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

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Abstract

Objective We aimed to detect the incidence and risk factors of type 2 diabetes mellitus (T2DM) development in the suburbs of Beijing.

Design Cohort study with record linkage to incidence data.

Setting We performed a 5-year follow-up study in a randomly selected suburban population including 1,114 subjects aged≥18 years living in the suburbs of Beijing.

Participants 118 subjects with T2DM in baseline according to the 1999 WHO criteria were excluded, and 895 subjects attended the follow-up assessment in 2012. The non-diabetic subjects at baseline were classified into two groups: normal glucose tolerance (NGT) group (n=673) and impaired glucose regulation (IGR) group(n=222), the incidence and risk factors of diabetes development in each group were investigated.

Outcome measures a structured questionnaire of sociodemographic characteristics, height, weight, waist circumference, hip circumference and blood pressure, oral glucose tolerance test, serum lipid levels.

Results Out of the 895 non-diabetic subjects, 67 developed diabetes with 29 in NGT group and 38 in IGR group respectively after 5-year follow-up, giving a overall 5-year cumulative incidence of diabetes of 13%. The incidence of diabetes was 15.5 cases per 1000 person-years, while 8.9 cases per 1000 person-years in NGT group and 35.7 cases per 1000 person-years in IGR group (P<0.01, RR=4.03, 95%CI:2.58-9.29). Binary logistic regression analysis showed that the risk factors of diabetes development included FPG in NGT group, while gender, WHR, FPG and DBP in IGR group.

Conclusions: During a mean follow-up of 5.0 years, the incidence of T2DM in the suburbs of Beijing was 15.5 per 1000 person-years. Early prevention of diabetes should focus on IGR subjects. Elevated FPG predicted diabetes development for both NGT and IGR subjects. Female, overweight/obesity and DBP were risk factors for diabetes development in IGR subjects.

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Strengths and limitations of this study

- 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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Introduction

Diabetes mellitus is a clinical syndrome characterized by disordered glycometabolism. The lack and/or insufficiency of insulin induces metabolic disorders related to saccharides, lipids, proteins, water and electrolytes, resulting in hyperglycemia as the main clinical feature. Long-term hyperglycemia leads to macrovascular and microvascular complications, which may result in disability and death.[1,2] Diabetes is increasingly prevalent, affecting 451 million (8.4%) adults worldwide, and these figures are expected to increase to 693 million (9.9%) by 2045.[3] Type 2 diabetes mellitus (T2DM) accounts for over 90% of diabetes cases. Diabetes, as a leading cause of death,[1,3,4] is becoming a public issue and placing a heavy burden on the health care system.[5] In 2017, approximately 5 million deaths of adults worldwide were attributed to diabetes, and the global healthcare expenditure associated with people with diabetes was estimated to be $850 billion.[3]

As T2DM is usually asymptomatic, it can remain undiagnosed for many years. Almost half of all people (49.7%) living with diabetes were undiagnosed in 2017.[3] Accordingly, screening for prediabetes/T2DM and preventing the evolution of diabetes in individuals with risk factors are essential. Currently, it is believed that the risk factors related to the development of T2DM may include age, body mass index (BMI), body fat distribution, family history of diabetes, history of cardiovascular disease (CVD), history of gestational diabetes mellitus (GDM), race/ethnicity, diet, physical inactivity, hypertension, dyslipidemia and prediabetes.[4,6-14] Some studies demonstrated that birth weight,[15,16] income,[17] socioeconomic status,[18,19] working hours,[19,20] occupation[21] and genetic factors[22-24] might also contribute to the development of T2DM.

Along with the process of urbanization, the aging of the population, changes in lifestyle, and the increasing prevalence of obesity and overweight, the prevalence of 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 2010[29] 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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pressure (SBP), FPG, PG2h, TGs, TC, LDL-C and duration of follow-up was statistically significant.

Incidence of T2DM

During the follow-up, T2DM developed in 67 subjects, 29 in the NGT group and 38 in the IGR group, resulting in T2DM onset rates of 15.45, 8.86 and 35.67 per 1,000 person-years in the total study population, the NGT group and the IGR group, respectively (Table 2). The difference in the incidence of T2DM between the NGT group and the IGR group was statistically significant (χ^2=37.38, P＜0.01, RR=4.03, 95% CI: 2.58-9.29).

The 5-year cumulative incidence of T2DM was 13%, with 10% in the NGT group and 20% in the IGR group. The mean follow-up duration was 5.008 years (SE=0.013, 95% CI: 4.982-5.033), with 5.003 years (SE=0.012, 95% CI: 5.010-5.056) in the NGT group and 4.933 years (SE=0.038, 95% CI: 4.859-5.007) in the IGR group. Using the log-rank test, we found that the cumulative incidence of T2DM in the IGR group was significantly higher than that in the NGT group (χ^2=36.905, P＜0.0001). The results of the Kaplan-Meier survival analyses are shown in Figure 1.

Analyses of the risk factors for diabetes development

The results of binary logistic regression analyses for the development of T2DM in the NGT and IGR groups are shown in Table 3. FPG contributed to the development of T2DM in the NGT group, and the OR was 6.111 (1.379, 27.070; P=0.017). Gender, WHR, DBP, and FPB contributed to the development of T2DM 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 from 20-79 years in 2017, there were an estimated 425 million

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cases of diabetes[3]. However, the astonishing prevalence may be partly attributable to the increase in population and the prolongation of the life-span.[35] 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)[36] and those described in a study conducted in Mexico (12.7 cases per 1,000 person-years from 1990 to 2008).[37] 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)[38] and in a study conducted in northern Spain (95.2 cases per 1,000 person-years during 1998 to 2005)[39] and is higher than that observed in a study conducted in Iran (10.6 cases per 1000 person-years from 1999 to 2011)[40] and in the SUPREME-DM project in the USA (11.5 cases per 1000 person-years from 2006 to 2011).[41] 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).[42] This difference may partly be due to the relatively higher standard of living in the suburbs of Beijing.

The development of diabetes is based on the interaction between genes and lifestyle and environmental factors.[43,44] 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, the development of diabetes was mainly the consequence of elevated FPG in the NGT group. Diabetes development was mainly associated with sex (female), abnormal WHR, elevated DBP and elevated FPG in the IGR group. The increase in the FPG level was a strong predictor of diabetes development in both the NGT group and the IGR group, with 6.111- and 7.243-times increased risk per unit increase, respectively.

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In our study, the WHR measurement was found to predict diabetes risk. Some studies have declared that WHR, as an obesity indicator, was superior to BMI and WC. [45,46] A meta-analysis demonstrated that either BMI or WC (WHR) predicted or was independently associated with type 2 diabetes, regardless of the controversial findings regarding which one was better.[47]

Age and family history of diabetes were widely believed to be risk factors for diabetes development.[4,6-14] However, we found only an increasing trend of diabetes development in the elderly population and in subjects with a family history of diabetes (P＞0.05). This finding might be related to the short period of follow-up and the subjects' unawareness of their family history of diabetes.

There is evidence that T2DM can be prevented in high-risk individuals by a lifestyle program of regular exercise.[48,49] Surprisingly, our study found that exercise did not exert a beneficial effect on diabetes incidence, a finding similar to that of the ATTICA study.[36,50] However, we did find a decreasing trend in diabetes incidence with increasing exercise time. 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).

The strengths of our study are that the study was based on a cohort selected by multiple stage sampling at baseline with a relatively long follow-up period. The limitation is that many variables assessed as risk factors were not updated regularly, which might have changed during the follow-up period, and the data were collected only at the baseline investigation and at the end of the study.

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 the incidence in many other areas worldwide. Compared with the NGT subjects, the IGR subjects were more susceptible to T2DM. To prevent diabetes development, all subjects should pay special attention to elevated FPG. In addition, sex, WHR, and DBP were predictors of T2DM in IGR subjects.

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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 formulating a protocol for diabetes prevention.

Authors' contributions

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.; 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.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Funding statement

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Ethics approval

Ethical approval was gained from Ethics Committee of Clinical Trials of Drugs/Devices in China-Japan Friendship Hospital (2011-049).

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281 **Table 1 Comparison of characteristics of the NGT and IGR subjects at baseline**

Variable at baseline	NGT group (n=673)	IGR group (n=222)	t or χ^2, *P* 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 (hours)	5.85±11.81	5.59±8.06	0.305, 0.761
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 (year)	4.85±0.32	4.79±0.56	2.081, 0.038

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BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; PG2h, 2-hour plasma glucose; TC, total cholesterol; TGs, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FH, family history. Exercise duration is expressed as hours per week.

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

	Cases of diabetes	Follow-up (person-years)	Incidence (per 1,000 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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Table 3. Multivariate logistic regression model for the development of T2DM

	NGT group		IGR group	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Sex	0.375 (0.067, 2.103)	0.265	7.293 (1.074, 49.549)	0.042
Age (years)	1.013 (0.962, 1.068)	0.615	1.019 (0.964, 1.077)	0.499
Weight (kg)	1.044 (0.927, 1.175)	0.478	1.056 (0.929, 1.200)	0.402
BMI (kg/m^2)	0.934 (0.653, 1.336)	0.710	0.971 (0.661, 1.427)	0.881
WC (cm)	1.073 (0.936, 1.230)	0.311	0.904 (0.748, 1.092)	0.295
WHR	0.006 (0.000, 7058.081)	0.473	2.874E8 (8.386, 9.847E15)	0.028
SBP (mmHg)	1.013 (0.976, 1.052)	0.492	0.992 (0.958, 1.026)	0.637
DBP (mmHg)	0.955 (0.890, 1.024)	0.198	1.068 (1.009, 1.130)	0.024
FPG (mmol/L)	6.111 (1.379, 27.070)	0.017	7.243 (2.314, 22.673)	0.001
TC (mmol/L)	2.719 (0.917, 8.067)	0.071	0.814 (0.141, 4.699)	0.818
TGs (mmol/L)	0.996 (0.589, 1.684)	0.989	0.926 (0.491, 1.749)	0.813
HDL-C (mmol/L)	2.536 (0.519, 12.395)	0.250	0.622 (0.071, 5.460)	0.669
LDL-C (mmol/L)	0.604 (0.206, 1.769)	0.358	1.070 (0.181, 6.321)	0.941
Exercise duration (hours)	1.013 (0.947, 1.084)	0.707	0.923 (0.847, 1.005)	0.066
FH of T2DM	1.868 (0.492, 7.090)	0.358	2.062 (0.656, 6.478)	0.215
Smoking history	0.766 (0.186, 3.162)	0.713	1.591 (0.346, 7.317)	0.551
Alcohol history	0.726 (0.202, 2.610)	0.624	1.685 (0.458, 6.203)	0.432

BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; TC, total cholesterol; TGs, triglycerides; HDL-C, high-density lipoprotein cholesterol; 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),

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smoking history was defined as no (n=1) or yes (n=2), and alcohol history was defined as no (n=1) or yes (n=2). Exercise duration was expressed as hours per week.

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Figure legend

Figure 1. Cumulative incidence of T2DM in the NGT group and the IGR group (log-rank test: χ^2=36.905, P<0.0001)

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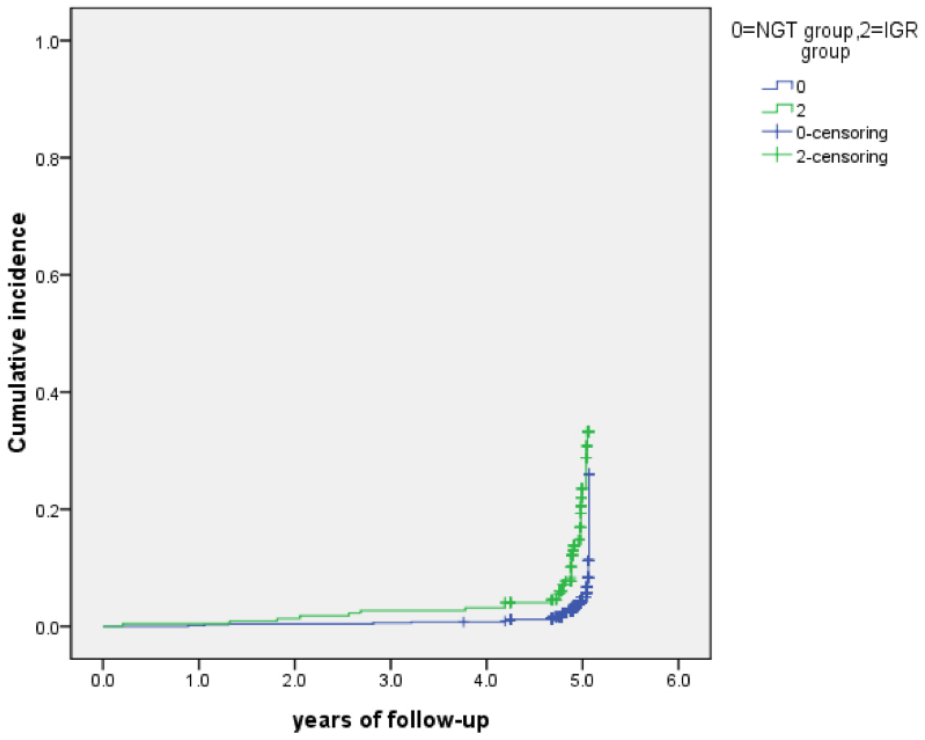
0=NGT group,2=IGR group
0
2
0-censoring
2-censoring
Cumulative incidence
1.0
0.8
0.6
0.4
0.2
0.0
0.0
1.0
2.0
3.0
4.0
5.0
6.0
years of follow-up

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

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) 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 recruitment, exposure, follow-up, and data collection	
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of 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, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) 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	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(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) and information on exposures and potential confounders	8
		(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

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Main results	16	(*a*) 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 (*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	9
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 information			
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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Epidemiology and risk factors for diabetes in the suburbs of Beijing: a retrospective cohort study

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Abstract

Objective We aimed to detect the incidence and risk factors of type 2 diabetes mellitus (T2DM) development in the suburbs of Beijing.

Design Cohort study with record linkage to incidence data.

Setting We performed a 5-year follow-up study in a randomly selected suburban population including 1,114 subjects aged≥18 years living in the suburbs of Beijing.

Participants 118 subjects with T2DM at baseline according to the 1999 WHO criteria were excluded, and 895 subjects attended the follow-up assessment in 2012. The non-diabetic subjects at baseline were classified into two groups: normal glucose tolerance (NGT) group (n=673) and impaired glucose regulation (IGR) group(n=222).The incidence and risk factors of diabetes development in each group were investigated.

Outcome measures A structured questionnaire about sociodemographic characteristics, height, weight, waist circumference, hip circumference , blood pressure, oral glucose tolerance test, and serum lipid levels.

Results Out of the 895 non-diabetic subjects, 67 developed diabetes with 29 in the NGT group and 38 in the IGR group respectively after a 5-year follow-up, producing an overall 5-year cumulative incidence of diabetes of 13%. The incidence of diabetes was 15.5 cases per 1000 person-years, 8.9 cases per 1000 person-years in the NGT group and 35.7 cases per 1000 person-years in the IGR group (P<0.01;RR=4.03; 95%CI:2.58-9.29). Binary logistic regression analysis showed that the risk factors for diabetes development included fasting plasma glucose (FPG) in the NGT group, and sex, the waist-to-hip ratio (WHR), FPG and diastolic blood pressure (DBP) in the IGR group.

Conclusions: During a mean follow-up of 5.0 years, the incidence of T2DM in the suburbs of Beijing was 15.5 per 1000 person-years. Early prevention of diabetes should focus on IGR subjects. Elevated FPG predicted diabetes development for both NGT and IGR subjects. Female sex, overweight/obesity and DBP are risk factors for diabetes development in IGR subjects**.**

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Strengths and limitations of this study

- Provides new data on the incidence of T2DM in the Beijing area.
- Has a longitudinal design.
- Selects a cohort by multiple-stage sampling at baseline.
- Has a relatively long follow-up period.
- Has the limitation 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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Introduction

Diabetes mellitus is a clinical syndrome characterized by disordered glycometabolism. The lack and/or insufficiency of insulin induces metabolic disorders related to saccharides, lipids, proteins, water and electrolytes, resulting in hyperglycemia as the main clinical feature. Long-term hyperglycemia leads to macrovascular and microvascular complications, which may result in disability and death.[1,2] Diabetes is increasingly prevalent, affecting 463 million (9.3%) adults worldwide, and these figures are expected to increase to 700 million (10.9%) by 2045.[3] Type 2 diabetes mellitus (T2DM) accounts for over 90% of diabetes cases. Diabetes, as a leading cause of death,[1,3,4] is becoming a public issue, placing a heavy burden on the health care system.[5] In 2017 approximately 5 million adult deaths worldwide were attributed to diabetes,[6] and the global healthcare expenditure associated with people with diabetes in 2019 was estimated to be USD 760 billion.[7] Because T2DM is usually asymptomatic, it can remain undiagnosed for many years. Almost half of all people (50.1%) living with diabetes were undiagnosed in 2019.[3] Accordingly, screening for prediabetes/T2DM and preventing the evolution of diabetes in individuals with risk factors are essential. Currently, the risk factors related to T2DM development may include age, the body mass index (BMI), body fat distribution, a family history of diabetes, a history of cardiovascular disease (CVD), a history of gestational diabetes mellitus (GDM), race/ethnicity, diet, physical inactivity, hypertension, dyslipidemia and prediabetes.[4,8-16] Some studies have demonstrated that birth weight,[17,18] income,[19] socioeconomic status,[20,21] working hours,[21,22] occupation[23] and genetic factors[24-26] might also contribute to T2DM development .

In addition to the process of urbanization, the population aging, changes in lifestyle, and increasing prevalence of obesity and overweight, the prevalence of diabetes in 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 2010[31] 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.

Materials and Methods

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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Sociodemographic characteristics—The data were collected by trained staff using a structured questionnaire via a face-to-face interview to assess general information (sex, age, nationality, education status, occupation, and per capita income), personal history (smoking history, alcohol history, physical activity, and dietary habits), family history (diabetes mellitus, hypertension, hyperlipidemia, myocardial infarction, stroke, and obesity), and history of current illness (diabetes, hypertension, hyperlipidemia, cardiovascular, cerebrovascular diseases, and 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 — The subjects were examined for height, weight, waist circumference (WC), hip circumference (HC) and blood pressure. All the subjects were asked to remove their shoes, socks, hats and coats, stand erectly and look 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 is the circumference of the waist at the horizontal line of the umbilicus measured in centimeters using a measuring tape, and the HC is the circumference of hips at the horizontal line of the anterior superior spine measured in centimeters using a measuring tape. The 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 measured 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 minutes before the measurement with their arms bare and placed at the chest level. All the clinical staff members were trained to measure blood pressure and obtain anthropometric measurements.

Laboratory examination — All the subjects were invited to undergo a blood test (including an OGTT) at the baseline and the end of follow-up. Venous blood samples

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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.

Patient and Public Involvement

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

Results

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 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.

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Continuous variables were expressed as means±standard deviation (sd) and were examined using a t test, while categorical variables were expressed as percentages and were examined using the χ^2 test. No significant difference was found between the NGT group and the IGR group in sex, height, family history of T2DM, smoking history, alcohol history, exercise time, diastolic blood pressure (DBP) or HDL-C. Age, weight, BMI, WC, WHR, systolic blood pressure (SBP), FPG, PG2h, TGs, TC and LDL-C in the IGR group were significantly higher than those in the NGT group.

Incidence of T2DM

During the follow-up, T2DM developed in 67 subjects, 29 in the NGT group and 38 in the IGR group, resulting in T2DM onset rates of 15.45, 8.86 and 35.67 per 1,000 person-years in the total study population, NGT group and IGR group, respectively (Table 2). The difference in the incidence of T2DM between the NGT group and IGR group was statistically significant (χ^2=37.38;P＜0.01;RR=4.03;95% CI: 2.58-9.29). The 5-year cumulative incidence of T2DM was 13%, with 10% in the NGT group and 20% in the IGR group. The mean follow-up duration was 5.008 years (SE=0.013; 95% CI: 4.982–5.033), with 5.003 years (SE=0.012;95% CI: 5.010–5.056) in the NGT group and 4.933 years (SE=0.038;95% CI: 4.859–5.007) in the IGR group. Using the log-rank test, we found that the cumulative incidence of T2DM in the IGR group was significantly higher than that in the NGT group (χ^2=36.905; P＜0.0001). The results of the Kaplan–Meier survival analyses are shown in Figure 1.

Analyses of the risk factors for diabetes development

The results of binary logistic regression analyses for T2DM development in the NGT and IGR groups are shown in Table 3. FPG contributed to T2DM development in the NGT group, and the OR was 6.111 (1.379, 27.070; P=0.017). Sex,WHR, DBP, and 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

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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 diabetes[3]. 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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group. Diabetes development was mainly associated with sex (female), abnormal WHR, elevated DBP and elevated FPG in the IGR group. The increase in the FPG level was a strong predictor of diabetes development in both the NGT group and IGR group, with 6.111- and 7.243-fold increased risk per unit increase, respectively.

In our study, the WHR measurement was found to predict diabetes risk. Some studies have declared that WHR, as an obesity indicator, is superior to BMI and WC. [47,48] A meta-analysis demonstrated that either BMI or WC (WHR) predicted or was independently associated with type 2 diabetes, regardless of the controversial findings regarding which was better.[49]

Age and family history of diabetes are considered risk factors for diabetes development.[4,8-16] However, we found only an increasing trend of diabetes development in the elderly population and subjects with a family history of diabetes ($P>0.05$). This finding might be related to the short period of follow-up and the subjects' unawareness of their family history of diabetes.

There is evidence that T2DM can be prevented in high-risk individuals by a lifestyle program of regular exercise.[50,51] Surprisingly, our study found that exercise did not exert a beneficial effect on diabetes incidence, a finding similar to that in the ATTICA study.[38,52] However, we found a decreasing trend in the diabetes incidence with increasing exercise time. 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).

The strength of our study is that it was based on a cohort selected by multiple stage sampling at baseline with a relatively long follow-up period. A limitation is that many variables assessed as risk factors were not updated regularly, and might have changed during the follow-up period. Additionally, the data were collected only at the baseline investigation and at the end of the study.

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

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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 formulating a protocol for diabetes prevention.

Authors' contributions

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.; 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.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Competing interests None declared.

Funding statement

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Ethics approval

Ethical approval was obtained from the Ethics Committee of Clinical Trials of

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Drugs/Devices in China-Japan Friendship Hospital (2011-049).

Data availability statement

All data included in this study are available from the corresponding author on reasonable request.

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

Variable at baseline	NGT group (n=673)	IGR group (n=222)	t or χ^2, *P* value
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, <0.001
PG2h (mmol/L)	5.90±1.01	8.29±1.52	-26.692, <0.001
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 (hours)	5.85±11.81	5.59±8.06	0.305, 0.761
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 (year)	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, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose;

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PG2h, 2-hour plasma glucose; TC, total cholesterol; TGs, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FH, family history. Exercise duration is expressed as hours per week.

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Table 2. Incidence of T2DM during the follow-up

	Cases of diabetes	Follow-up (person-years)	Incidence (per 1,000 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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Table 3. Multivariate logistic regression model for T2DM development

	NGT group		IGR group	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Sex	0.375 (0.067, 2.103)	0.265	7.293 (1.074, 49.549)	0.042
Age (years)	1.013 (0.962, 1.068)	0.615	1.019 (0.964, 1.077)	0.499
Weight (kg)	1.044 (0.927, 1.175)	0.478	1.056 (0.929, 1.200)	0.402
BMI (kg/m^2)	0.934 (0.653, 1.336)	0.710	0.971 (0.661, 1.427)	0.881
WC (cm)	1.073 (0.936, 1.230)	0.311	0.904 (0.748, 1.092)	0.295
WHR	0.006 (0.000, 7058.081)	0.473	2.874E8 (8.386, 9.847E15)	0.028
SBP (mmHg)	1.013 (0.976, 1.052)	0.492	0.992 (0.958, 1.026)	0.637
DBP (mmHg)	0.955 (0.890, 1.024)	0.198	1.068 (1.009, 1.130)	0.024
FPG (mmol/L)	6.111 (1.379, 27.070)	0.017	7.243 (2.314, 22.673)	0.001
TC (mmol/L)	2.719 (0.917, 8.067)	0.071	0.814 (0.141, 4.699)	0.818
TGs (mmol/L)	0.996 (0.589, 1.684)	0.989	0.926 (0.491, 1.749)	0.813
HDL-C (mmol/L)	2.536 (0.519, 12.395)	0.250	0.622 (0.071, 5.460)	0.669
LDL-C (mmol/L)	0.604 (0.206, 1.769)	0.358	1.070 (0.181, 6.321)	0.941
Exercise duration (hours)	1.013 (0.947, 1.084)	0.707	0.923 (0.847, 1.005)	0.066
FH of T2DM	1.868 (0.492, 7.090)	0.358	2.062 (0.656, 6.478)	0.215
Smoking history	0.766 (0.186, 3.162)	0.713	1.591 (0.346, 7.317)	0.551
Alcohol history	0.726 (0.202, 2.610)	0.624	1.685 (0.458, 6.203)	0.432

BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; TC, total cholesterol; TGs, triglycerides; HDL-C, high-density lipoprotein cholesterol; 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),

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smoking history was defined as no (n=1) or yes (n=2), and alcohol history was defined as no (n=1) or yes (n=2). Exercise duration is expressed as hours per week.

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Figure legend

Figure 1. Cumulative incidence of T2DM in the NGT and IGR groups (log-rank test: χ^2=36.905;P<0.0001)

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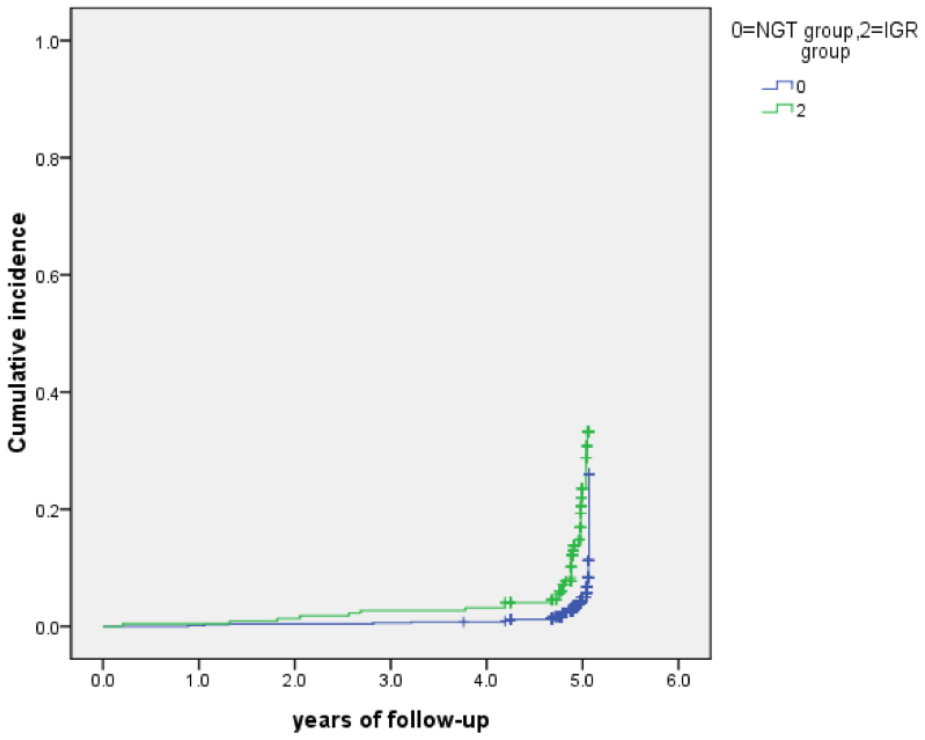
0=NGT group,2=IGR group
0
2
Cumulative incidence
1.0
0.8
0.6
0.4
0.2
0.0
0.0
1.0
2.0
3.0
4.0
5.0
6.0
years of follow-up

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

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) 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 recruitment, exposure, follow-up, and data collection	
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of 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, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) 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	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(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) and information on exposures and potential confounders	8
		(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

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Main results	16	(*a*) 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 (*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	9
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 information			
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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Epidemiology and risk factors for diabetes in the suburbs of Beijing: a retrospective cohort study

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

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Abstract

Objective We aimed to detect the incidence and risk factors of type 2 diabetes mellitus (T2DM) development in the suburbs of Beijing.

Design Cohort study with record linkage to incidence data.

Setting We performed a 5-year follow-up study in a randomly selected suburban population including 1,114 subjects aged≥18 years living in the suburbs of Beijing.

Participants 118 subjects with T2DM at baseline according to the 1999 WHO criteria were excluded, and 895 subjects attended the follow-up assessment in 2012. The non-diabetic subjects at baseline were classified into two groups: normal glucose tolerance (NGT) group (n=673) and impaired glucose regulation (IGR) group(n=222).The incidence and risk factors of diabetes development in each group were investigated.

Outcome measures A structured questionnaire about sociodemographic characteristics, height, weight, waist circumference, hip circumference , blood pressure, oral glucose tolerance test, and serum lipid levels.

Results Out of the 895 non-diabetic subjects, 67 developed diabetes with 29 in the NGT group and 38 in the IGR group respectively after a 5-year follow-up, producing an overall 5-year cumulative incidence of diabetes of 13%. The incidence of diabetes was 15.5 cases per 1000 person-years, 8.9 cases per 1000 person-years in the NGT group and 35.7 cases per 1000 person-years in the IGR group (P<0.01;RR=4.03; 95%CI:2.58-9.29). Binary logistic regression analysis showed that the risk factors for diabetes development included fasting plasma glucose (FPG) in the NGT group, and sex, the waist-to-hip ratio (WHR), FPG and diastolic blood pressure (DBP) in the IGR group.

Conclusions: During a mean follow-up of 5.0 years, the incidence of T2DM in the suburbs of Beijing was 15.5 per 1000 person-years. Early prevention of diabetes should focus on IGR subjects. Elevated FPG predicted diabetes development for both NGT and IGR subjects. Female sex, overweight/obesity and DBP are risk factors for diabetes development in IGR subjects**.**

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Strengths and limitations of this study

- This study is a retrospective cohort survey of the incidence of T2DM and 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 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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Introduction

Diabetes mellitus is a clinical syndrome characterized by disordered glycometabolism. The lack and/or insufficiency of insulin induces metabolic disorders related to saccharides, lipids, proteins, water and electrolytes, resulting in hyperglycemia as the main clinical feature. Long-term hyperglycemia leads to macrovascular and microvascular complications, which may result in disability and death.[1,2] Diabetes is increasingly prevalent, affecting 463 million (9.3%) adults worldwide, and these figures are expected to increase to 700 million (10.9%) by 2045.[3] Type 2 diabetes mellitus (T2DM) accounts for over 90% of diabetes cases. Diabetes, as a leading cause of death,[1,3,4] is becoming a public issue, placing a heavy burden on the health care system.[5] In 2017 approximately 5 million adult deaths worldwide were attributed to diabetes,[6] and the global healthcare expenditure associated with people with diabetes in 2019 was estimated to be USD 760 billion.[7] Because T2DM is usually asymptomatic, it can remain undiagnosed for many years. Almost half of all people (50.1%) living with diabetes were undiagnosed in 2019.[3] Accordingly, screening for prediabetes/T2DM and preventing the evolution of diabetes in individuals with risk factors are essential. Currently, the risk factors related to T2DM development may include age, the body mass index (BMI), body fat distribution, a family history of diabetes, a history of cardiovascular disease (CVD), a history of gestational diabetes mellitus (GDM), race/ethnicity, diet, physical inactivity, hypertension, dyslipidemia and prediabetes.[4,8-16] Some studies have demonstrated that birth weight,[17,18] income,[19] socioeconomic status,[20,21] working hours,[21,22] occupation[23] and genetic factors[24-26] might also contribute to T2DM development .

In addition to the process of urbanization, the population aging, changes in lifestyle, and increasing prevalence of obesity and overweight, the prevalence of diabetes in 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 2010[31] 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.

Materials and Methods

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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Data collection

Sociodemographic characteristics—The data were collected by trained staff using a structured questionnaire via a face-to-face interview to assess general information (sex, age, nationality, education status, occupation, and per capita income), personal history (smoking history, alcohol history, physical activity, and dietary habits), family history (diabetes mellitus, hypertension, hyperlipidemia, myocardial infarction, stroke, and obesity), and history of current illness (diabetes, hypertension, hyperlipidemia, cardiovascular, cerebrovascular diseases, and 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 — The subjects were examined for height, weight, waist circumference (WC), hip circumference (HC) and blood pressure. All the subjects were asked to remove their shoes, socks, hats and coats, stand erectly and look 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 is the circumference of the waist at the horizontal line of the umbilicus measured in centimeters using a measuring tape, and the HC is the circumference of hips at the horizontal line of the anterior superior spine measured in centimeters using a measuring tape. The 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 measured 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 minutes before the measurement with their arms bare and placed at the chest level. All the clinical staff members were trained to measure blood pressure and obtain anthropometric measurements.

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Laboratory examination —All the subjects were invited to undergo a blood test (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 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.

Patient and Public Involvement

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

Results

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 were diagnosed with diabetes by OGTT at baseline and one subject with severe data

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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 were expressed as means±standard deviation (sd) and were examined using a t test, while categorical variables were expressed as percentages and were examined using the χ^2 test. No significant difference was found between the NGT group and the IGR group in sex, height, family history of T2DM, smoking history, alcohol history, exercise time, diastolic blood pressure (DBP) or HDL-C. Age, weight, BMI, WC, WHR, systolic blood pressure (SBP), FPG, PG2h, TGs, TC and LDL-C in the IGR group were significantly higher than those in the NGT group.

Incidence of T2DM

During the follow-up, T2DM developed in 67 subjects, 29 in the NGT group and 38 in the IGR group, resulting in T2DM onset rates of 15.45, 8.86 and 35.67 per 1,000 person-years in the total study population, NGT group and IGR group, respectively (Table 2). The difference in the incidence of T2DM between the NGT group and IGR group was statistically significant (χ^2=37.38;P＜0.01;RR=4.03;95% CI: 2.58-9.29). The 5-year cumulative incidence of T2DM was 13%, with 10% in the NGT group and 20% in the IGR group. The mean follow-up duration was 5.008 years (SE=0.013; 95% CI: 4.982–5.033), with 5.003 years (SE=0.012;95% CI: 5.010–5.056) in the NGT group and 4.933 years (SE=0.038;95% CI: 4.859–5.007) in the IGR group. Using the log-rank test, we found that the cumulative incidence of T2DM in the IGR group was significantly higher than that in the NGT group (χ^2=36.905; P＜0.0001). The results of the Kaplan–Meier survival analyses are shown in Figure 1.

Analyses of the risk factors for diabetes development

The results of binary logistic regression analyses for T2DM development in the NGT and IGR groups are shown in Table 3. FPG contributed to T2DM development in the NGT group, and the OR was 6.111 (1.379, 27.070; P=0.017). Sex, WHR, DBP, and FPB contributed to T2DM development in the IGR group, and the ORs were 7.293

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(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 diabetes[3]. 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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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 group. Diabetes development was mainly associated with sex (female), abnormal WHR, elevated DBP and elevated FPG in the IGR group. The increase in the FPG level was a strong predictor of diabetes development in both the NGT group and IGR group, with 6.111- and 7.243-fold increased risk per unit increase, respectively.

In our study, the WHR measurement was found to predict diabetes risk. Some studies have declared that WHR, as an obesity indicator, is superior to BMI and WC. [47,48] A meta-analysis demonstrated that either BMI or WC (WHR) predicted or was independently associated with type 2 diabetes, regardless of the controversial findings regarding which was better.[49]

Age and family history of diabetes are considered risk factors for diabetes development.[4,8-16] However, we found only an increasing trend of diabetes development in the elderly population and subjects with a family history of diabetes (P＞0.05). This finding might be related to the short period of follow-up and the subjects' unawareness of their family history of diabetes.

There is evidence that T2DM can be prevented in high-risk individuals by a lifestyle program of regular exercise.[50,51] Surprisingly, our study found that exercise did not exert a beneficial effect on diabetes incidence, a finding similar to that in the ATTICA study.[38,52] However, we found a decreasing trend in the diabetes incidence with increasing exercise time. 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).

The strength of our study is that it was based on a cohort selected by multiple stage sampling at baseline with a relatively long follow-up period. A limitation is that many variables assessed as risk factors were not updated regularly, and might have changed during the follow-up period. Secondly, the follow-up could not be random due to the limitations of the conditions. Additionally, the data were collected only at the baseline investigation and at the end of the study.

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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 formulating a protocol for diabetes prevention.

Authors' contributions

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.; 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.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Competing interests None declared.

Funding statement

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Ethics approval

Ethical approval was obtained from the Ethics Committee of Clinical Trials of Drugs/Devices in China-Japan Friendship Hospital (2011-049).

Data availability statement

All data included in this study are available from the corresponding author on reasonable request.

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

Variable at baseline	NGT group (n=673)	IGR group (n=222)	t or χ^2, *P* value
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, <0.001
PG2h (mmol/L)	5.90±1.01	8.29±1.52	-26.692, <0.001
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 (hours)	5.85±11.81	5.59±8.06	0.305, 0.761
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 (year)	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, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose;

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PG2h, 2-hour plasma glucose; TC, total cholesterol; TGs, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FH, family history. Exercise duration is expressed as hours per week.

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Table 2. Incidence of T2DM during the follow-up

	Cases of diabetes	Follow-up (person-years)	Incidence (per 1,000 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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Table 3. Multivariate logistic regression model for T2DM development

	NGT group		IGR group	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Sex	0.375 (0.067, 2.103)	0.265	7.293 (1.074, 49.549)	0.042
Age (years)	1.013 (0.962, 1.068)	0.615	1.019 (0.964, 1.077)	0.499
Weight (kg)	1.044 (0.927, 1.175)	0.478	1.056 (0.929, 1.200)	0.402
BMI (kg/m^2)	0.934 (0.653, 1.336)	0.710	0.971 (0.661, 1.427)	0.881
WC (cm)	1.073 (0.936, 1.230)	0.311	0.904 (0.748, 1.092)	0.295
WHR	0.006 (0.000, 7058.081)	0.473	2.874E8 (8.386, 9.847E15)	0.028
SBP (mmHg)	1.013 (0.976, 1.052)	0.492	0.992 (0.958, 1.026)	0.637
DBP (mmHg)	0.955 (0.890, 1.024)	0.198	1.068 (1.009, 1.130)	0.024
FPG (mmol/L)	6.111 (1.379, 27.070)	0.017	7.243 (2.314, 22.673)	0.001
TC (mmol/L)	2.719 (0.917, 8.067)	0.071	0.814 (0.141, 4.699)	0.818
TGs (mmol/L)	0.996 (0.589, 1.684)	0.989	0.926 (0.491, 1.749)	0.813
HDL-C (mmol/L)	2.536 (0.519, 12.395)	0.250	0.622 (0.071, 5.460)	0.669
LDL-C (mmol/L)	0.604 (0.206, 1.769)	0.358	1.070 (0.181, 6.321)	0.941
Exercise duration (hours)	1.013 (0.947, 1.084)	0.707	0.923 (0.847, 1.005)	0.066
FH of T2DM	1.868 (0.492, 7.090)	0.358	2.062 (0.656, 6.478)	0.215
Smoking history	0.766 (0.186, 3.162)	0.713	1.591 (0.346, 7.317)	0.551
Alcohol history	0.726 (0.202, 2.610)	0.624	1.685 (0.458, 6.203)	0.432

BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; TC, total cholesterol; TGs, triglycerides; HDL-C, high-density lipoprotein cholesterol; 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),

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smoking history was defined as no (n=1) or yes (n=2), and alcohol history was defined as no (n=1) or yes (n=2). Exercise duration is expressed as hours per week.

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Figure legend

Figure 1. Cumulative incidence of T2DM in the NGT and IGR groups (log-rank test: χ^2=36.905;P<0.0001)

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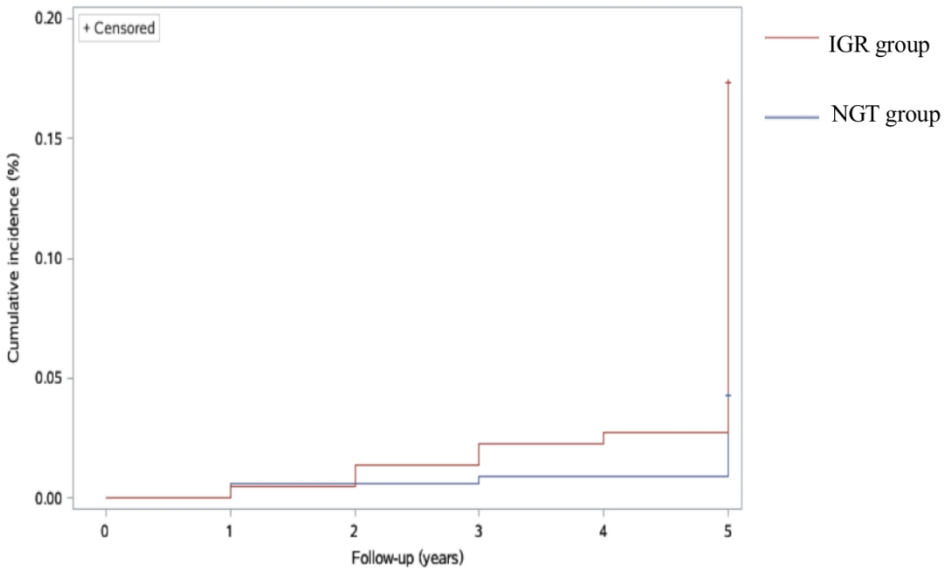
+ Censored
0.20
0.15
0.10
0.05
0.00
Cumulative incidence (%)
0
1
2
3
4
5
Follow-up (years)
IGR group
NGT group

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

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) 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 recruitment, exposure, follow-up, and data collection	
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of 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, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) 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	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(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) and information on exposures and potential confounders	8
		(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

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Main results	16	(*a*) 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 (*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	9
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 information			
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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