InterAct Project:
25	407	an examination of the interaction of genetic and lifestyle factors on the incidence of type 2 diabetes in
26 27	408	the EPIC Study. Diabetologia 2011;54:2272-2282.
27	409	45. Zhao X, Zhu X, Zhang H, et al. Prevalence of diabetes and predictions of its risks using
29	410	anthropometric measures in southwest rural areas of China. BMC Public Health 2012;12:821.
30 31	411	46. Gupta R, Rastogi P, Sarna M, et al. Body-mass index, waist-size, waist-hip ratio and
32	412	cardiovascular risk factors in urban subejcts. J Assoc Physicians India 2007;55:621-627.
33	413	47. Qiao Q, Nyamdorj R. Is the association of type II diabetes with waist circumference or waist-to-
34 35	414	hip ratio stronger than that with body mass index? Eur J Clin Nutr 2010;64:30-34.
36	415	48. Dela F, Prats C, Helge JW. Exercise interventions to prevent and manage type 2 diabetes:
37	416	physiological mechanisms. Med Sport Sci 2014;60:36-47.
38 39	417	49. Teixeira-Lemos E, Nunes S, Teixeira F, et al. Regular physical exercise training assists in
40	418	preventing type 2 diabetes development: focus on its antioxidant and anti-inflammatory properties.
41 42	419	Cardiovasc Diabetol 2011;10:12.
42 43	420	50. Panagiotakos DB, Pitsavos C, Skoumas Y, et al. Five-year incidence of type 2 diabetes mellitus
44	421	among cardiovascular disease-free Greek adults: findings from the ATTICA study. Vasc Health Risk
45 46	422	Manag 2008;4:691-698.
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STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Pag No
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	1
		(<i>b</i>) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of	
C		recruitment, exposure, follow-up, and data collection	
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of	7
-		participants. Describe methods of follow-up	
		(b) For matched studies, give matching criteria and number of exposed and	7
		unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and	7
		effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	7
measurement		assessment (measurement). Describe comparability of assessment methods if	
		there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,	7
		describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for	8
		confounding	
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) If applicable, explain how loss to follow-up was addressed	
		(<i>e</i>) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially	8
		eligible, examined for eligibility, confirmed eligible, included in the study,	
		completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social)	8
		and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	9

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their	9
		precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.	1
		Discuss both direction and magnitude of any potential bias	1
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	1
Generalisability	21	Discuss the generalisability (external validity) of the study results	1
Other informati	ion		
		Give the source of funding and the role of the funders for the present study and, if	1
Funding	22	Give the source of running and the role of the runders for the present study and, if	

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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BMJ Open

Epidemiology and risk factors for diabetes in the suburbs of Beijing: a retrospective cohort study

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Complete List of Authors:	Xie, Lingding; China-Japan Friendship Hospital Zhao, Xu; Civil Aviation General Hospital Zhang, Bo; China-Japan Friendship Hospital, Zhu, Haiqing; China Meitan General Hospital
Primary Subject Heading :	Epidemiology
Secondary Subject Heading:	Diabetes and endocrinology
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, EPIDEMIOLOGY, PUBLIC HEALTH





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6 7 8	2	Beijing: a retrospective cohort study
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60	23	

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	24	Abstract
	25	Objective We aimed to detect the incidence and risk factors of type 2 diabetes
	26	mellitus (T2DM) development in the suburbs of Beijing.
)	27	Design Cohort study with record linkage to incidence data.
2 2	28	Setting We performed a 5-year follow-up study in a randomly selected suburban
5 1 -	29	population including 1,114 subjects aged >18 years living in the suburbs of Beijing.
5	30	Participants 118 subjects with T2DM at baseline according to the 1999 WHO criteria
3	31	were excluded, and 895 subjects attended the follow-up assessment in 2012. The non-
)	32	diabetic subjects at baseline were classified into two groups: normal glucose tolerance
<u>)</u> 2	33	(NGT) group (n=673) and impaired glucose regulation (IGR) group(n=222). The
1	34	incidence and risk factors of diabetes development in each group were investigated.
5 7	35	Outcome measures A structured questionnaire about sociodemographic
3	36	characteristics, height, weight, waist circumference, hip circumference, blood
) 	37	pressure, oral glucose tolerance test, and serum lipid levels.
2 3	38	Results Out of the 895 non-diabetic subjects, 67 developed diabetes with 29 in the
1	39	NGT group and 38 in the IGR group respectively after a 5-year follow-up, producing
5	40	an overall 5-year cumulative incidence of diabetes of 13%. The incidence of diabetes
3	41	was 15.5 cases per 1000 person-years, 8.9 cases per 1000 person-years in the NGT
)	42	group and 35.7 cases per 1000 person-years in the IGR group (P<0.01;RR=4.03;
<u>2</u> 3	43	95%CI:2.58-9.29). Binary logistic regression analysis showed that the risk factors for
1 5	44	diabetes development included fasting plasma glucose (FPG) in the NGT group, and
5 7	45	sex, the waist-to-hip ratio (WHR), FPG and diastolic blood pressure (DBP) in the IGR
3	46	group.
) 	47	Conclusions: During a mean follow-up of 5.0 years, the incidence of T2DM in the
<u>2</u> 3	48	suburbs of Beijing was 15.5 per 1000 person-years. Early prevention of diabetes
1 5	49	should focus on IGR subjects. Elevated FPG predicted diabetes development for both
5 7	50	NGT and IGR subjects. Female sex, overweight/obesity and DBP are risk factors for
3	51	diabetes development in IGR subjects.
)		

Strengths and limitations of this study Provides new data on the incidence of T2DM in the Beijing area. \geq \triangleright Has a longitudinal design. Selects a cohort by multiple-stage sampling at baseline. Has a relatively long follow-up period. \triangleright Has the limitation that many variables assessed as risk factors were not \triangleright updated regularly, and the data were collected only at the baseline investigation and at the end of the study.

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	65	
	66	Introduction
	67	Diabetes mellitus is a clinical syndrome characterized by disordered
	68	glycometabolism. The lack and/or insufficiency of insulin induces metabolic disorders
	69	related to saccharides, lipids, proteins, water and electrolytes, resulting in
,	70	hyperglycemia as the main clinical feature. Long-term hyperglycemia leads to
,	71	macrovascular and microvascular complications, which may result in disability and
,	72	death. ^{1,2} Diabetes is increasingly prevalent, affecting 463 million (9.3%) adults
,	73	worldwide, and these figures are expected to increase to 700 million (10.9%) by
,	74	2045. ³ Type 2 diabetes mellitus (T2DM) accounts for over 90% of diabetes cases.
,	75	Diabetes, as a leading cause of death, ^{1,3,4} is becoming a public issue, placing a heavy
,	76	burden on the health care system. ⁵ In 2017 approximately 5 million adult deaths
,	77	worldwide were attributed to diabetes, ⁶ and the global healthcare expenditure
,	78	associated with people with diabetes in 2019 was estimated to be USD 760 billion. ⁷
,	79	Because T2DM is usually asymptomatic, it can remain undiagnosed for many years.
:	80	Almost half of all people (50.1%) living with diabetes were undiagnosed in $2019.^3$
:	81	Accordingly, screening for prediabetes/T2DM and preventing the evolution of
:	82	diabetes in individuals with risk factors are essential. Currently, the risk factors
:	83	related to T2DM development may include age, the body mass index (BMI), body fat
:	84	distribution, a family history of diabetes, a history of cardiovascular disease (CVD), a
:	85	history of gestational diabetes mellitus (GDM), race/ethnicity, diet, physical
:	86	inactivity, hypertension, dyslipidemia and prediabetes.4,8-16 Some studies have
:	87	demonstrated that birth weight, ^{17,18} income, ¹⁹ socioeconomic status, ^{20,21} working
:	88	hours, ^{21,22} occupation ²³ and genetic factors ²⁴⁻²⁶ might also contribute to T2DM
:	89	development.
2	90	In addition to the process of urbanization, the population aging, changes in lifestyle,
2	91	and increasing prevalence of obesity and overweight, the prevalence of diabetes in
2	92	China has increased over the past three decades. The prevalence of diabetes in China

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was 0.67% in 1980,²⁷ 2.12% in 1995,²⁸ 5.5% in 2001,²⁹ 9.7% in 2008,³⁰ 9.7% in
2010³¹ and 10.4% in 2013.³² As the capital city, limited information is available
regarding the incidence of diabetes and prediabetes in Beijing. Certain studies have
suggested that different diabetic risk patterns might exist in Asian populations.³³⁻³⁶
This study aimed to determine the incidence of and risk factors for T2DM among
Chinese adults in the suburbs of Beijing.

99 Materials and Methods

100 Study population

The study population comprised residents living in the suburbs (Huairou, Pinggu and Hepingli) of Beijing. The three suburbs were randomly selected from the Beijing countryside. Individuals aged 18 years or older who were willing to participate and provided informed consent were eligible to participate in the study. People with a history of diabetes were excluded from the study. Pregnant women were also excluded from the study.

We performed a 5-year perspective cohort study. The baseline survey occurred from June 2007 to September 2008 using a random sampling method with a follow-up examination from May to July 2012. All the subjects were asked to undergo a personal interview, physical examination and blood test [including an oral glucose tolerance test (OGTT)]. Through OGTT, subjects with diabetes at baseline were excluded, and the nondiabetic subjects at baseline were divided into the normal glucose tolerance (NGT) group and impaired glucose regulation (IGR) group. We analyzed the incidence and risk factors of diabetes development in each group. Diabetes mellitus was defined according to the 1990 WHO criteria or self-reported prior diagnosis of diabetes with current medication use. IGR was determined if the subjects had a fasting plasma glucose (FPG) level of 6.1-6.9 mmol/L and/or a 2-hour plasma glucose level of 7.8–11.0 mmol/L. **Data collection**

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120 **Sociodemographic characteristics**—The data were collected by trained staff using a structured questionnaire via a face-to-face interview to assess general information 121 (sex, age, nationality, education status, occupation, and per capita income), personal 122 123 history (smoking history, alcohol history, physical activity, and dietary habits), family history (diabetes mellitus, hypertension, hyperlipidemia, myocardial infarction, 124 stroke, and obesity), and history of current illness (diabetes, hypertension, 125 hyperlipidemia, cardiovascular, cerebrovascular diseases, and kidney diseases). 126 127 Subjects who were diagnosed with T2DM between recruitment and the end of followup were asked to report the date of diagnosis. 128 Anthropometric measurements — The subjects were examined for height, weight, 129 waist circumference (WC), hip circumference (HC) and blood pressure. All the 130 subjects were asked to remove their shoes, socks, hats and coats, stand erectly and 131 look forward with their arms relaxed and their heels together. Height was measured in 132 centimeters using a height bar, and weight was measured in kilograms using a digital 133 weighing scale. The WC is the circumference of the waist at the horizontal line of the 134 umbilicus measured in centimeters using a measuring tape, and the HC is the 135 circumference of hips at the horizontal line of the anterior superior spine measured in 136 centimeters using a measuring tape. The BMI was calculated as weight in kilograms 137 138 divided by the square of height in meters (kg/m^2) , while the waist-to-hip ratio (WHR) was calculated as WC (cm) divided by HC (cm). The blood pressure values used were 139 140 an average of three measurements, which were measured 2 min apart using a mercury 141 sphygmomanometer. The subjects were asked to stop smoking and consuming alcohol 142 the day before the examination and to sit quietly in a chair for at least 5 minutes before the measurement with their arms bare and placed at the chest level. All the 143 144 clinical staff members were trained to measure blood pressure and obtain anthropometric measurements. 145 **Laboratory examination** — All the subjects were invited to undergo a blood test 146

147 (including an OGTT) at the baseline and the end of follow-up. Venous blood samples

after 8–14 hours of fasting were obtained from the subjects to measure FPG, total cholesterol (TC), triglycerides (TGs), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C). Venous blood samples, after a 75 g oral glucose load, were obtained to measure the 2-hour plasma glucose (PG2h). The subjects were instructed to maintain normal physical activity without dietary limit (the intake of saccharides should be no less than 150 g per day) before proceeding with the OGTT. Statistical analysis We used the P-P plot to test the normality of the numerical variables. The differences in continuous and categorical variables between the NGT and IGR groups were examined using t test and the χ^2 test statistic, respectively. Kaplan–Meier survival estimates were used to calculate the 5-year cumulative incidence of T2DM. The log-rank test was used to compare the survival curves. The Mantel-Haenszel χ^2 test of trends was used to analyze the ordinal data. Binary logistic regression analyses were used to estimate the odds ratio and 95% confidence interval for diabetes development. All the analyses were performed using SPSS statistical software version 17.0, and a P value<0.05 was considered statistically significant.

- 165 Patient and Public Involvement
- 166 Patients or the public were not involved in the design, or conduct, or reporting, or
- 167 dissemination plans of our research.
 - **Results**

169 Characteristics of the study population at baseline

In total, 1,114 residents participated in the study, and 1,014 subjects completed the
follow-up, with an overall response rate of 91.0%. After eliminating 118 subjects who

- 172 were diagnosed with diabetes at baseline and one subject with severe data deficiency,
- 173 895 subjects (308 men and 587 women) with a mean age of 48.1±11.9 years were
- included in the analysis, with 673 in the NGT group and 222 in the IGR group. The
- baseline characteristics of the 895 subjects in the study are shown in Table 1.

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176	Continuous variables were expressed as means±standard deviation (sd) and were
177	examined using a t test, while categorical variables were expressed as percentages and
178	were examined using the χ^2 test. No significant difference was found between the
179	NGT group and the IGR group in sex, height, family history of T2DM, smoking
180	history, alcohol history, exercise time, diastolic blood pressure (DBP) or HDL-C.
181	Age, weight, BMI, WC, WHR, systolic blood pressure (SBP), FPG, PG2h, TGs, TC
182	and LDL-C in the IGR group were significantly higher than those in the NGT group.
183	Incidence of T2DM
184	During the follow-up, T2DM developed in 67 subjects, 29 in the NGT group and 38
185	in the IGR group, resulting in T2DM onset rates of 15.45, 8.86 and 35.67 per 1,000
186	person-years in the total study population, NGT group and IGR group, respectively
187	(Table 2). The difference in the incidence of T2DM between the NGT group and IGR
188	group was statistically significant (χ^2 =37.38;P<0.01;RR=4.03;95% CI: 2.58-9.29).
189	The 5-year cumulative incidence of T2DM was 13%, with 10% in the NGT group and
190	20% in the IGR group. The mean follow-up duration was 5.008 years (SE=0.013;
191	95% CI: 4.982–5.033), with 5.003 years (SE=0.012;95% CI: 5.010–5.056) in the
192	NGT group and 4.933 years (SE=0.038;95% CI: 4.859–5.007) in the IGR group.
193	Using the log-rank test, we found that the cumulative incidence of T2DM in the IGR
194	group was significantly higher than that in the NGT group (χ^2 =36.905; P<0.0001).
195	The results of the Kaplan–Meier survival analyses are shown in Figure 1.
196	Analyses of the risk factors for diabetes development
197	The results of binary logistic regression analyses for T2DM development in the NGT
198	and IGR groups are shown in Table 3. FPG contributed to T2DM development in the
199	NGT group, and the OR was 6.111 (1.379, 27.070; P=0.017). Sex,WHR, DBP, and
200	FPB contributed to T2DM development in the IGR group, and the ORs were 7.293
201	(1.074, 49.549;P=0.042), 2.874E8 (8.386, 9.847E15; P=0.028), 1.068 (1.009, 1.130;
202	P=0.024) and 7.243 (2.314, 22.673; P=0.001), respectively. The increase in exercise

time slightly decreased the risk of T2DM in the IGR group, with an OR of 0.923
(0.847, 1.005; P=0.066).

Discussion

The prevalence of diabetes mellitus has been increasing markedly in recent decades. Among adults aged 20–79 years in 2019, there were an estimated 463 million cases of diabetes³. However, the striking prevalence may be partly attributable to the increase in population and prolongation of the life-span.³⁷ Accordingly, we studied the growing trend of T2DM by investigating the cumulative incidence of T2DM. Our results showed that 15.45 new cases of diabetes per 1,000 people-years were diagnosed during the five-year observation period (2007–2012). This marked trend is consistent with diabetes incidence rates worldwide, such as those described in the ATTICA study in Greece (12.9 cases per 1,000 person-years from 2002 to 2012)³⁸ and those described in a study conducted in Mexico (12.7 cases per 1,000 person-years from 1990 to 2008).³⁹ The incidence rate found in our study is lower than that in a study of Pima Indians (23.5 cases per 1,000 person-years during 1991 to 2003)⁴⁰ and in a study conducted in northern Spain (95.2 cases per 1,000 person-years during 1998 to 2005)⁴¹ and is higher than that observed in a study conducted in Iran (10.6 cases per 1000 person-years from 1999 to 2011)⁴² and in the SUPREME-DM project in the USA (11.5 cases per 1000 person-years from 2006 to 2011).⁴³ The T2DM incidence in the suburbs of Beijing is higher than that identified in the investigation conducted by Wang C et al in a Chinese population in 2010 (9.5 cases per 1000 person-years in men and 9.2 in women).⁴⁴ This difference may partly be due to the relatively higher standard of living in the suburbs of Beijing. Diabetes development is based on the interaction between genes and lifestyle and environmental factors.^{45,46} Compared with the NGT group that had an incidence of 8.86 cases per 1,000 person-years, the IGR group (35.67 cases per 1,000 person-years) had a higher incidence rate (RR=4.03;95% CI: 2.58–9.29;P<0.01). In our

study, diabetes development was mainly the consequence of elevated FPG in the NGT

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- 3 4	231	group. Diabetes development was mainly associated with sex (female), abnormal
5 6	232	WHR, elevated DBP and elevated FPG in the IGR group. The increase in the FPG
7 8	233	level was a strong predictor of diabetes development in both the NGT group and IGR
9 10	234	group, with 6.111- and 7.243-fold increased risk per unit increase, respectively.
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12 13	235	In our study, the WHR measurement was found to predict diabetes risk. Some studies
14 15	236	have declared that WHR, as an obesity indicator, is superior to BMI and WC. 47,48 A
16 17	237	meta-analysis demonstrated that either BMI or WC (WHR) predicted or was
18 19	238	independently associated with type 2 diabetes, regardless of the controversial findings
20 21	239	regarding which was better. ⁴⁹
22 23	240	Age and family history of diabetes are considered risk factors for diabetes
23 24 25	241	development. ^{4,8-16} However, we found only an increasing trend of diabetes
25 26 27	242	development in the elderly population and subjects with a family history of diabetes
28 29	243	(P>0.05). This finding might be related to the short period of follow-up and the
30 31	244	subjects' unawareness of their family history of diabetes.
32 33	245	There is evidence that T2DM can be prevented in high-risk individuals by a lifestyle
34 35	246	program of regular exercise. ^{50,51} Surprisingly, our study found that exercise did not
36 37	247	exert a beneficial effect on diabetes incidence, a finding similar to that in the ATTICA
38 39	248	study. ^{38,52} However, we found a decreasing trend in the diabetes incidence with
40 41	249	increasing exercise time. The increase in exercise time slightly decreased the risk of
42 43	250	T2DM in the IGR group, with an OR of 0.923 (0.847, 1.005; P=0.066).
44 45	251	The strength of our study is that it was based on a cohort selected by multiple stage
46 47	252	sampling at baseline with a relatively long follow-up period. A limitation is that many
48 49	253	variables assessed as risk factors were not updated regularly, and might have changed
50 51	254	during the follow-up period. Additionally, the data were collected only at the baseline
52 53	255	investigation and at the end of the study.
54 55	256	Conclusions
56 57	257	During a mean follow-up of 5.0 years, the incidence of T2DM in the suburbs of
58 59	258	Beijing was 15.45 cases per 1000 person-years, which was relatively higher than that

in many other areas worldwide. Compared with the NGT subjects, the IGR subjects

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260	were more susceptible to T2DM. To prevent diabetes development, all the subjects
261	should be evaluated for elevated FPG. Additionally, sex, WHR, and DBP were
262	predictors of T2DM in IGR subjects.
263	The findings in this study provide new data on the incidence of T2DM in the Beijing
264	area. The predictors of T2DM reported in the present study may be conducive to
265	formulating a protocol for diabetes prevention.
266	Authors' contributions
267	Conceptualization, B.Z.; Data curation, H.Z.; Formal analysis, H.Z.; Investigation,
268	L.X. and X.Z.; Methodology, B.Z.; Project administration, L.X., X.Z. and B.Z.;
269	Writing – original draft, L.X. and X.Z.; Writing – review & editing, B.Z All authors
270	read and approved the final manuscript, as well as the submission of this work. B.Z.
271	supervised and managed the data. B.Z. is the guarantor of this work.
272	
273	Conflicts of interest
274	The authors declare that they have no conflicts of interest.
275	
276	Competing interests None declared.
277	
278	Funding statement
279	The study was supported by grants from the 11th Five-year National Science and
280	Technology Support Program (2009BAI80B04).
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282	Ethics approval
283	Ethical approval was obtained from the Ethics Committee of Clinical Trials of

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- 3 4	284	Drugs/Devices in China-Japan Friendship Hospital (2011-049).
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7 8	286	Data availability statement
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12 13	287	All data included in this study are available from the corresponding author on
14 15	288	reasonable request.
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baseline

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291 Table 1 Comparison of the characteristics of the NGT and IGR subjects at

Variable at baseline	NGT group	IGR group	t or χ^2 , <i>P</i> value
	(n=673)	(n=222)	
Sex(%male)	34.9	32.9	0.306, 0.625
Age (years)	46.75±11.57	52.01±12.03	-5.813, <0.001
Height (cm)	161.85±7.94	161.18±7.83	1.092, 0.275
Weight (kg)	64.32±10.75	67.49±11.05	-3.777, <0.001
BMI (kg/m ²)	24.52±3.40	25.93±3.50	-5.332, <0.001
WC (cm)	83.04±9.75	86.82±9.20	-5.075, <0.001
WHR	0.87±0.07	0.89±0.06	-3.495, <0.001
SBP (mmHg)	119.71±18.37	125.18±20.13	-3.582, <0.001
DBP (mmHg)	78.02±11.21	79.75±12.66	-1.843, 0.066
FPG (mmol/L)	5.25±0.42	5.82±0.61	-15.875, <0.00
PG2h (mmol/L)	5.90±1.01	8.29±1.52	-26.692, <0.00
TGs (mmol/L)	1.42±1.17	1.61±1.08	-2.165, 0.031
TC (mmol/L)	4.56±0.92	4.84±0.95	-3.865, <0.001
HDL-C (mmol/L)	1.35±0.34	1.34±0.36	0.464, 0.643
LDL-C (mmol/L)	2.77±0.77	3.08±0.81	-4.648, <0.001
Exercise duration	5.85±11.81	5.59±8.06	0.305, 0.761
(hours)			
FH of T2DM (%)	15.5	21.4	3.722, 0.068
Smoking history (%)	22.4	20.7	0.286, 0.641
Alcohol history (%)	27.9	28.8	0.076, 0.796
Years of follow-up	4.85±0.32	4.79±0.56	2.081, 0.038

BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; SBP,

294 systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose;

1 2		
3 4	295	PG2h, 2-hour plasma glucose; TC, total cholesterol; TGs, triglycerides; HDL-C, high-
5 6	296	density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FH,
7 8	297	family history. Exercise duration is expressed as hours per week.
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299 Table 2. Incidence of T2DM during the follow-up

	Cases of diabetes	Follow-up (person-	Incidence (per 1,000
NGT group	29	years) 3,271.5	person-years) 8.86
IGR group	38	1,065.3	35.67
Total	67	4,336.8	15.45

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	NGT group		IGR group	
	OR (95% CI)	P value	OR (95% CI)	
Sex	0.375 (0.067, 2.103)	0.265	7.293 (1.074, 49.549)	
Age (years)	1.013 (0.962, 1.068)	0.615	1.019 (0.964, 1.077)	
Weight (kg)	1.044 (0.927, 1.175)	0.478	1.056 (0.929, 1.200)	
BMI (kg/m ²)	0.934 (0.653, 1.336)	0.710	0.971 (0.661, 1.427)	
WC (cm)	1.073 (0.936, 1.230)	0.311	0.904 (0.748, 1.092)	
WHR	0.006 (0.000,	0.473	2.874E8 (8.386,	
	7058.081)		9.847E15)	
SBP (mmHg)	1.013 (0.976, 1.052)	0.492	0.992 (0.958, 1.026)	
DBP (mmHg)	0.955 (0.890, 1.024)	0.198	1.068 (1.009, 1.130)	
FPG (mmol/L)	6.111 (1.379, 27.070)	0.017	7.243 (2.314, 22.673)	
TC (mmol/L)	2.719 (0.917, 8.067)	0.071	0.814 (0.141, 4.699)	
TGs (mmol/L)	0.996 (0.589, 1.684)	0.989	0.926 (0.491, 1.749)	
HDL-C (mmol/L)	2.536 (0.519, 12.395)	0.250	0.622 (0.071, 5.460)	
LDL-C (mmol/L)	0.604 (0.206, 1.769)	0.358	1.070 (0.181, 6.321)	
Exercise duration	1.013 (0.947, 1.084)	0.707	0.923 (0.847, 1.005)	
(hours)				
FH of T2DM	1.868 (0.492, 7.090)	0.358	2.062 (0.656, 6.478)	
Smoking history	0.766 (0.186, 3.162)	0.713	1.591 (0.346, 7.317)	
Alcohol history	0.726 (0.202, 2.610)	0.624	1.685 (0.458, 6.203)	
BMI, body mass index;	WC, waist circumference;	WHR, wa	ist-to-hip ratio; SBP,	
- <u>-</u> -	DBP, diastolic blood pres	ŕ	1	

306 LDL-C, low-density lipoprotein cholesterol; FH, family history. Sex is defined as

307 male (n=1) or female (n=2), FH of T2DM is defined as no (n=1) or yes (n=2),

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308	smoking history was defined as no (n=1) or yes (n=2), and alcohol history was
309	defined as no (n=1) or yes (n=2). Exercise duration is expressed as hours per week.
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1 2		
3 4	313	Figure legend
5 6	314	Figure 1. Cumulative incidence of T2DM in the NGT and IGR groups (log-rank test:
7 8	315	χ ² =36.905;P<0.0001)
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3 4	321	References
5	322	
6		1. Mortality GBD, Causes of Death C. Global, regional, and national age-sex specific all-cause and
7 8	323	cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global
9	324	Burden of Disease Study 2013. <i>Lancet</i> 2015;385:117-71.
10	325	2. Wong E, Backholer K, Gearon E, et al. Diabetes and risk of physical disability in adults: a
11 12	326	systematic review and meta-analysis. Lancet Diabetes Endocrinol 2013;1:106-14.
12 13	327	3. Sinclair A, Saeedi P, Kaundal A, Karuranga S, Malanda B, Williams R. Diabetes and global
14	328	ageing among 65-99-year-old adults: Findings from the International Diabetes Federation Diabetes
15	329	Atlas, 9(th) edition. Diabetes Res Clin Pract 2020;162:108078.
16 17	330	4. Mc Donald Posso AJ, Bradshaw Meza RA, Mendoza Morales EA, Jaen Y, Cumbrera Ortega A,
18	331	Mendoza Posada EJ. Diabetes in Panama: Epidemiology, Risk Factors, and Clinical Management. Ann
19	332	<i>Glob Health</i> 2015;81:754-64.
20 21	333	5. Bommer C, Sagalova V, Heesemann E, et al. Global Economic Burden of Diabetes in Adults:
22	334	Projections From 2015 to 2030. <i>Diabetes Care</i> 2018;41:963-70.
23	335	6. Cho NH, Shaw JE, Karuranga S, et al. IDF Diabetes Atlas: Global estimates of diabetes
24 25	336	prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract 2018;138:271-81.
26	337	7. Williams R, Karuranga S, Malanda B, et al. Global and regional estimates and projections of
27	338	diabetes-related health expenditure: Results from the International Diabetes Federation Diabetes Atlas,
28 29	339	9th edition. Diabetes Res Clin Pract 2020;162:108072.
30	340	8. Weber MB, Oza-Frank R, Staimez LR, Ali MK, Narayan KM. Type 2 diabetes in Asians:
31	341	prevalence, risk factors, and effectiveness of behavioral intervention at individual and population
32 33	342	levels. Annu Rev Nutr 2012;32:417-39.
34	343	9. Perez CM, Soto-Salgado M, Suarez E, Guzman M, Ortiz AP. High Prevalence of Diabetes and
35	344	Prediabetes and Their Coexistence with Cardiovascular Risk Factors in a Hispanic Community. J
36 37	345	Immigr Minor Health 2015;17:1002-9.
38	346	10. Aljoudi AS, Taha AZ. Knowledge of diabetes risk factors and preventive measures among
39	347	attendees of a primary care center in eastern Saudi Arabia. Ann Saudi Med 2009;29:15-9.
40 41	348	11. American Diabetes A. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in
42	349	Diabetes-2018. <i>Diabetes Care</i> 2018;41:S13-S27.
43	350	12. Fletcher B, Gulanick M, Lamendola C. Risk factors for type 2 diabetes mellitus. <i>J Cardiovasc</i>
44 45	351	Nurs 2002;16:17-23.
45	352	13. Karter AJ, Schillinger D, Adams AS, et al. Elevated rates of diabetes in Pacific Islanders and
47	353	Asian subgroups: The Diabetes Study of Northern California (DISTANCE). <i>Diabetes Care</i>
48 49	354	2013;36:574-9.
49 50	355	14. Harjo TC, Perez A, Lopez V, Wong ND. Prevalence of diabetes and cardiovascular risk factors
51	356	among California Native American adults compared to other ethnicities: the 2005 California Health
52		
53 54	357	Interview Survey. <i>Metab Syndr Relat Disord</i> 2011;9:49-54.
55	358	15. Akter S, Rahman MM, Abe SK, Sultana P. Prevalence of diabetes and prediabetes and their risk
56 57	359	factors among Bangladeshi adults: a nationwide survey. <i>Bull World Health Organ</i> 2014;92:204-13,
57 58	360	
59	361	16. Amarasinghe S, Balakumar S, Arasaratnam V. Prevalence and risk factors of diabetes mellitus
60	362	among adults in Jaffna District. Ceylon Med J 2015;60:107-10.

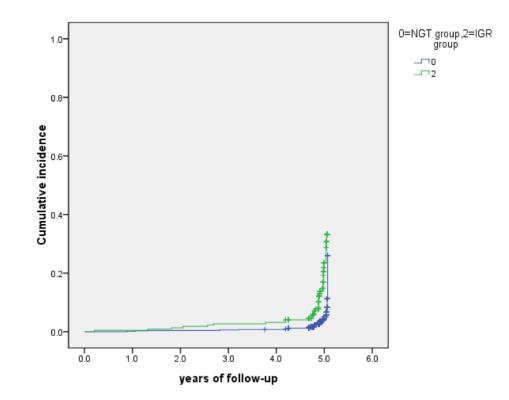
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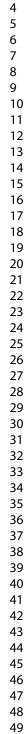
1 2

3 4	363	17. Pettitt DJ, Jovanovic L. Low birth weight as a risk factor for gestational diabetes, diabetes, and
5	364	impaired glucose tolerance during pregnancy. Diabetes Care 2007;30 Suppl 2:S147-9.
б	365	18. Harder T, Rodekamp E, Schellong K, Dudenhausen JW, Plagemann A. Birth weight and
7 8	366	subsequent risk of type 2 diabetes: a meta-analysis. Am J Epidemiol 2007;165:849-57.
9	367	19. Barker L, Crespo R, Gerzoff RB, Denham S, Shrewsberry M, Cornelius-Averhart D. Residence in
10	368	a distressed county in Appalachia as a risk factor for diabetes, Behavioral Risk Factor Surveillance
11 12	369	System, 2006-2007. Prev Chronic Dis 2010;7:A104.
12	370	20. Espelt A, Arriola L, Borrell C, Larranaga I, Sandin M, Escolar-Pujolar A. Socioeconomic position
14	371	and type 2 diabetes mellitus in Europe 1999-2009: a panorama of inequalities. Curr Diabetes Rev
15 16	372	2011;7:148-58.
17	373	21. Kivimaki M, Virtanen M, Kawachi I, et al. Long working hours, socioeconomic status, and the
18	374	risk of incident type 2 diabetes: a meta-analysis of published and unpublished data from 222 120
19 20	375	individuals. Lancet Diabetes Endocrinol 2015;3:27-34.
21	376	22. Bannai A, Yoshioka E, Saijo Y, Sasaki S, Kishi R, Tamakoshi A. The Risk of Developing
22	377	Diabetes in Association With Long Working Hours Differs by Shift Work Schedules. J Epidemiol
23 24	378	2016;26:481-7.
25	379	23. Honda T, Kuwahara K, Nakagawa T, Yamamoto S, Hayashi T, Mizoue T. Leisure-time,
26	380	occupational, and commuting physical activity and risk of type 2 diabetes in Japanese workers: a
27 28	381	cohort study. <i>BMC Public Health</i> 2015;15:1004.
29	382	24. Ma RC, Hu C, Tam CH, et al. Genome-wide association study in a Chinese population identifies a
30	383	susceptibility locus for type 2 diabetes at 7q32 near PAX4. <i>Diabetologia</i> 2013;56:1291-305.
31 32	384	25. Grarup N, Sandholt CH, Hansen T, Pedersen O. Genetic susceptibility to type 2 diabetes and
33	385	obesity: from genome-wide association studies to rare variants and beyond. <i>Diabetologia</i>
34 35	386	2014;57:1528-41.
36	387	26. Florez JC, Jablonski KA, Bayley N, et al. TCF7L2 polymorphisms and progression to diabetes in
37	388	the Diabetes Prevention Program. N Engl J Med 2006;355:241-50.
38 39	389	27. Gruop NDrC. A mass survey of diabetes mellitus in a population of 300,000 in 14 provinces and
40	390	municipalities in China (author's transl). Zhonghua Nei Ke Za Zhi 1981;20:678-83.
41	391	28. Pan XR, Yang WY, Li GW, Liu J. Prevalence of diabetes and its risk factors in China, 1994.
42 43	392	National Diabetes Prevention and Control Cooperative Group. <i>Diabetes Care</i> 1997;20:1664-9.
44	393	29. Chan JC, Malik V, Jia W, et al. Diabetes in Asia: epidemiology, risk factors, and
45	394	pathophysiology. JAMA 2009;301:2129-40.
46 47	395	30. Yang W, Lu J, Weng J, et al. Prevalence of diabetes among men and women in China. <i>N Engl J</i>
48	396	Med 2010;362:1090-101.
49 50	397	31. Xu Y, Wang L, He J, et al. Prevalence and control of diabetes in Chinese adults. JAMA
50 51	398	2013;310:948-59.
52	399	32. Wang L, Gao P, Zhang M, et al. Prevalence and Ethnic Pattern of Diabetes and Prediabetes in
53 54	400	China in 2013. <i>JAMA</i> 2017;317:2515-23.
54 55	401	33. Narayan KM, Aviles-Santa L, Oza-Frank R, et al. Report of a National Heart, Lung, And Blood
56	402	Institute Workshop: heterogeneity in cardiometabolic risk in Asian Americans In the U.S.
57 58	403	Opportunities for research. J Am Coll Cardiol 2010;55:966-73.
59		
60		

34. Oza-Frank R, Ali MK, Vaccarino V, Narayan KM. Asian Americans: diabetes prevalence across U.S. and World Health Organization weight classifications. Diabetes Care 2009;32:1644-6. 35. Ma RC, Chan JC. Type 2 diabetes in East Asians: similarities and differences with populations in Europe and the United States. Ann NY Acad Sci 2013;1281:64-91. 36. Gujral UP, Pradeepa R, Weber MB, Narayan KM, Mohan V. Type 2 diabetes in South Asians: similarities and differences with white Caucasian and other populations. Ann NY Acad Sci 2013;1281:51-63. 37. Gulland A. Global life expectancy has risen, reports WHO. BMJ 2014;348:g3369. 38. Koloverou E, Panagiotakos DB, Pitsavos C, et al. 10-year incidence of diabetes and associated risk factors in Greece: the ATTICA study (2002-2012). Rev Diabet Stud 2014;11:181-9. 39. Gonzalez-Villalpando C, Davila-Cervantes CA, Zamora-Macorra M, Trejo-Valdivia B, Gonzalez-Villalpando ME. Incidence of type 2 diabetes in Mexico: results of the Mexico City Diabetes Study after 18 years of follow-up. Salud Publica Mex 2014;56:11-7. 40. Pavkov ME, Hanson RL, Knowler WC, Bennett PH, Krakoff J, Nelson RG. Changing patterns of type 2 diabetes incidence among Pima Indians. Diabetes Care 2007;30:1758-63. 41. Valdes S, Botas P, Delgado E, Alvarez F, Cadorniga FD. Population-based incidence of type 2 diabetes in northern Spain: the Asturias Study. Diabetes Care 2007;30:2258-63. 42. Derakhshan A, Sardarinia M, Khalili D, Momenan AA, Azizi F, Hadaegh F. Sex specific incidence rates of type 2 diabetes and its risk factors over 9 years of follow-up: Tehran Lipid and Glucose Study. PLoS One 2014;9:e102563. 43. Nichols GA, Schroeder EB, Karter AJ, et al. Trends in diabetes incidence among 7 million insured adults, 2006-2011: the SUPREME-DM project. Am J Epidemiol 2015;181:32-9. 44. Wang C, Li J, Xue H, et al. Type 2 diabetes mellitus incidence in Chinese: contributions of overweight and obesity. Diabetes Res Clin Pract 2015;107:424-32. 45. Murea M, Ma L, Freedman BI. Genetic and environmental factors associated with type 2 diabetes and diabetic vascular complications. Rev Diabet Stud 2012;9:6-22. 46. InterAct C, Langenberg C, Sharp S, et al. Design and cohort description of the InterAct Project: an examination of the interaction of genetic and lifestyle factors on the incidence of type 2 diabetes in the EPIC Study. Diabetologia 2011;54:2272-82. 47. Zhao X, Zhu X, Zhang H, et al. Prevalence of diabetes and predictions of its risks using anthropometric measures in southwest rural areas of China. BMC Public Health 2012;12:821. 48. Gupta R, Rastogi P, Sarna M, Gupta VP, Sharma SK, Kothari K. Body-mass index, waist-size, waist-hip ratio and cardiovascular risk factors in urban subejcts. J Assoc Physicians India 2007;55:621-7. 49. Qiao Q, Nyamdorj R. Is the association of type II diabetes with waist circumference or waist-to-hip ratio stronger than that with body mass index? Eur J Clin Nutr 2010;64:30-4. 50. Dela F, Prats C, Helge JW. Exercise interventions to prevent and manage type 2 diabetes: physiological mechanisms. Med Sport Sci 2014;60:36-47. 51. Teixeira-Lemos E, Nunes S, Teixeira F, Reis F. Regular physical exercise training assists in preventing type 2 diabetes development: focus on its antioxidant and anti-inflammatory properties. Cardiovasc Diabetol 2011;10:12.

2 3		
4	445	52. Panagiotakos DB, Pitsavos C, Skoumas Y, Lentzas Y, Stefanadis C. Five-year incidence of type 2
5	446	diabetes mellitus among cardiovascular disease-free Greek adults: findings from the ATTICA study.
6 7	447	Vasc Health Risk Manag 2008;4:691-8.
8	448	
9 10		
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STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Pag No
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	1
		(<i>b</i>) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			1
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of	
-		recruitment, exposure, follow-up, and data collection	
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of	7
		participants. Describe methods of follow-up	
		(b) For matched studies, give matching criteria and number of exposed and	7
		unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and	7
		effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	7
measurement		assessment (measurement). Describe comparability of assessment methods if	
		there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,	7
		describe which groupings were chosen and why	
Statistical methods	12	(<i>a</i>) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) If applicable, explain how loss to follow-up was addressed	
		(<u>e</u>) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially	8
i unicipanto	15	eligible, examined for eligibility, confirmed eligible, included in the study,	
		completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social)	8
		and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of inferest	
		(b) Indicate number of participants with missing data for each variable of interest(c) Summarise follow-up time (eg, average and total amount)	

Main results	16	(<i>a</i>) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other informati	on		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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BMJ Open

Epidemiology and risk factors for diabetes in the suburbs of Beijing: a retrospective cohort study

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Primary Subject Heading :	Epidemiology
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Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, EPIDEMIOLOGY, PUBLIC HEALTH





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12 13	4	Lingding Xie*, ¹ Xu Zhao*, ² Bo Zhang, ¹ Haiqing Zhu ³
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	24	Abstract
	25	Objective We aimed to detect the incidence and risk factors of type 2 diabetes
	26	mellitus (T2DM) development in the suburbs of Beijing.
)	27	Design Cohort study with record linkage to incidence data.
2 2	28	Setting We performed a 5-year follow-up study in a randomly selected suburban
3 1 -	29	population including 1,114 subjects aged >18 years living in the suburbs of Beijing.
5	30	Participants 118 subjects with T2DM at baseline according to the 1999 WHO criteria
3	31	were excluded, and 895 subjects attended the follow-up assessment in 2012. The non-
)	32	diabetic subjects at baseline were classified into two groups: normal glucose tolerance
<u>)</u> 2	33	(NGT) group (n=673) and impaired glucose regulation (IGR) group(n=222). The
1	34	incidence and risk factors of diabetes development in each group were investigated.
5 7	35	Outcome measures A structured questionnaire about sociodemographic
3	36	characteristics, height, weight, waist circumference, hip circumference, blood
) 	37	pressure, oral glucose tolerance test, and serum lipid levels.
2 3	38	Results Out of the 895 non-diabetic subjects, 67 developed diabetes with 29 in the
1	39	NGT group and 38 in the IGR group respectively after a 5-year follow-up, producing
5	40	an overall 5-year cumulative incidence of diabetes of 13%. The incidence of diabetes
3	41	was 15.5 cases per 1000 person-years, 8.9 cases per 1000 person-years in the NGT
)	42	group and 35.7 cases per 1000 person-years in the IGR group (P<0.01;RR=4.03;
<u>2</u> 3	43	95%CI:2.58-9.29). Binary logistic regression analysis showed that the risk factors for
1 5	44	diabetes development included fasting plasma glucose (FPG) in the NGT group, and
5 7	45	sex, the waist-to-hip ratio (WHR), FPG and diastolic blood pressure (DBP) in the IGR
3	46	group.
) 	47	Conclusions: During a mean follow-up of 5.0 years, the incidence of T2DM in the
<u>2</u> 3	48	suburbs of Beijing was 15.5 per 1000 person-years. Early prevention of diabetes
1 5	49	should focus on IGR subjects. Elevated FPG predicted diabetes development for both
5 7	50	NGT and IGR subjects. Female sex, overweight/obesity and DBP are risk factors for
3	51	diabetes development in IGR subjects.
)		

AAAA	rengths and limitations of this study This study is a retrospective cohort survey of the incidence of T2E risk factors in the suburbs of Beijing. Has a longitudinal design. Selects a cohort by multiple-stage sampling at baseline. Has a relatively long follow-up period. limitations include that many variables assessed as risk factors we updated regularly, and the data were collected only at the baseline investigation and at the end of the study.

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65	
66	Introduction
67	Diabetes mellitus is a clinical syndrome characterized by disordered
68	glycometabolism. The lack and/or insufficiency of insulin induces metabolic disorders
69	related to saccharides, lipids, proteins, water and electrolytes, resulting in
70	hyperglycemia as the main clinical feature. Long-term hyperglycemia leads to
71	macrovascular and microvascular complications, which may result in disability and
72	death. ^{1,2} Diabetes is increasingly prevalent, affecting 463 million (9.3%) adults
73	worldwide, and these figures are expected to increase to 700 million (10.9%) by
74	2045. ³ Type 2 diabetes mellitus (T2DM) accounts for over 90% of diabetes cases.
75	Diabetes, as a leading cause of death, ^{1,3,4} is becoming a public issue, placing a heavy
76	burden on the health care system. ⁵ In 2017 approximately 5 million adult deaths
77	worldwide were attributed to diabetes, ⁶ and the global healthcare expenditure
78	associated with people with diabetes in 2019 was estimated to be USD 760 billion. ⁷
79	Because T2DM is usually asymptomatic, it can remain undiagnosed for many years.
80	Almost half of all people (50.1%) living with diabetes were undiagnosed in $2019.^3$
81	Accordingly, screening for prediabetes/T2DM and preventing the evolution of
82	diabetes in individuals with risk factors are essential. Currently, the risk factors
83	related to T2DM development may include age, the body mass index (BMI), body fat
84	distribution, a family history of diabetes, a history of cardiovascular disease (CVD), a
85	history of gestational diabetes mellitus (GDM), race/ethnicity, diet, physical
86	inactivity, hypertension, dyslipidemia and prediabetes.4,8-16 Some studies have
87	demonstrated that birth weight, ^{17,18} income, ¹⁹ socioeconomic status, ^{20,21} working
88	hours, ^{21,22} occupation ²³ and genetic factors ²⁴⁻²⁶ might also contribute to T2DM
89	development.
90	In addition to the process of urbanization, the population aging, changes in lifestyle,
91	and increasing prevalence of obesity and overweight, the prevalence of diabetes in
92	China has increased over the past three decades. The prevalence of diabetes in China

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was 0.67% in 1980,²⁷ 2.12% in 1995,²⁸ 5.5% in 2001,²⁹ 9.7% in 2008,³⁰ 9.7% in
2010³¹ and 10.4% in 2013.³² As the capital city, limited information is available
regarding the incidence of diabetes and prediabetes in Beijing. Certain studies have
suggested that different diabetic risk patterns might exist in Asian populations.³³⁻³⁶
This study aimed to determine the incidence of and risk factors for T2DM among
Chinese adults in the suburbs of Beijing.

99 Materials and Methods

100 Study population

 The study population comprised residents living in the suburbs (Huairou, Pinggu and Hepingli) of Beijing. We used a multistage, stratified sampling method to randomly select the three suburbs from the Beijing countryside.³⁰ The details of its sampling methods have been described previously.³⁰ Individuals aged 18 years or older who were willing to participate and provided informed consent were eligible to participate in the study. People with a history of diabetes were excluded from the study. Pregnant women were also excluded from the study.

We performed a 5-year retrospective cohort study. The baseline survey occurred from June 2007 to September 2008 using a random sampling method with a follow-up examination from May to July 2012. All the subjects were asked to undergo a personal interview, physical examination and blood test [including an oral glucose tolerance test (OGTT)]. Subjects diagnosed as diabetes by OGTT at baseline were excluded. The nondiabetic subjects at baseline were divided into the normal glucose tolerance (NGT) group and impaired glucose regulation (IGR) group according to OGTT. We analyzed the incidence and risk factors of diabetes development in each group. Diabetes mellitus was defined according to the 1990 WHO criteria or self-reported prior diagnosis of diabetes with current medication use. IGR was determined if the subjects had a fasting plasma glucose (FPG) level of 6.1-6.9 mmol/L and/or a 2-hour plasma glucose level of 7.8-11.0 mmol/L. NGT was defined as FPG less than 6.0mmol/L and a 2-hour plasma glucose level less than 11.1mmol/L.

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3 4	121	Data collection
5 6	122	Sociodemographic characteristics—The data were collected by trained staff using a
7 8	123	structured questionnaire via a face-to-face interview to assess general information
9 10	124	(sex, age, nationality, education status, occupation, and per capita income), personal
11 12	125	history (smoking history, alcohol history, physical activity, and dietary habits), family
13 14	126	history (diabetes mellitus, hypertension, hyperlipidemia, myocardial infarction,
15 16 17	127	stroke, and obesity), and history of current illness (diabetes, hypertension,
17 18 19	128	hyperlipidemia, cardiovascular, cerebrovascular diseases, and kidney diseases).
20 21	129	Subjects who were diagnosed with T2DM between recruitment and the end of follow-
21 22 23	130	up were asked to report the date of diagnosis.
23 24 25	131	Anthropometric measurements — The subjects were examined for height, weight,
26 27	132	waist circumference (WC), hip circumference (HC) and blood pressure. All the
28 29	133	subjects were asked to remove their shoes, socks, hats and coats, stand erectly and
30 31	134	look forward with their arms relaxed and their heels together. Height was measured in
32 33	135	centimeters using a height bar, and weight was measured in kilograms using a digital
34 35	136	weighing scale. The WC is the circumference of the waist at the horizontal line of the
36 37	137	umbilicus measured in centimeters using a measuring tape, and the HC is the
38 39	138	circumference of hips at the horizontal line of the anterior superior spine measured in
40 41	139	centimeters using a measuring tape. The BMI was calculated as weight in kilograms
42 43	140	divided by the square of height in meters (kg/m ²), while the waist-to-hip ratio (WHR)
44 45	141	was calculated as WC (cm) divided by HC (cm). The blood pressure values used were
46 47	142	an average of three measurements, which were measured 2 min apart using a mercury
48 49	143	sphygmomanometer. The subjects were asked to stop smoking and consuming alcohol
50 51	144	the day before the examination and to sit quietly in a chair for at least 5 minutes
52 53	145	before the measurement with their arms bare and placed at the chest level. All the
54 55	146	clinical staff members were trained to measure blood pressure and obtain
56 57 58	147	anthropometric measurements.

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148 **Laboratory examination**—All the subjects were invited to undergo a blood test 149 (including an OGTT) at baseline. The nondiabetic subjects at baseline undergo a secondary blood test (including an OGTT) at the end of follow-up. Venous blood 150 151 samples after 8–14 hours of fasting were obtained from the subjects to measure FPG, total cholesterol (TC), triglycerides (TGs), high-density lipoprotein cholesterol (HDL-152 C) and low-density lipoprotein cholesterol (LDL-C). Venous blood samples, after a 153 75 g oral glucose load, were obtained to measure the 2-hour plasma glucose (PG2h). 154 155 The subjects were instructed to maintain normal physical activity without dietary limit (the intake of saccharides should be no less than 150 g per day) before proceeding 156 with the OGTT. 157 **Statistical analysis** 158

We used the P-P plot to test the normality of the numerical variables. The differences 159 in continuous and categorical variables between the NGT and IGR groups were 160 examined using t test and the χ^2 test statistic, respectively. Kaplan–Meier survival 161 estimates were used to calculate the 5-year cumulative incidence of T2DM. The log-162 rank test was used to compare the survival curves. The Mantel–Haenszel χ^2 test of 163 trends was used to analyze the ordinal data. Binary logistic regression analyses were 164 used to estimate the odds ratio and 95% confidence interval for diabetes development. 165 166 All the analyses were performed using SPSS statistical software version 17.0, and a P value<0.05 was considered statistically significant. 167

168 **Patient and Public Involvement**

Patients or the public were not involved in the design, or conduct, or reporting, ordissemination plans of our research.

171 Results

172 Characteristics of the study population at baseline

173 In total, 1,114 residents participated in the study, and 1,014 subjects completed the

- 174 follow-up, with an overall response rate of 91.0%. After eliminating 118 subjects who
- 175 were diagnosed with diabetes by OGTT at baseline and one subject with severe data

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176	deficiency, 895 subjects (308 men and 587 women) with a mean age of 48.1±11.9
177	years were included in the analysis, with 673 in the NGT group and 222 in the IGR
178	group. The baseline characteristics of the 895 subjects in the study are shown in Table
179	1. Continuous variables were expressed as means±standard deviation (sd) and were
180	examined using a t test, while categorical variables were expressed as percentages and
181	were examined using the χ^2 test. No significant difference was found between the
182	NGT group and the IGR group in sex, height, family history of T2DM, smoking
183	history, alcohol history, exercise time, diastolic blood pressure (DBP) or HDL-C.
184	Age, weight, BMI, WC, WHR, systolic blood pressure (SBP), FPG, PG2h, TGs, TC
185	and LDL-C in the IGR group were significantly higher than those in the NGT group.
186	Incidence of T2DM
187	During the follow-up, T2DM developed in 67 subjects, 29 in the NGT group and 38
188	in the IGR group, resulting in T2DM onset rates of 15.45, 8.86 and 35.67 per 1,000
189	person-years in the total study population, NGT group and IGR group, respectively
190	(Table 2). The difference in the incidence of T2DM between the NGT group and IGR
191	group was statistically significant (χ^2 =37.38;P<0.01;RR=4.03;95% CI: 2.58-9.29).
192	The 5-year cumulative incidence of T2DM was 13%, with 10% in the NGT group and
193	20% in the IGR group. The mean follow-up duration was 5.008 years (SE=0.013;
194	95% CI: 4.982–5.033), with 5.003 years (SE=0.012;95% CI: 5.010–5.056) in the
195	NGT group and 4.933 years (SE=0.038;95% CI: 4.859–5.007) in the IGR group.
196	Using the log-rank test, we found that the cumulative incidence of T2DM in the IGR
197	group was significantly higher than that in the NGT group ($\chi^2=36.905$; P<0.0001).
198	The results of the Kaplan–Meier survival analyses are shown in Figure 1.
199	Analyses of the risk factors for diabetes development
200	The results of binary logistic regression analyses for T2DM development in the NGT
201	and IGR groups are shown in Table 3. FPG contributed to T2DM development in the
202	NGT group, and the OR was 6.111 (1.379, 27.070; P=0.017). Sex, WHR, DBP, and
203	FPB contributed to T2DM development in the IGR group, and the ORs were 7.293

(1.074, 49.549; P=0.042), 2.874E8 (8.386, 9.847E15; P=0.028), 1.068 (1.009, 1.130; P=0.024) and 7.243 (2.314, 22.673; P=0.001), respectively. The increase in exercise time slightly decreased the risk of T2DM in the IGR group, with an OR of 0.923 (0.847, 1.005; P=0.066). Discussion The prevalence of diabetes mellitus has been increasing markedly in recent decades. Among adults aged 20–79 years in 2019, there were an estimated 463 million cases of diabetes³. However, the striking prevalence may be partly attributable to the increase in population and prolongation of the life-span.³⁷ Accordingly, we studied the growing trend of T2DM by investigating the cumulative incidence of T2DM. Our results showed that 15.45 new cases of diabetes per 1,000 people-years were diagnosed during the five-year observation period (2007–2012). This marked trend is consistent with diabetes incidence rates worldwide, such as those described in the ATTICA study in Greece (12.9 cases per 1,000 person-years from 2002 to 2012)³⁸ and those described in a study conducted in Mexico (12.7 cases per 1,000 person-years from 1990 to 2008).³⁹ The incidence rate found in our study is lower than that in a study of Pima Indians (23.5 cases per 1,000 person-years during 1991 to 2003)⁴⁰ and in a study conducted in northern Spain (95.2 cases per 1,000 person-years during 1998 to 2005)⁴¹ and is higher than that observed in a study conducted in Iran (10.6 cases per 1000 person-years from 1999 to 2011)⁴² and in the SUPREME-DM project in the USA (11.5 cases per 1000 person-years from 2006 to 2011).⁴³ The T2DM incidence in the suburbs of Beijing is higher than that identified in the investigation conducted by Wang C et al in a Chinese population in 2010 (9.5 cases per 1000 person-years in men and 9.2 in women).⁴⁴ This difference may partly be due to the relatively higher standard of living in the suburbs of Beijing. Diabetes development is based on the interaction between genes and lifestyle and environmental factors.^{45,46} Compared with the NGT group that had an incidence of 8.86 cases per 1,000 person-years, the IGR group (35.67 cases per 1,000 person-

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3 4	232	years) had a higher incidence rate (RR=4.03;95% CI: 2.58–9.29;P<0.01). In our
5 6	233	study, diabetes development was mainly the consequence of elevated FPG in the NGT
7 8	234	group. Diabetes development was mainly associated with sex (female), abnormal
9 10	235	WHR, elevated DBP and elevated FPG in the IGR group. The increase in the FPG
11 12	236	level was a strong predictor of diabetes development in both the NGT group and IGR
13 14	237	group, with 6.111- and 7.243-fold increased risk per unit increase, respectively.
15 16	238	In our study, the WHR measurement was found to predict diabetes risk. Some studies
17 18	239	have declared that WHR, as an obesity indicator, is superior to BMI and WC. 47,48 A
19 20	240	meta-analysis demonstrated that either BMI or WC (WHR) predicted or was
21 22	241	independently associated with type 2 diabetes, regardless of the controversial findings
23 24	242	regarding which was better.49
25 26 27	243	Age and family history of diabetes are considered risk factors for diabetes
27 28 20	244	development. ^{4,8-16} However, we found only an increasing trend of diabetes
29 30 31	245	development in the elderly population and subjects with a family history of diabetes
32 33	246	(P>0.05). This finding might be related to the short period of follow-up and the
34 35	247	subjects' unawareness of their family history of diabetes.
36 37	248	There is evidence that T2DM can be prevented in high-risk individuals by a lifestyle
38 39	249	program of regular exercise.50,51 Surprisingly, our study found that exercise did not
40 41	250	exert a beneficial effect on diabetes incidence, a finding similar to that in the ATTICA
42 43	251	study. ^{38,52} However, we found a decreasing trend in the diabetes incidence with
44 45	252	increasing exercise time. The increase in exercise time slightly decreased the risk of
46 47	253	T2DM in the IGR group, with an OR of 0.923 (0.847, 1.005; P=0.066).
48 49	254	The strength of our study is that it was based on a cohort selected by multiple stage
50 51	255	sampling at baseline with a relatively long follow-up period. A limitation is that many
52 53	256	variables assessed as risk factors were not updated regularly, and might have changed
54 55	257	during the follow-up period. Secondly, the follow-up could not be random due to the
56 57	258	limitations of the conditions. Additionally, the data were collected only at the baseline
58 59	259	investigation and at the end of the study.
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260 **Conclusions**

During a mean follow-up of 5.0 years, the incidence of T2DM in the suburbs of
Beijing was 15.45 cases per 1000 person-years, which was relatively higher than that
in many other areas worldwide. Compared with the NGT subjects, the IGR subjects
were more susceptible to T2DM. To prevent diabetes development, all the subjects
should be evaluated for elevated FPG. Additionally, sex, WHR, and DBP were
predictors of T2DM in IGR subjects.
The findings in this study provide new data on the incidence of T2DM in the Beijing

area. The predictors of T2DM reported in the present study may be conducive to

269 formulating a protocol for diabetes prevention.

270 Authors' contributions

- 271 Conceptualization, B.Z.; Data curation, H.Z.; Formal analysis, H.Z.; Investigation,
- L.X. and X.Z.; Methodology, B.Z.; Project administration, L.X., X.Z. and B.Z.;
- 273 Writing original draft, L.X. and X.Z.; Writing review & editing, B.Z.. All authors
- read and approved the final manuscript, as well as the submission of this work. B.Z.
- supervised and managed the data. B.Z. is the guarantor of this work.

276

- 277 **Conflicts of interest**
- 278 The authors declare that they have no conflicts of interest.

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280 **Competing interests** None declared.

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282 Funding statement

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 - 284 Technology Support Program (2009BAI80B04).

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5 6	286	Ethics approval
7 8	287	Ethical approval was obtained from the Ethics Committee of Clinical Trials of
9 10	288	Drugs/Devices in China-Japan Friendship Hospital (2011-049).
11 12	289	
13 14 15 16	290	Data availability statement
17 18 19	291	All data included in this study are available from the corresponding author on
20 21	292	reasonable request.
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baseline

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295	Table 1 Comparison of the characteristics of the NGT and IGR subjects at
	1 U

Variable at baseline	NGT group	IGR group	t or χ^2 , <i>P</i> value
	(n=673)	(n=222)	
Sex(%male)	34.9	32.9	0.306, 0.625
Age (years)	46.75±11.57	52.01±12.03	-5.813, <0.001
Height (cm)	161.85±7.94	161.18±7.83	1.092, 0.275
Weight (kg)	64.32±10.75	67.49±11.05	-3.777, <0.001
BMI (kg/m ²)	24.52±3.40	25.93±3.50	-5.332, <0.001
WC (cm)	83.04±9.75	86.82±9.20	-5.075, <0.001
WHR	0.87±0.07	0.89±0.06	-3.495, <0.001
SBP (mmHg)	119.71±18.37	125.18±20.13	-3.582, <0.001
DBP (mmHg)	78.02±11.21	79.75±12.66	-1.843, 0.066
FPG (mmol/L)	5.25±0.42	5.82±0.61	-15.875, <0.00
PG2h (mmol/L)	5.90±1.01	8.29±1.52	-26.692, <0.00
TGs (mmol/L)	1.42±1.17	1.61±1.08	-2.165, 0.031
TC (mmol/L)	4.56±0.92	4.84±0.95	-3.865, <0.001
HDL-C (mmol/L)	1.35±0.34	1.34±0.36	0.464, 0.643
LDL-C (mmol/L)	2.77±0.77	3.08±0.81	-4.648, <0.001
Exercise duration	5.85±11.81	5.59±8.06	0.305, 0.761
(hours)			
FH of T2DM (%)	15.5	21.4	3.722, 0.068
Smoking history (%)	22.4	20.7	0.286, 0.641
Alcohol history (%)	27.9	28.8	0.076, 0.796
Years of follow-up	4.85±0.32	4.79±0.56	2.081, 0.038

BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; SBP,

298 systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose;

1 2		
3 4	299	PG2h, 2-hour plasma glucose; TC, total cholesterol; TGs, triglycerides; HDL-C, high-
5 6	300	density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FH,
7 8	301	family history. Exercise duration is expressed as hours per week.
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303 Table 2. Incidence of T2DM during the follow-up

	Cases of diabetes	Follow-up (person-	Incidence (per 1,000
		years)	person-years)
NGT group	29	3,271.5	8.86
IGR group	38	1,065.3	35.67
Total	67	4,336.8	15.45

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	NGT group IGR grou		
	OR (95% CI)	P value	OR (95% CI)
	0.275 (0.077, 0.102)	0.265	7 202 (1 074 40 540
Sex	0.375 (0.067, 2.103)	0.265	7.293 (1.074, 49.549)
Age (years)	1.013 (0.962, 1.068)	0.615	1.019 (0.964, 1.077)
Weight (kg)	1.044 (0.927, 1.175)	0.478	1.056 (0.929, 1.200)
BMI (kg/m ²)	0.934 (0.653, 1.336)	0.710	0.971 (0.661, 1.427)
WC (cm)	1.073 (0.936, 1.230)	0.311	0.904 (0.748, 1.092)
WHR	0.006 (0.000,	0.473	2.874E8 (8.386,
	7058.081)		9.847E15)
SBP (mmHg)	1.013 (0.976, 1.052)	0.492	0.992 (0.958, 1.026)
DBP (mmHg)	0.955 (0.890, 1.024)	0.198	1.068 (1.009, 1.130)
FPG (mmol/L)	6.111 (1.379, 27.070)	0.017	7.243 (2.314, 22.673)
TC (mmol/L)	2.719 (0.917, 8.067)	0.071	0.814 (0.141, 4.699)
TGs (mmol/L)	0.996 (0.589, 1.684)	0.989	0.926 (0.491, 1.749)
HDL-C (mmol/L)	2.536 (0.519, 12.395)	0.250	0.622 (0.071, 5.460)
LDL-C (mmol/L)	0.604 (0.206, 1.769)	0.358	1.070 (0.181, 6.321)
Exercise duration	1.013 (0.947, 1.084)	0.707	0.923 (0.847, 1.005)
(hours)			
FH of T2DM	1.868 (0.492, 7.090)	0.358	2.062 (0.656, 6.478)
Smoking history	0.766 (0.186, 3.162)	0.713	1.591 (0.346, 7.317)
Alcohol history	0.726 (0.202, 2.610)	0.624	1.685 (0.458, 6.203)
BMI, body mass index;	WC, waist circumference;	WHR, wa	ist-to-hip ratio; SBP,
systolic blood pressure;	DBP, diastolic blood pres	sure [.] FPG	fasting plasma glucose

LDL-C, low-density lipoprotein cholesterol; FH, family history. Sex is defined as

male (n=1) or female (n=2), FH of T2DM is defined as no (n=1) or yes (n=2),

3 4	312	smoking history was defined as no (n=1) or yes (n=2), and alcohol history was
5 6	313	defined as no (n=1) or yes (n=2). Exercise duration is expressed as hours per week.
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3 4	317	Figure legend
5 6	318	Figure 1. Cumulative incidence of T2DM in the NGT and IGR groups (log-rank test:
7 8	319	χ ² =36.905;P<0.0001)
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3	325	References
4 5		
6	326	1. Mortality GBD, Causes of Death C. Global, regional, and national age-sex specific all-cause and
7	327	cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global
8 9	328	Burden of Disease Study 2013. Lancet 2015;385:117-71.
9 10	329	2. Wong E, Backholer K, Gearon E, et al. Diabetes and risk of physical disability in adults: a
11	330	systematic review and meta-analysis. Lancet Diabetes Endocrinol 2013;1:106-14.
12	331	3. Sinclair A, Saeedi P, Kaundal A, Karuranga S, Malanda B, Williams R. Diabetes and global
13 14	332	ageing among 65-99-year-old adults: Findings from the International Diabetes Federation Diabetes
15	333	Atlas, 9(th) edition. Diabetes Res Clin Pract 2020;162:108078.
16	334	4. Mc Donald Posso AJ, Bradshaw Meza RA, Mendoza Morales EA, Jaen Y, Cumbrera Ortega A,
17 18	335	Mendoza Posada EJ. Diabetes in Panama: Epidemiology, Risk Factors, and Clinical Management. Ann
19	336	<i>Glob Health</i> 2015;81:754-64.
20	337	5. Bommer C, Sagalova V, Heesemann E, et al. Global Economic Burden of Diabetes in Adults:
21 22	338	Projections From 2015 to 2030. Diabetes Care 2018;41:963-70.
23	339	6. Cho NH, Shaw JE, Karuranga S, et al. IDF Diabetes Atlas: Global estimates of diabetes
24	340	prevalence for 2017 and projections for 2045. <i>Diabetes Res Clin Pract</i> 2018;138:271-81.
25 26	341	7. Williams R, Karuranga S, Malanda B, et al. Global and regional estimates and projections of
20	342	diabetes-related health expenditure: Results from the International Diabetes Federation Diabetes Atlas,
28	343	9th edition. <i>Diabetes Res Clin Pract</i> 2020;162:108072.
29	344	 Weber MB, Oza-Frank R, Staimez LR, Ali MK, Narayan KM. Type 2 diabetes in Asians:
30 31		
32	345	prevalence, risk factors, and effectiveness of behavioral intervention at individual and population
33	346	levels. Annu Rev Nutr 2012;32:417-39.
34 35	347	9. Perez CM, Soto-Salgado M, Suarez E, Guzman M, Ortiz AP. High Prevalence of Diabetes and
36	348	Prediabetes and Their Coexistence with Cardiovascular Risk Factors in a Hispanic Community. J
37	349	Immigr Minor Health 2015;17:1002-9.
38	350	10. Aljoudi AS, Taha AZ. Knowledge of diabetes risk factors and preventive measures among
39 40	351	attendees of a primary care center in eastern Saudi Arabia. Ann Saudi Med 2009;29:15-9.
41	352	11. American Diabetes A. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in
42	353	Diabetes-2018. Diabetes Care 2018;41:S13-S27.
43 44	354	12. Fletcher B, Gulanick M, Lamendola C. Risk factors for type 2 diabetes mellitus. J Cardiovasc
45	355	Nurs 2002;16:17-23.
46	356	13. Karter AJ, Schillinger D, Adams AS, et al. Elevated rates of diabetes in Pacific Islanders and
47 48	357	Asian subgroups: The Diabetes Study of Northern California (DISTANCE). Diabetes Care
49	358	2013;36:574-9.
50	359	14. Harjo TC, Perez A, Lopez V, Wong ND. Prevalence of diabetes and cardiovascular risk factors
51 52	360	among California Native American adults compared to other ethnicities: the 2005 California Health
53	361	Interview Survey. Metab Syndr Relat Disord 2011;9:49-54.
54	362	15. Akter S, Rahman MM, Abe SK, Sultana P. Prevalence of diabetes and prediabetes and their risk
55 56	363	factors among Bangladeshi adults: a nationwide survey. Bull World Health Organ 2014;92:204-13,
56 57	364	13A.
58	365	16. Amarasinghe S, Balakumar S, Arasaratnam V. Prevalence and risk factors of diabetes mellitus
59	366	among adults in Jaffna District. <i>Ceylon Med J</i> 2015;60:107-10.
60	500	among adunts in Janna District. Ceyton intea 5 2015,00.107-10.

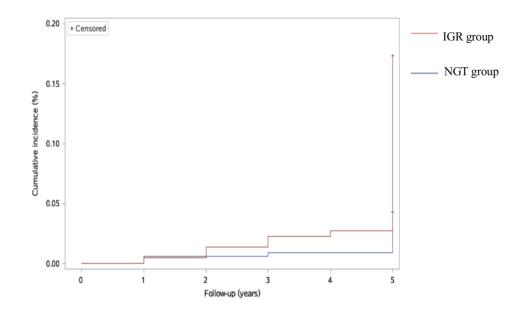
Page 21 of 25

1 2

3	367	17. Pettitt DJ, Jovanovic L. Low birth weight as a risk factor for gestational diabetes, diabetes, and
4 5	368	impaired glucose tolerance during pregnancy. Diabetes Care 2007;30 Suppl 2:S147-9.
6	369	18. Harder T, Rodekamp E, Schellong K, Dudenhausen JW, Plagemann A. Birth weight and
7	370	subsequent risk of type 2 diabetes: a meta-analysis. Am J Epidemiol 2007;165:849-57.
8 9	371	19. Barker L, Crespo R, Gerzoff RB, Denham S, Shrewsberry M, Cornelius-Averhart D. Residence in
10	372	a distressed county in Appalachia as a risk factor for diabetes, Behavioral Risk Factor Surveillance
11 12	373	System, 2006-2007. Prev Chronic Dis 2010;7:A104.
12	374	20. Espelt A, Arriola L, Borrell C, Larranaga I, Sandin M, Escolar-Pujolar A. Socioeconomic position
14	375	and type 2 diabetes mellitus in Europe 1999-2009: a panorama of inequalities. Curr Diabetes Rev
15 16	376	2011;7:148-58.
17	377	21. Kivimaki M, Virtanen M, Kawachi I, et al. Long working hours, socioeconomic status, and the
18	378	risk of incident type 2 diabetes: a meta-analysis of published and unpublished data from 222 120
19 20	379	individuals. Lancet Diabetes Endocrinol 2015;3:27-34.
21	380	22. Bannai A, Yoshioka E, Saijo Y, Sasaki S, Kishi R, Tamakoshi A. The Risk of Developing
22	381	Diabetes in Association With Long Working Hours Differs by Shift Work Schedules. <i>J Epidemiol</i>
23 24	382	2016;26:481-7.
25	383	23. Honda T, Kuwahara K, Nakagawa T, Yamamoto S, Hayashi T, Mizoue T. Leisure-time,
26	384	occupational, and commuting physical activity and risk of type 2 diabetes in Japanese workers: a
27 28	385	cohort study. <i>BMC Public Health</i> 2015;15:1004.
29	386	24. Ma RC, Hu C, Tam CH, et al. Genome-wide association study in a Chinese population identifies a
30	387	susceptibility locus for type 2 diabetes at 7q32 near PAX4. <i>Diabetologia</i> 2013;56:1291-305.
31 32	388	25. Grarup N, Sandholt CH, Hansen T, Pedersen O. Genetic susceptibility to type 2 diabetes and
33	389	obesity: from genome-wide association studies to rare variants and beyond. <i>Diabetologia</i>
34 25	390	2014;57:1528-41.
35 36	391	26. Florez JC, Jablonski KA, Bayley N, et al. TCF7L2 polymorphisms and progression to diabetes in
37	392	the Diabetes Prevention Program. N Engl J Med 2006;355:241-50.
38 39	393	27. Gruop NDrC. A mass survey of diabetes mellitus in a population of 300,000 in 14 provinces and
39 40	394	municipalities in China (author's transl). <i>Zhonghua Nei Ke Za Zhi</i> 1981;20:678-83.
41	395	28. Pan XR, Yang WY, Li GW, Liu J. Prevalence of diabetes and its risk factors in China, 1994.
42 43	396	National Diabetes Prevention and Control Cooperative Group. <i>Diabetes Care</i> 1997;20:1664-9.
44	397	29. Chan JC, Malik V, Jia W, et al. Diabetes in Asia: epidemiology, risk factors, and
45	398	pathophysiology. JAMA 2009;301:2129-40.
46 47	399	30. Yang W, Lu J, Weng J, et al. Prevalence of diabetes among men and women in China. <i>N Engl J</i>
48	400	Med 2010;362:1090-101.
49 50	401	31. Xu Y, Wang L, He J, et al. Prevalence and control of diabetes in Chinese adults. <i>JAMA</i>
50 51	402	2013;310:948-59.
52	403	32. Wang L, Gao P, Zhang M, et al. Prevalence and Ethnic Pattern of Diabetes and Prediabetes in
53 54	404	China in 2013. <i>JAMA</i> 2017;317:2515-23.
54 55	405	33. Narayan KM, Aviles-Santa L, Oza-Frank R, et al. Report of a National Heart, Lung, And Blood
56	406	Institute Workshop: heterogeneity in cardiometabolic risk in Asian Americans In the U.S.
57 58	407	Opportunities for research. <i>J Am Coll Cardiol</i> 2010;55:966-73.
58 59		· · · · · · · · · · · · · · · · · · ·
60		

34. Oza-Frank R, Ali MK, Vaccarino V, Narayan KM. Asian Americans: diabetes prevalence across U.S. and World Health Organization weight classifications. Diabetes Care 2009;32:1644-6. 35. Ma RC, Chan JC. Type 2 diabetes in East Asians: similarities and differences with populations in Europe and the United States. Ann NY Acad Sci 2013;1281:64-91. 36. Gujral UP, Pradeepa R, Weber MB, Narayan KM, Mohan V. Type 2 diabetes in South Asians: similarities and differences with white Caucasian and other populations. Ann NY Acad Sci 2013;1281:51-63. 37. Gulland A. Global life expectancy has risen, reports WHO. BMJ 2014;348:g3369. 38. Koloverou E, Panagiotakos DB, Pitsavos C, et al. 10-year incidence of diabetes and associated risk factors in Greece: the ATTICA study (2002-2012). Rev Diabet Stud 2014;11:181-9. 39. Gonzalez-Villalpando C, Davila-Cervantes CA, Zamora-Macorra M, Trejo-Valdivia B, Gonzalez-Villalpando ME. Incidence of type 2 diabetes in Mexico: results of the Mexico City Diabetes Study after 18 years of follow-up. Salud Publica Mex 2014;56:11-7. 40. Pavkov ME, Hanson RL, Knowler WC, Bennett PH, Krakoff J, Nelson RG. Changing patterns of type 2 diabetes incidence among Pima Indians. Diabetes Care 2007;30:1758-63. 41. Valdes S, Botas P, Delgado E, Alvarez F, Cadorniga FD. Population-based incidence of type 2 diabetes in northern Spain: the Asturias Study. Diabetes Care 2007;30:2258-63. 42. Derakhshan A, Sardarinia M, Khalili D, Momenan AA, Azizi F, Hadaegh F. Sex specific incidence rates of type 2 diabetes and its risk factors over 9 years of follow-up: Tehran Lipid and Glucose Study. PLoS One 2014;9:e102563. 43. Nichols GA, Schroeder EB, Karter AJ, et al. Trends in diabetes incidence among 7 million insured adults, 2006-2011: the SUPREME-DM project. Am J Epidemiol 2015;181:32-9. 44. Wang C, Li J, Xue H, et al. Type 2 diabetes mellitus incidence in Chinese: contributions of overweight and obesity. Diabetes Res Clin Pract 2015;107:424-32. 45. Murea M, Ma L, Freedman BI. Genetic and environmental factors associated with type 2 diabetes and diabetic vascular complications. Rev Diabet Stud 2012;9:6-22. 46. InterAct C, Langenberg C, Sharp S, et al. Design and cohort description of the InterAct Project: an examination of the interaction of genetic and lifestyle factors on the incidence of type 2 diabetes in the EPIC Study. Diabetologia 2011;54:2272-82. 47. Zhao X, Zhu X, Zhang H, et al. Prevalence of diabetes and predictions of its risks using anthropometric measures in southwest rural areas of China. BMC Public Health 2012;12:821. 48. Gupta R, Rastogi P, Sarna M, Gupta VP, Sharma SK, Kothari K. Body-mass index, waist-size, waist-hip ratio and cardiovascular risk factors in urban subejcts. J Assoc Physicians India 2007;55:621-7. 49. Qiao Q, Nyamdorj R. Is the association of type II diabetes with waist circumference or waist-to-hip ratio stronger than that with body mass index? Eur J Clin Nutr 2010;64:30-4. 50. Dela F, Prats C, Helge JW. Exercise interventions to prevent and manage type 2 diabetes: physiological mechanisms. Med Sport Sci 2014;60:36-47. 51. Teixeira-Lemos E, Nunes S, Teixeira F, Reis F. Regular physical exercise training assists in preventing type 2 diabetes development: focus on its antioxidant and anti-inflammatory properties. Cardiovasc Diabetol 2011;10:12.

1 2		
3	449	52. Panagiotakos DB, Pitsavos C, Skoumas Y, Lentzas Y, Stefanadis C. Five-year incidence of type 2
4 5	450	diabetes mellitus among cardiovascular disease-free Greek adults: findings from the ATTICA study.
6	451	Vasc Health Risk Manag 2008;4:691-8.
o 7 8 9 10 11 12 13 14 15 16 17 18 9 20 21 22 32 42 52 6 27 28 29 30 132 33 435 36 37 839 40 41 42 43 445 46 47 48 9 50 152 53 455 67 89 60	451	Vasc Health Kisk Manag 2008;4:691-8.



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STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Pag No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the	1
		abstract	
		(b) Provide in the abstract an informative and balanced summary of what was	2
		done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of	
		recruitment, exposure, follow-up, and data collection	
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of	7
		participants. Describe methods of follow-up	
		(b) For matched studies, give matching criteria and number of exposed and	7
		unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and	7
		effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	7
measurement		assessment (measurement). Describe comparability of assessment methods if	
		there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,	7
~		describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for	8
		confounding	
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) If applicable, explain how loss to follow-up was addressed	
		(<u>e</u>) Describe any sensitivity analyses	
Results			0
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially	8
		eligible, examined for eligibility, confirmed eligible, included in the study,	
		completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	0
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social)	8
		and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	9

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their	9
		precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.	10
		Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations,	10
-		multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other informati	on		•
Funding	22	Give the source of funding and the role of the funders for the present study and, if	12
		applicable, for the original study on which the present article is based	

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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