Protocol



Data Resource Profile: A Protocol of China National Diabetic Chronic Complications Study*

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Diabetes affects approximately 10.5% of adults worldwide, and its chronic complications lead to severely disabling sequelae and premature death, thus placing a heavy healthcare burden on both patients affected and society^[1]. China has experienced a dramatic increase in diabetes prevalence from 0.67% in $1980^{[2]}$ to 12.8% in $2018^{[3]}$ and has approximately one-quarter of people with diabetes worldwide^[1]. It is therefore essential to understand the epidemiologic characteristics of the chronic complications and co-morbidities of diabetes, and the current status of diabetes management to guide planning for appropriate diabetes care and intervention for these complications and co-morbidities at the national level^[4-7]. To date, however, no national populationbased epidemiologic studies regarding diabetesrelated complications and co-morbidities have been reported in China.

The China National Diabetic Chronic Complications Study (China DiaChronic Study) was conducted to investigate the epidemiologic characteristics of multiple chronic complications and co-morbidities of diabetes [retinopathy, nephropathy, peripheral neuropathy, peripheral arterial disease (PAD), and cardiovascular disease (CVD)] and related factors, as well as to assess the attainment rates of metabolic targets and the implementation of standardized diagnosis and treatments in Chinese adults with diagnosed diabetes between March 2018 and January 2020.

The China DiaChronic Study group consisted of members from the Chinese Diabetes Society (CDS)

and the National Center for Chronic Noncommunicable Disease Control and Prevention of the Chinese Center for Disease Control and Prevention (China CDC, referred to as CDC hereafter), who formed national, provincial, and local working groups. The national working group developed technical plans, questionnaires, and training materials, designed a system platform for sampling, information collection, and management (Supplementary Figure S1, available in www. besjournal.com), and conducted unified first-tier training for the provincial working group representatives. The provincial working groups conducted second-tier training for the provincial and local working staff. Under the guidance and supervision of the national working group, the provincial working groups organized and carried out the on-site surveys in their provinces in cooperation with the local working groups and uploaded survey data to the system platform. The results of the medical tests and evaluation reports were input into the system platform and were then printed and given out to the participants by the local working groups.

A sample size of approximately 49,800 was estimated according to the following formula [8]:

$$n = \frac{1.96^{2} \rho (1-\rho) (\text{Deff}) N}{(p * \sigma)^{2}}$$

A prevalence of peripheral arterial disease of 10.7% was drawn from the Shanghai diabetic

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complications study^[9], and prevalence of peripheral arterial disease was estimated to be 8.56% (or 10.7 x 0.8) at the China national level, which was expected to be the lowest among the rates of various diabetes-related complications. Then, the prevalence (p) of 8.56% was used to estimate the sample size for this survey. The two-sided significant level was 0.05, the design effect was 2 (Deff), the desired level of relative precision was 0.1 (σ), and the number of stratification (N) was 6 (sex and geographical regions). Then, based on an assumed 90% response rate, a nationally representative sample size was estimated to be 55,333 individuals.

The multistage sampling scheme (stratification, clustering, and random) was used to sample study participants based on the disease surveillance points (DSPs) started in 2013 from the China Chronic Disease and Risk Factors Surveillance (CCDRFS)^[10-11]. The CCDRFS was designed to reflect the epidemiologic characteristics of chronic diseases and related factors at both the national and provincial levels and covered all 31 provinces, autonomous regions, and municipalities of mainland China. One DSP from the CCDRFS usually represented a rural county or an urban district. Every county/district in mainland China has a diabetes management registration system for its local patients.

In the first stage, generally, four DSPs were selected from each province after considering urbanization levels. Three municipalities (Beijing, Tianjin, and Shanghai) have been fully urbanized; one rural DSP was added in three provinces (Sichuan, Henan, and Shandong) with larger population sizes, and the number of DSPs was reduced in one province (Qinghai) and two autonomous regions (Tibet and Xinjiang) with smaller population sizes. Then, a total of 122 DSPs (65 urban and 57 rural DSPs) from the 2013 CCDRFS were invited to participate. Of the DSPs invited, 15 refused to participate and were replaced with other CDC sites (not included in the 2013 CCDRFS) in the same province with similar urbanization levels (referred to as study sites hereafter), as shown in Supplementary Figure S2, available in www.besjournal.com. Approximately 1.68 million patients with diagnosed diabetes have been registered in the diabetes management registration system in these 122 study sites.

In the second stage, four neighborhoods in urban areas or four villages in rural areas were selected from each study site, and a total of 488 neighborhoods/villages were obtained.

In the third stage, the national sample size of

55.333 was divided 488 equally by neighborhoods/villages, then 113 study participants were sampled at each neighborhood/village. Subsequently, an age structure of 16% of the younger individuals (18-44 years), 44% of the middle-aged individuals (45-59 years), and 40% of the elderly individuals (60-74 years) according to the CCDRFS 2013 diabetes data^[12], and an equal ratio of male to female participants were adopted. Finally, we set the sample size at 120 individuals for each neighborhood/village, then increased the national sample size to 58,560 individuals. The multistage stratified sampling procedure is depicted in Figure 1.

The China DiaChronic Study was approved by the Ethical Review Committee (Approval No: 2018-010) and was registered in the Chinese Clinical Trial registry (ChiCTR1800014432). Written informed consent was obtained from each participant prior to data collection.

People with diagnosed diabetes aged 18–74 years, and who had resided in the study sites for at least 6 months of the last year before the survey were eligible for participating in this survey. Pregnant women or people with severe health conditions or illnesses that prevented them from participating, including the bedridden or the intellectually disabled, were excluded.

All data collection was performed at a local hospital or community health service center by the CDS and CDC medical staff. All investigators completed a training program and were qualified to use specific tools and methods before participating in on-site surveys. The flowchart of fieldwork is shown in Supplementary Figure S3, available in www.besjournal.com. Data collection consisted of the following four examination components: questionnaire surveys, physical examinations, laboratory testing, and special examinations [electrocardiogram (ECG), diabetic retinopathy, peripheral neuropathy, and peripheral vascular]. A summary of the four examination components is presented in Supplementary Tables S1-S4, available in www.besjournal.com.

Face-to-face personal interviews were conducted through a digital questionnaire using a portable Android device. The questionnaire consisted of the following items: 1) demographic and socioeconomic information; 2) lifestyle factors, including smoking, alcohol intake, tea and coffee consumption, diet, physical activity, and sleep; 3) family history of disease; 4) medical history; 5) weight measurement and control; and 6) menstrual and obstetric history (Supplementary Table S1). A global physical activity

questionnaire was adopted for physical activities [13]. A metabolic equivalent (MET) was calculated according to the total of moderate- and vigorous-intensity physical activity (the moderate MET value was 4.0 and the vigorous MET value was 8.0) for work, in-transit activity, and leisure time throughout a week [13]. If the participant had difficulties in answering the above questions, the family members who were most familiar with him/her would respond. In the survey of diet and physical activity, images for estimating dietary portion size and a classification table for physical activity were provided as a reference for the participants (Supplementary Table S5, available in www. besjournal.com).

The physical examinations included blood

pressure, heart and anthropometric rate. measurements (height, weight, and circumference), and were performed in a fasting state in the morning according to a standard protocol^[14]. Blood pressure was measured in the left arm three times consecutively with a 1-min interval between the measurements with the participant in a seated position after 5 minutes of rest using an automated device. Waist circumference was measured in the horizontal plane midway between the lower edge of the costal arch and the upper edge of the iliac crest (Supplementary Table S2).

After a 10-hour overnight fast, a 15-mL blood sample and a random urine sample were collected from each participant. The fasting plasma glucose level was measured within 48 hours by local

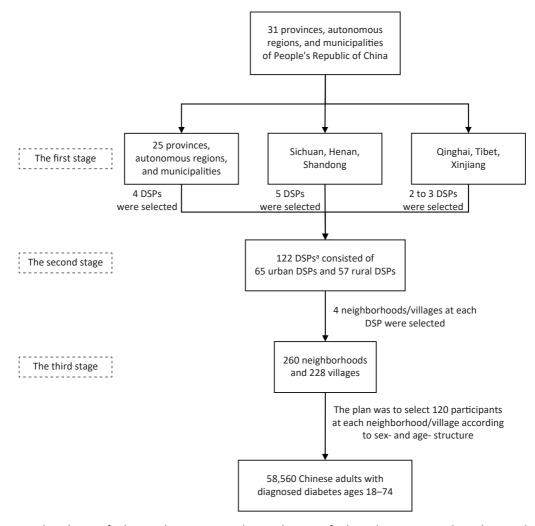


Figure 1. Flowchart of the multistage sampling scheme of the China National Diabetic Chronic Complications Study. ^aOf the 122 DSPs, 15 were replaced with other CDC sites (not included in the 2013 CCDRFS) in the same province with similar urbanization levels. CCDRFS, China Chronic Disease and Risk Factors Surveillance; CDC, Center for Disease Control and Prevention; DSPs, disease surveillance points.

laboratories that had completed a standardization and certification program. The day after the survey, the blood and urine specimens were shipped to the Guangzhou KingMed Diagnostics Group Co., Ltd. (Guangzhou, China) in a refrigerator with a temperature range of 2–8 °C to test for glycated hemoglobin (HbA1c), lipid, liver function (alanine transaminase, glutamyl transferase, aspartate transaminase, albumin, and total protein), kidney function (creatinine, urea, and uric acid), urinary albumin, and urinary creatinine concentrations (Supplementary Table S3).

An ECG and screening for diabetic retinopathy, peripheral neuropathy, and peripheral arterial disease were performed using uniform medical equipment. A six-channel automatic analysis electrocardiograph (FX-8222T; Fukuda Denshi Co., Ltd., Tokyo, Japan) was used to perform a standard 12-lead electrocardiography, resting adding additional leads if necessary. These electrocardiograms were reviewed and interpreted by medical professionals who were blinded to the conditions of the participants. In addition, electrocardiograms were characterized as ECG coronary probable (ST-segment elevation pathologic Q waves), ECG coronary possible (detected ST-segment depression and T-wave changes), ECG coronary unlikely (all other remaining abnormal ECG records), and a normal ECG according to the European Society of Cardiology/American Heart Association recommendations. The ophthalmic examinations included a visual acuity test and fundus photography. Logarithm of the minimal angle of resolution (log-MAR) charts were used at a distance of five meters with each eye tested separately. Two 45-degree color fundus photographs were taken for each eye; one was centered on the optic disc and another on the macula, using a digital non-mydriatic retinal camera (Canon CR-2; Canon Inc., Tokyo, Japan or TRC-NW400; Topcon Corporation, Tokyo, Japan). The severity of diabetic retinopathy was graded into the following five levels according to the 2002 International Clinical Diabetic Retinopathy Disease Severity Scales $^{[15]}$: no apparent retinopathy; mild, moderate, and severe nonproliferative proliferative retinopathy; and retinopathy. Every photograph was reviewed and rated by two ophthalmologists, and if the diagnosis or the grading of diabetic retinopathy was inconsistent, the photograph was reviewed by another senior ophthalmologist. ophthalmologists were blinded to the participants' conditions and the results graded by other ophthalmologists. An inspection of the feet and evaluation of ankle reflexes, and pinprick, pressure, temperature, and vibration sensations were carried out for neuropathy testing using a reflex hammer with a sensory needle, 10-g monofilament, and Tip-Therm (Beijing Laxons Technology Co., Ltd., Beijing, China), and 128-Hz tuning fork (Berchtold GmbH & CO.KG, Esslingen, Germany), respectively. Peripheral neuropathy was scored according to the 1994 Michigan Neuropathy Screening Instrument^[16]. Peripheral vascular lesions were assessed by palpation of the dorsalis pedis, posterior tibial, and popliteal arteries. Intermittent claudication was using the Edinburgh intermittent claudication questionnaire (Supplementary Table **S4**).

Data are presented as the mean (standard deviation) for continuous variables and number (percentage) for categorical variables. The difference in means and proportions between two groups was tested using a t-test and χ^2 test, respectively. All analyses were conducted using SAS (version 9.4; SAS Institute, Cary, NC, USA). The map was created using R (version 4.0.4; R Foundation for Statistical Computing, Vienna, Austria). All tests were two-sided and a P < 0.05 was considered statistically significant.

The response rate for each item in the China DiaChronic Study for the 58,560 participants is shown in Table 1. The overall response rate was 91.2% (males, 90.4%; females, 92.0%; young 74.7%; middle-aged participants, participants, 93.9%; and elderly participants, 95.1%). Some participants were excluded from the response rate calculation for a given complication because the participants were ineligible for the examination (e.g., a participant with a two-leg amputation was not eligible for a peripheral nerve examination). Then, under the condition of a complete interview, the individual response rates for anthropometric measurements, blood pressure measurements, blood sample testing, and urine sample testing were 91.2%, 91.1%, 91.1%, and 90.6%, respectively. The individual response rates for of ECG examination, visual acuity test, and diabetic retinopathy, peripheral neuropathy, and peripheral arterial disease screening were 90.3%, 90.6%, 90.1%, 90.5%, and 90.5%, respectively.

A total of 53,401 patients, with a mean age of 57.1 years, had complete interviews. Among them, 49.6% were males, 13.7% were young (18–44 years), 44.6% were middle-aged (45–59 years), 41.7% were elderly, 46.7% lived in rural areas, 37.2% resided in

Table 1. Response rates in the China National Diabetic Chronic Complications study

		Questionnaire	ing	indices		Blood pressure	Bloo	Blood test	Uri	Urine test	Electroca	rdiogram	Electrocardiogram Visual acuity test	uity test	Diabetic retinopathy	etic pathy	Perip	Peripheral neuropathy	Peripheral arterial disease	heral disease
Population	2	Response rate (%)	2	Response rate (%)	>	Response rate (%)	<	Response rate (%)	2	Response rate (%)	>	Response rate (%)	< < < < < < < < < < < < < < < < < < <	Response rate (%)	× ×	Response rate (%)	S	Response rate (%)	S	Response rate (%)
Total	53,401	1 91.2	53,378	91.2	53,359	91.1	53,367	91.1	53,064	9.06	52,872	90.3	52,875	9.06	52,134	90.1	53,002	90.5	52,967	90.5
Sex																				
Men	26,471	1 90.4	26,459	90.4	26,447	90.3	26,453	90.3	26,361	0.06	26,182	89.4	26,226	8.68	25,884	89.4	26,255	89.7	26,236	9.68
Women	Women 26,930	0.26	26,919	91.9	26,912	91.9	26,914	91.9	26,703	91.2	26,690	91.2	26,649	91.4	26,250	6.06	26,747	91.4	26,731	91.3
Age group, years	, years																			
18–44	7,289	74.7	7,288	74.7	7,284	74.6	7,279	74.6	7,193	73.7	7,201	73.8	7,185	73.9	7,134	73.5	7,215	74.0	7,209	73.9
45–59	23,834	6.£6 t	23,822	93.9	23,815	93.8	23,823	93.9	23,730	93.5	23,588	93.0	23,631	93.4	23,390	93.0	23,662	93.3	23,645	93.2
60–74	22,278	3 95.1	22,268	95.1	22,260	95.0	22,265	95.1	22,141	94.5	22,083	94.3	22,059	94.5	21,610	94.0	22,125	94.5	22,113	94.4
Setting																				
Urban	28,457	7 91.2	28,449	91.2	28,437	91.1	28,435	91.1	28,279	9.06	28,115	90.1	28,216	200.7	27,744	0.06	28,259	9.06	28,240	90.5
Rural	24,944	1 91.2	24,929	91.1	24,922	91.1	24,932	91.1	24,785	9.06	24,757	90.5	24,659	90.5	24,390	90.2	24,743	90.5	24,727	90.4
Geographical region	ical regio	ū																		
Eastern	Eastern 19,865	92.0	19,858	91.9	19,856	91.9	19,854	91.9	19,748	91.4	19,657	91.0	19,695	91.4	19,437	91.2	19,711	91.3	19,699	91.2
Central	14,539	91.8	14,536	91.8	14,527	91.7	14,526	91.7	14,442	91.2	14,389	8.06	14,364	6.06	14,208	8.06	14,453	91.3	14,435	91.2
Westeri	Western 18,997	6.68 7	18,984	89.9	18,976	8.68	18,987	89.9	18,874	89.4	18,826	89.1	18,816	89.5	18,489	88.6	18,838	89.2	18,833	89.2

Note. For the visual acuity test, and diabetic retinopathy, peripheral neuropathy, and peripheral arterial disease screening, 197, 714, 15, and 13 participants were excluded, respectively, from the response rate calculation because the participants were ineligible for these examinations (e.g., a subject with a two-leg amputation was not eligible for a peripheral nerve examination). In addition, the definition of completion of all above examinations was under the condition of a complete interview (date of diabetes diagnosis and approximately 80% of the questions in our questionnaire were completed). eastern regions, 27.2% in central regions, 35.6% in western regions, and 25.3% had high school or greater education levels. Males had a lower mean age and higher education level compared to females. The mean duration of diabetes was 7.0 years and the mean BMI was 25.7 kg/m² (Table 2).

Based on the existing evidence, which was derived mostly from developed countries, patients with diabetes had a 20%-50% prevalence of various microvascular complications, as follows: diabetic retinopathy, the leading cause of blindness, affects approximately one-third of adults with diabetes [17-19]; diabetic nephropathy, the most common cause of end-stage renal disease^[20-21], occurs in 20%-40% of patients with diabetes^[22-24]; and diabetic peripheral neuropathy [DPN] may be present in approximately 50% of patients with diabetes^[25]. Compared to those without diabetes, patients with diabetes have a 1.5fold higher risk of developing CVD during their lifetime, which accounts for two-thirds of their deaths^[26-27]. The reported prevalence of PAD varies greatly, and together with DPN, is related to an increased risk of lower extremity amputation^[28].

Large-scale population-based studies regarding diabetes-related complications are currently focused on Europe, North America, and other high-income countries^[29], while there is limited data available for the low- and middle-income countries with the largest increases in diabetes prevalence, such as China.

The China DiaChronic Study is the first database to be used for determining the epidemiologic characteristics of multiple chronic complications and co-morbidities of diabetes (retinopathy, nephropathy, peripheral neuropathy, PAD, and CVD), assess the attainment rates of metabolic targets, and implement standardized diagnosis and treatments in Chinese adults with diagnosed diabetes at the national level. The main implication of this study was to provide the scientific basis for the government to formulate prevention and control measures for chronic complications and co-morbidities of diabetes in China.

This study had several apparent strengths. First, this study was the first large-scale survey of multiple chronic complications and co-morbidities of diabetes based on primary health care management populations, while previous data on these

Table 2. Characteristics of study participants with a complete interview

Characteristic	Tatal	S	ex	0
Cnaracteristic	Total	Male	Female	- P value
N (%)	53,401 (100.0)	26,471 (49.6)	26,930 (50.4)	0.047
Age, years	57.1 (10.1)	57.0 (10.1)	57.3 (10.0)	0.009
Age group (years), n (%)				0.125
18–44	7,289 (13.7)	3,694 (14.0)	3,595 (13.4)	
45–59	23,834 (44.6)	11,774 (44.5)	12,060 (44.8)	
60–74	22,278 (41.7)	11,003 (41.6)	11,275 (41.9)	
Setting, n (%)				0.166
Urban	28,457 (53.3)	14,186 (53.6)	14,271 (53.0)	
Rural	24,944 (46.7)	12,285 (46.4)	12,659 (47.0)	
Geographical region, n (%)				0.127
Eastern	19,865 (37.2)	9,806 (37.0)	10,059 (37.4)	
Central	14,539 (27.2)	7,139 (27.0)	7,400 (27.5)	
Western	18,997 (35.6)	9,526 (36.0)	9,471 (35.2)	
Educational levels, n (%)				< 0.001
Middle school and below	39,910 (74.7)	18,111 (68.4)	21,799 (81.0)	
High school and above	13,491 (25.3)	8,360 (31.6)	5,131 (19.1)	
Diabetes duration, years	7.0 (5.9)	7.1 (6.0)	7.0 (5.9)	0.137
Body mass index, kg/m ²	25.7 (3.6)	25.7 (3.5)	25.7 (3.8)	0.825

Note. Data were presented as the mean (standard deviation) for continuous variables and number (percentage) for categorical variables.

complications and co-morbidities were mainly drawn from hospitals or regional areas, or only focused on a single disease^[19,30-32]. Second, the sample was nationally representative through multistage stratified random sampling over 31 provinces, autonomous regions, and municipalities in China. Third, a unified protocol, the unified medical equipment, and the unified testing laboratory (except for fasting blood glucose levels in a local laboratory with unified quality control) were used for all study sites, ensuring the consistency and reliability of the data. Fourth, stringent quality control was implemented across the entire survey process. Before the investigation, all investigators and research staff underwent a training session. During the investigation, provincial supervisors selected at least 5% of the participants to be reexamined to confirm whether the investigators followed the standardized procedures for physical examination, peripheral neuropathy screening, and PAD screening. After the investigation, all collected data were uploaded to the information management platform, reviewed, and checked. Fifth, two fundus photographs were taken for each eye (one was centered on the optic disc and another on the macula), which reduced the likelihood of a missed diagnosis of diabetic retinopathy.

The study had several limitations. First, as a cross-sectional survey, causal relationships were not drawn. Second, lower response rates were found in younger participants in some study sites. However, the total sample size of the young participants was sufficient for a national analysis. Finally, some behavior-related questionnaires required the participant to recall situations in the past year (mainly the dietary survey), and there may be some recall biases.

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Conflicts of Interest The authors declare that they have no conflicts of interest.

Author Contributions JIA Wei Ping, HOU Xu Hong, WANG Li Min, and HUANG Zheng Jing designed the study protocol. JIA Wei Ping, HOU Xu Hong, WANG Li Min, and ZHANG Mei developed the questionnaire. JIA Wei Ping, HOU Xu Hong, WANG Li Min, CHEN Si Yu, and WU Jing drafted the manuscript. All authors made substantial contributions to the study

conception and design. All authors have read and approved the final manuscript.

Members of the China National Diabetic Chronic Complications Study Group are listed in Supplementary Table S6, available in www.besjournal.com.

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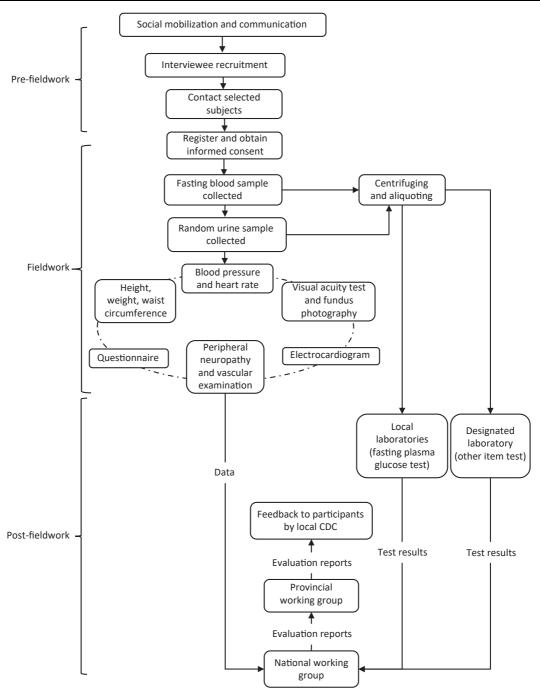
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中国糖尿病并发症研究	中国糖尿病并发症研究	中国糖尿病并发症研究
China National Diabetic Chronic Complications Study	China National Diabetic Chronic Complications Study	China National Diabetic Chronic Complications Study
工作手册	实验室工作手册	信息平台操作手册
Techinique Manual	Laboratory Operation Manual	User Manual of Information Platform
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Supplementary Figure S1. The front cover of the technique manuals.



Supplementary Figure S2. Geographical distribution of the 122 study sites in the 31 provinces, autonomous regions, and municipalities of mainland China.



Supplementary Figure S3. Flowchart of fieldwork.

Supplementary Table S1. Summary of the questionnaire

Part	Item	Content
1	Demographic and socioeconomic information	Patient ID, Sex, Date of birth, Race, Education, Occupation, Residence, Income and expenses, Marriage status, and Medical insurance
2	Smoking status	Current cigarette consumption (frequency, duration), Cigarette cessation, and Passive smoking
3	Alcohol, tea, and coffee consumption	Current alcohol consumption (frequency, degree, duration), Alcohol cessation, Tea consumption (frequency, species), and Coffee consumption (frequency)
4	Diet	Fourteen kinds of food: grains (rice, noodles, steamed bread, etc.), whole grains (corn, buckwheat, millet, etc.), potatoes (russet potato, yam, yuca root, sweet potato, etc.), soybean products, fresh vegetables, fresh fruits, dairy foods, red meat (pork, beef, lamb, etc.), poultry (chicken, duck, etc.), seafood, eggs, nuts, sugar-sweetened beverages, and fresh juices
5	Physical activity and sleep	Work, agriculture, and housework; Transit; Recreational activities and exercise; Total/leisure- time sedentary behavior; and Sleep behavior
6	Family history	Family history of hypertension, diabetes, obesity, coronary heart disease, stroke, tumor, and dyslipidemia
7	Medical history	Medical history of diabetes, hypertension, coronary heart disease, stroke, dyslipidemia, urinary system diseases, chronic hepatitis, hepatocirrhosis, and malignancy (date of diagnosis and/or treatment of the disease)
8	Medication	Current medication for diabetes, hypertension, coronary heart disease, stroke, dyslipidemia, and other diseases (names of medicines taken)
9	Weight and its control	Frequency of weight measuring and weight change in a year
10	Menstrual and obstetrical history ^a	Age at first menstruation, Menopausal status, Age at menopause, History of gestational hypertension, gestational diabetes, and ovarian surgery

Note. ^aOnly applicable for female participants.

Supplementary Table S2. Summary of physical examinations

Item	No. of measurements	Equipment used	Precision
Height (cm)	1	TGZ height gauge	0.1
Weight (kg)	1	TANITA HD-390 body weight scale	0.1
Waist circumference (cm)	2	1.5 Meter soft retractable measuring tape	0.1
Blood pressure (mmHg)	3	Omron blood pressure monitor ^a	1
Heart rate (beats/min)	3	Omron blood pressure monitor ^a	1

 $\it Note.\ ^{\it a}$ Models included HBP-1300, HEM-7207, HEM-7071, HEM-770A, HEM-7118, HEM-7133, HEM-7130, and HEM-8102A.

Supplementar	y Table S3.	Summary of	of laboratory	tests /
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Item	Method	Equipment used	Precision
Blood			
FPG (mmol/L) ^a	Glucose oxidase or hexokinase method	Equipment available in local laboratories ^a	0.01
HbA1c (%) ^b	High-performance liquid chromatography	BioRad D10 Hemoglobin Analyzer	0.1
Lipid (mmol/L) ^{b,c}	Enzymatic method	Roche cobas c701/702	0.01
Creatinine (µmol/L) ^b	Enzymatic method	Roche cobas c701/702	1
Urine			
Urinary albumin (mg/L)	Immunoturbidimetry	Roche cobas c701/702	0.1
Urinary creatine (µmol/L)	Enzymatic method	Roche cobas c701/702	1

Note. ^aFPG was measured by local laboratories with a unified quality control plan, as follows. Before carrying out fasting blood glucose testing, each laboratory was required to verify the testing system using uniformly-issued serum chemistry controls: 1) repeatability precision verification [the staff aliquoted 20 copies of the low-, medium-, and high-concentration quality control products, performed repeated tests (a total of 60 measurement data), and the verification pass standard was that the coefficients of variation (CV) of each concentration were < 2.5%]; and 2) intermediate precision verification [the staff took one quality control product with low, medium, and high concentrations, tested once every hour, repeated four times a day for five days (20 data for each concentration; a total of 60 data), and the verification standards included that for each concentration, the means and the CVs of the daily test results were within the ranges declared by the manufacturer]. During the test period, each laboratory was required to perform real-time quality control using quality control products. On each experimental day, the staff needed to test quality controls in three levels (before, during, and after testing). If the test results met the following conditions, they were considered to be under quality control: 1) the test results of a specific concentration level cannot exceed the target value ± 3 standard deviations (SDs) within one day or exceed the target value ± 2 SDs for two consecutive days; and 2) the test results of two specific concentration levels cannot exceed the target value by ± 2 SDs at the same time within one day. After the test, we summarized the quality control results of each laboratory. The data showed that the CVs were all < 3.3% (0.05%-3.18%) and the cumulative target values [hexokinase method (level 1, 3.06-3.62; level 2, 6.08-7.02; level 3, 18.40-21.02); glucose oxidase method (level 1, 3.11-3.39; level 2, 6.16-6.75; level 3, 18.60-20.55)] were within the range declared by the manufacturer [hexokinase method (level 1, 2.89–3.68; level 2, 5.94–7.13; level 3, 18.20–22.20); glucose oxidase method (level 1, 2.66–3.91; level 2, 5.54-7.58; level 3, 17.40-23.80)]. ^bHbA1c, lipids, and creatinine, as well as urinary albumin and creatinine, were centrally measured and HbA1c was measured with a national glycohemoglobin standardization programcertified method. ^cLipid test included triglycerides, total cholesterol, high-density lipoprotein-cholesterol, and low-density lipoprotein-cholesterol. FPG, fasting plasma glucose; HbA1c, hemoglobin A1c.

Supplementary Table S4. Summary of special examinations

Item	Description	Equipment used
Electrocardiogram	A standard resting 12-lead electrocardiogram was performed and additional leads were completed if necessary	Six-channel automatic electrocardiography (Mode FX-8222T)
Visual acuity test	It was measured at a distance of five meters with each eye tested separately	Log-MAR visual acuity chart
Diabetic retinopathy	Two 45-degree color fundus photographs were taken for each eye; one was centered on the optic disc and the other on the macula	Digital non-mydriatic retinal camera (Canon CR-2 or TRC-NW400)
Peripheral neuropathy	An inspection of the feet and evaluation of ankle reflexes, pinprick, and vibration, pressure, and temperature sensations were carried out	Diabetic foot sensory examination kit, including 10 g monofilament, Tip-Therm, 128-Hz tuning fork, and a reflex hammer with sensory needle
Peripheral arterial disease	Peripheral vascular lesions were assessed by palpation of the dorsalis pedis, posterior tibial, and popliteal arteries, and by the Edinburgh intermittent claudication questionnaire	/

Supplementary Table S5. Physical activity classification

Work, agriculture	Work, agriculture, and housework	Recreational activities and exercise	ties and exercise	Sedentary behavior
Moderate-intensity physical activity ^a	High-intensity physical activity ^b	Moderate-intensity physical activity ^a	High-intensity physical activity ^b	Sitting, leaning, or lying outside of sleep time
Examples: Cleaning (such as vacuuming, mopping the floor, polishing the floor, wiping the table, sweeping the floor, ironing, etc.), Washing (brushing carpet, hand laundry, etc.), Gardening work (such as watering, soiling, fertilizing, etc.), Manual milking, Hand-weaving, Woodworking (carve, sawing softwood, etc.), Using tools such as mills and shovels to mix cement, sand, etc., Carrying/moving moderate loads (< 20 kg), Lifting water, Stocking livestock, etc.	Examples: Forestry work (cutting and moving timber), Sawing hardwood, Cultivating land, Sowing, Harvesting crops (wheat, rice, sugar cane, etc.), Gardening work (excavation, heavy loads, etc.), Artificial grinding (using tweezers or stone grinders, etc.), Construction work (moving building materials, building walls, etc.), Carrying/moving heavy loads (> 20 kg), Fitness coaching (such as spinning, aerobics, yoga, etc.), Courier work (on foot or by bike), Pulling, picking up rickshaws, pushing wheelbarrows, operating jackhammers, etc.	Examples: Bicycling, Jogging, Dancing, Riding, Tai Chi, Yoga, Pilates, Yangge, Dance, etc.	Examples: Long-distance running, Playing football, Playing soccer, Playing tennis, Spinning/cycling, Lifting dumbbells, barbells, Ballet, Swimming, etc.	Examples:Working, Studying, Reading, Watching TV, Using a computer, Riding a motor vehicle, Resting, etc.

Note. ^aPhysical activity requires a moderate amount of effort and noticeably accelerates the heart rate. ^bPhysical activity requires a large amount of effort and causes rapid breathing and a substantial increase in heart rate.

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