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Hypertension and diabetes on cognitive impairment: a case–control study in China

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Abstract

Background Cognitive impairment, hypertension and diabetes are prevalent chronic conditions in populations of older ages. Previous studies have shown that hypertension and diabetes are risk factors for the development of cognitive impairment. However, the impact of hypertension combined with diabetes (HD) and their cumulative effects on cognitive impairment remain unclear. We aimed to investigate whether HD influences development of cognitive impairment and whether the effect is cumulative.

Methods A case–control study was conducted. From 40,103 subjects aged 60 years or older, enrolled from 28 representative communities of 9 provinces of China between January 2015 and December 2021 into the Prevention and Intervention on Neurodegenerative Disease for Elderly in China program using multi-stage stratified random sampling, individuals not meeting our propensity score matching criteria were excluded, and 13,252 individuals were finally selected for the study. Exposure factors included hypertension, diabetes and their comorbidity. Odds ratios (ORs) of exposure factors on cognitive impairment were measured using multiple logistic regression.

Results We found significant impacts of hypertension, diabetes and their comorbidity on cognitive impairment occurrence. The OR values for dementia were 1.18 for individuals with hypertension only, 1.26 for those with diabetes only, and 1.53 for those with HD. Compared to participants without hypertension and diabetes, the OR values for mild cognitive impairment (MCI) were 1.11 for individuals with hypertension only, 1.32 for those with diabetes only, and 1.27 for those with HD. For subjects with HD longer than 5 years, the comorbidity significantly impacted on MCI and dementia, and the degree of impact increased with the duration of comorbidity. For hypertension, the influence of hypertension on dementia were most influential in middle-aged (45–64 years old) people. By contrast, the influence of diabetes on people younger than 45-year-old was most significant, with the middle-age group being the second most impacted subjects.

Conclusions The elderly with HD have a heightened risk of developing cognitive impairment, particularly dementia, compared to those with either hypertension or diabetes alone. The study revealed a significant cumulative impact of HD on cognitive impairment.

Keywords Cognitive impairment, Hypertension, Diabetes, Elderly, Case–control study

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Background

Cognitive impairment is a prevalent condition in the elderly, encompassing three main types, namely, subjective cognitive decline (SCD), mild cognitive impairment (MCI) and dementia. Dementia has emerged as a costly, fatal and burdensome disease in recent decades, garnering serious attention worldwide. Globally, the number of cases of dementia is expected to increase from 57.4 million in 2019 to 152.8 million by 2050 [1]. Moreover, dementia is the seventh leading cause of mortality in the world, resulting in 1.6 million deaths and accounting for 25.3 million disability-adjusted life-years in 2019 [2, 3]. Costs linked to dementia are projected to rise from $1.3 trillion per year worldwide in 2019 to $2.8 trillion by 2030 [4].

Like cognitive impairment, hypertension and diabetes are also two major prevalent chronic conditions among the elderly [5–10]. Of note, previous studies have shown that in midlife population either hypertension or diabetes alone represents an important risk factor for development of cognitive impairment, especially for dementia [11–16], yet controversies still exist on whether effective treatment of hypertension and diabetes alleviates cognitive impairment [11, 17]. While most relevant studies examined the effects of hypertension and diabetes separately, the joint effect of both conditions on cognitive function has been less well investigated [11–17]. A few existing reports suggest a possible correlation between the hypertension/diabetes comorbidity and cognition, but the study populations were limited to developed countries [18, 19]. No large sample study has been conducted on low- and middle-income countries (LMICs), such as China with a population of 1.4 billion. Furthermore, the effects of key parameters of hypertension and diabetes, such as the age of diagnosis, sex and compliance to standard treatments on cognitive function in LMICs remain largely unclear, making evidence-based development and implementation of coping strategies for cognitive impairment in elderly patients with diabetes and hypertension difficult. Thus, to address the above unanswered issues, we performed a case control study involving 13,252 subjects using data collected in the database of the Prevention and Intervention on Neurodegenerative Disease for Elderly in China (PINDEC) program to further investigate whether the combination and the disease course lengths of hypertension and diabetes have significant impacts on cognitive impairment in the elderly, and whether compliance to medication influences the development of cognitive impairment, aiming to provide evidence that can facilitate prevention and control of cognitive impairment in the elderly.

Methods

Study population and design

Based on data derived from the Chinese PINDEC program [20], a case–control study was conducted. The study was approved by the Ethics Review Committee of the National Center for Chronic and Noncommunicable Disease Control and Prevention, the Chinese Center for Disease Control and Prevention (Batch No.: 201620; 201,902), and all participants provided informed consent before enrollment.

From January 2015 to December 2021, 40,103 subjects aged 60 and above were randomly enrolled using multistage clustered sampling method from 28 communities in 9 of the 31 provinces of mainland China, which were selected to be nationally representative for geographic locations, population sizes and levels of socioeconomic development, as shown in Fig. 1 [21]. Participants included had resided in the area for a minimum of 12 months before the survey. Subjects who refused to participate, had a life-threatening illness, were hospitalized or were institutionalized by senior care facilities were excluded [21]. Furthermore, 12,770 participants with a SCD label determined by self-evaluation of cognitive impairment inclination were removed from the study due to its subjective nature. Moreover, 3474 participants were excluded due to having been diagnosed as either hypertension alone, diabetes alone, or both conditions combined for less than 3 years. In addition, participants not meeting the propensity score matching criteria were also excluded. Resultantly, a total of 13,252 participants were finally included in the study, as demonstrated in Fig. 1 as the sampling scheme.

After the above-described exclusion, the subjects in the case group were those diagnosed with cognitive impairment by physicians, including MCI and dementia. More specifically, the DSM-IV-R criteria were employed for the diagnosis of dementia [22], and SCD was defined as having AD8 score lower than 2 and complaining of subjective decline of memory or other cognitive function but not sufficiently meeting the DSM-IV-R criteria for a dementia diagnosis [23]. For the diagnosis of MCI, the following criteria were applied: AD8 score ≥ 2 but not meeting the DSM-IV-R criteria for dementia diagnosis. By contrast, the control group comprises cognitively normal subjects, as defined as the AD8 score being lower than 2 without subjective decline of memory or other cognitive function and not meeting the DSM-IV-R criteria for dementia diagnosis. For subjects who were unable to communicate adequately, proxy respondents were taken.

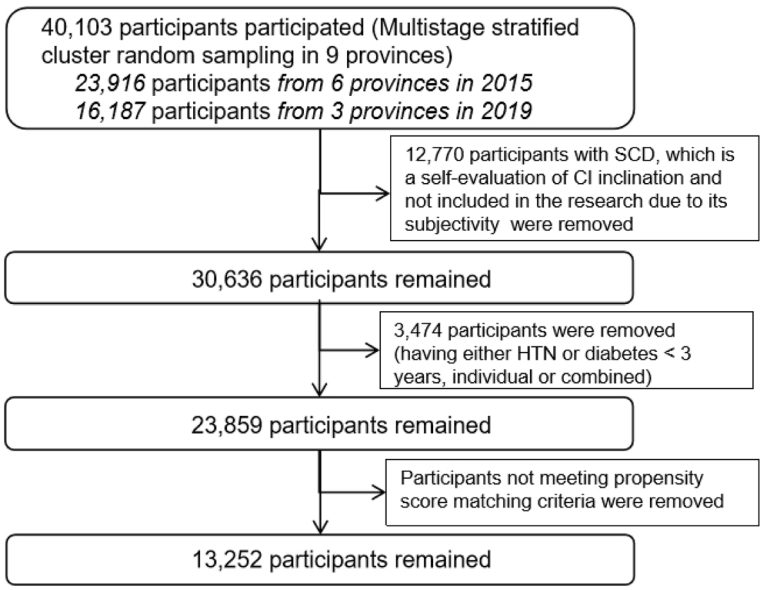

Fig. 1 Selection of individuals for study inclusion. Abbreviations: HTN, hypertension; SCD, subjective cognitive decline

Measurement of exposure factors

Questionnaire surveys were independently conducted through face-to-face interviews by medical personnel who had received standardized training, which included an introduction to the survey protocol, process for signing informed consent forms, procedures for examination and testing operations, utilization of the survey information system, quality control measures and considerations to be taken into account during the survey process [21]. All questionnaires were administered using a tablet with automatic skip pattern and logic check. All interviews were audio-recorded, and 5% of the questionnaires were randomly selected for quality check [21]. The survey questionnaires covered demographic characters, physiological indicators, genetic factors, lifestyle behaviors and other relevant information as shown in Table 1 and Table S1 in Additional file 1.

Exposure factors were hypertension, diabetes, and their comorbidity. The diagnosis of hypertension was based on the 2018 Chinese Guidelines for the Management of hypertension [24], and diabetes was diagnosed according to the Guideline for the Management of Diabetes Mellitus in the Elderly in China (2024 Edition) [25].

Expanded from potential risk factors indicated in previously published reports [11, 12], we included the following covariates in five categories: demographic factors (age, sex, marital status, occupation and education level), genetic factors (family history of dementia), physiological factors (cerebrovascular disease, coronary heart disease, chronic obstructive pulmonary disease, chronic kidney disease, asthma, arthritis, cervical spondylosis, chronic insomnia, chronic constipation, obesity, depression and sensory function status), behavioral factors (alcohol consumption, smoking, tea consumption, social isolation, physical inactivity, playing poker cards, using internet, reading and neighbor interaction), and environmental factors (residence location, region and $PM_{2.5}$ exposure); and the definition for each covariate is provided in Table S1 of Additional file 1.

Statistical analysis

Propensity score matching was employed to reduce the interference of confounding factors [26]. For patients with MCI or dementia versus normal-group subjects in each community, we utilized the binary logistic regression model based on independent variables, including age and sex, to estimate every individual's propensity to develop MCI or dementia, respectively. Moreover, each case of MCI or dementia was matched with the control group (individuals with normal cognitive function) by 1:1 nearest neighbor matching according to propensity score results, with a caliper of 0.02.

Multiple logistic regression methods were used to estimate the odds ratio (OR) and 95% CI between each of the exposure factors and cognitive function. The degree of cognitive function was divided into three grades, namely, cognitively normal, MCI and dementia, with normal cognitive status used as reference. In a full-adjusted model to explore the effect, and cumulative dynamic progressive impact of hypertension, diabetes and their comorbidity on cognitive function,

we adjusted for all covariates of demographic, genetic, physiological and environmental factors.

Based on a whole population analysis, we categorized the population by sex (male vs female), age (60–64 years vs 65 years and older), educational level (high vs low education), and residence areas (urban vs rural) to comparatively analyze the effects of comorbidity of hypertension and diabetes on cognitive function in subgroups. Several sensitivity analyses were performed to test the robustness of our methods and the findings. Specifically, we used comorbidity of hypertension and diabetes as a single factor for regression analysis and performed adjustment for covariates of age, sex, marital status, educational level and occupation. Statistical analysis was conducted utilizing the SPSS 24.0 software, and propensity score matching was performed using the MatchIt package in R 4.3.1. A bilateral p-value below 0.05 was considered to be statistically significant.

Results

Baseline characteristics of participants

Among 13,252 participants included in the current study, 7,336 subjects were in the cognitive impairment case group, consisting of 4,964 MCI and 2,372 dementia cases, and the control group comprised 5,916 individuals (Table 1; Additional file 1: Tables S2 to S3). The percentages of subjects aged 65 years or older; females; individuals who were divorced, unmarried or widowed; manual labor workers; and subjects with less education based on years of education were lower in the control group (75.3%, 57.7%, 22.1%, 58.7% and 64.0%, respectively) and MCI group (72.9%, 58.3%, 21.3%, 59.9% and 68.1%, respectively) as compared with those in the dementia group (86.3%, 62.5%, 35.3%, 76.3% and 86.4%, respectively) (Table 1).

Among all participants, proportions of individuals with hypertension or diabetes alone, and HD, respectively, were 25.1%, 4.1% and 7.5%, and 1.7% subjects fell into the category with 1–2 years of interval time between the first-time diagnosis of HD and the first-time diagnosis of cognitive impairment or the date of the survey. Whereas, 2.4% individuals possessed such an interval $\geq$ 10 years (Table 2), exhibiting that the majority of individuals included had a duration of HD lasting for 10 years or more among the HD population.

In the entire cohort of subjects, nearly 31.6% had either hypertension or diabetes alone, or HD undergoing standard treatments, whereas 5.3% subjects who had such diseases without treatment or only received treatment occasionally as defined in Table 2, revealing that the majority was individuals receiving standard treatment.

Impact of hypertension and diabetes and their disease course duration on MCI and dementia occurrence

The possibility of hypertension, diabetes and HD, respectively, being risk factors for cognitive impairment occurrence was analyzed. Our results showed that compared with participants without hypertension and diabetes, subjects with either hypertension or diabetes had a higher risk of developing dementia and MCI, with the OR value for dementia among patients with hypertension being 1.19 (95%CI, 1.04–1.36), as opposed to the OR value for dementia in individuals with neither hypertension nor diabetes. Similarly, compared with individuals without diabetes, OR values for dementia and MCI among subjects with diabetes were 1.29 (95%CI, 1.06–1.59) and 1.21 (95%CI, 1.05–1.40), respectively (Fig. 2).

Our data also showed that hypertension and diabetes had cumulatively effects on the development of MCI and dementia, with their impact on dementia being more significant than that on MCI. Notably, influences of diabetes on dementia occurrence for people diagnosed with diabetes for 3 years, 5 years or 10 years were significant, and such an impact increased as the duration of diabetes prolonged. It is also notable that the influence of diabetes on MCI development in people with diabetes for more than 10 years was significant. By contrast, the effect of hypertension on dementia and MCI development in subjects diagnosed with hypertension for more than 3 years was significant, but insignificant in those with hypertension for more than 5 or 10 years (Fig. 3). Our study implicated that the earlier the prevention and control of diabetes was implemented, the lower the risk of developing cognitive impairment.

Of note, compared with individuals without diabetes, those who had been diagnosed as diabetes patients for 3, 5 and 10 years or longer, respectively, displayed OR values for dementia of 1.37 (95% CI, 1.11–1.70), 1.45 (95% CI, 1.01–2.07) and 1.49 (1.16–1.91); while OR for MCI in individuals with the duration of diabetes for 10 years or more was 1.25 (95% CI, 1.04–1.49). Moreover, as compared to those without hypertension, the OR values for dementia and MCI, respectively, in subjects having hypertension for 3 years or more were 1.22 (95% CI, 1.07–1.40) and 1.10 (95%CI, 1.00–1.22) (Fig. 3). Taken together, these data suggest that both hypertension and diabetes are risk factors for the development of cognitive impairment, with diabetes exhibiting a cumulative effect on cognitive impairment.

The age of initial diagnosis of hypertension or diabetes influences the development of MCI and dementia

To investigate whether the age at which the first-time diagnosis of hypertension and/or diabetes is made effects

Table 1 Baseline characteristics of participants

Characteristic		Controls, No. (%)	Cases, No. (%)		Total ($n=13,252$)
		Cognitively normal ($n=5916$)	MCI ($n=4964$)	Dementia ($n=2372$)	
Demographic factors [a]	Age				
	65 +	4455 (75.3)	3617 (72.9)	2047 (86.3)	10,119 (76.4)
	60 ~ 65	1461 (24.7)	1347 (27.1)	325 (13.7)	3133 (23.6)
	Sex				
	Female	3413 (57.7)	2892 (58.3)	1482 (62.5)	7787 (58.8)
	Male	2503 (42.3)	2072 (41.7)	890 (37.5)	5465 (41.2)
	Marital status				
	Divorced, unmarried or widowed	1307 (22.1)	1058 (21.3)	837(35.3)	3202 (24.2)
	Married	4609 (77.9)	3906 (78.7)	1535(64.7)	10,050 (75.8)
	Occupation [b]				
	Manual workers	3472 (58.7)	2974(59.9)	1810(76.3)	8256 (62.3)
	Mental workers	650 (11.0)	388(7.8)	122(5.1)	1160 (8.8)
	Less education				
	Yes	3787 (64.0)	3382(68.1)	2049(86.4)	9218 (69.6)
	No	2129 (36.0)	1582(31.9)	323(13.6)	4034 (30.4)
Genetic factors [a]	Family history of dementia				
	Yes	108 (1.8)	163(3.3)	70(3.0)	341 (2.6)
	No	5808 (98.2)	4801(96.7)	2302(97.0)	12,911 (97.4)
Physiological factors [a]	Cerebrovascular disease				
	Yes	417 (7.0)	618(12.4)	402(16.9)	1437 (10.8)
	No	5499 (93.0)	4346(87.6)	1970(83.1)	11,815 (89.2)
	Obesity				
	Yes	371 (6.3)	296(6.0)	127(5.4)	794 (6.0)
	No	5500 (93.7)	4640(94.0)	2216(94.6)	12,356 (94.0)
	Coronary heart disease				
	Yes	608 (10.3)	765(15.4)	365(15.4)	1738 (13.1)
	No	5308 (89.7)	4199(84.6)	2007(84.6)	11,514 (86.9)
	Chronic obstructive pulmonary disease				
	Yes	418 (7.1)	635(12.8)	382(16.1)	1435 (10.8)
	No	5498 (92.9)	4329(87.2)	1990(83.9)	11,817 (89.2)
	Asthma				
	Yes	151 (2.6)	223(4.5)	120(5.1)	494 (3.7)
	No	5765 (97.4)	4741(95.5)	2252(94.9)	12,758 (96.3)
	Chronic kidney disease				
	Yes	88 (1.5)	143(2.9)	74(3.1)	305 (2.3)
	No	5828 (98.5)	4821(97.1)	2298(96.9)	12,947 (97.7)
	Arthritis				
	Yes	362 (6.1)	528(10.6)	256(10.8)	1146 (8.6)
	No	5554 (93.9)	4436(89.4)	2116(89.2)	12,106 (91.4)

Table 1 (continued)

Characteristic		Controls, No. (%)	Cases, No. (%)		Total ($n=13,252$)
		Cognitively normal ($n=5916$)	MCI ($n=4964$)	Dementia ($n=2372$)	
	Cervical spondylosis				
	Yes	579 (9.8)	855(17.2)	265(11.2)	1699 (12.8)
	No	5337 (90.2)	4109(82.8)	2107(88.8)	11,553 (87.2)
	Chronic insomnia				
	Yes	1192 (20.1)	1908(38.4)	918(38.7)	4018 (30.3)
	No	4724 (79.9)	3056(61.6)	1454(61.3)	9234 (69.7)
	Chronic constipation				
	Yes	452 (7.6)	883(17.8)	504(21.2)	1839 (13.9)
	No	5464 (92.4)	4081(82.2)	1868(78.8)	11,413 (86.1)
	Depression				
	Yes	436 (8.4)	1104(24.4)	640(34.0)	2180 (18.8)
	No	4745 (91.6)	3427(75.6)	1240(66.0)	9412 (81.2)
	Sensory function status				
	Normal	4741 (80.1)	3292(66.3)	1581(66.7)	9614 (72.5)
	One SD	1046 (17.7)	1355(27.3)	648(27.3)	3049 (23.0)
	Two SDs	127 (2.1)	296(6.0)	127(5.4)	550 (4.2)
	Three SDs	2 (0.1)	21(0.4)	16(0.7)	39 (0.3)
Behavioral factors [a]	Alcohol				
	Yes	548 (9.3)	491(9.9)	168(7.1)	1207 (9.1)
	No	5368 (90.7)	4473(90.1)	2204(92.9)	12,045 (90.9)
	Smoking				
	Yes	1782 (30.1)	1606(32.4)	629(26.5)	4017 (30.3)
	No	4134 (69.9)	3358(67.6)	1743(73.5)	9235 (69.7)
	Tea drinking				
	No	4318 (73.0)	3779(76.1)	2037(85.9)	10,134 (76.5)
	Yes	1598 (27.0)	1185(23.9)	335(14.1)	3118 (23.5)
	Social isolation				
	Yes	3479 (58.8)	3200(64.5)	1732(73.0)	8411 (63.5)
	No	2437 (41.2)	1764(35.5)	640(27.0)	4841 (36.5)
	Physical inactivity				
	Yes	1040 (17.6)	1028(20.7)	795(33.5)	2863 (21.6)
	No	4876 (82.4)	3936(79.3)	1577(66.5)	10,389 (78.4)
	Playing cards				
	No	4491 (75.9)	3957(79.7)	2120(89.4)	10,568 (79.7)
	Yes	1425 (24.1)	1007(20.3)	252(10.6)	2684 (20.3)
	Using Internet				
	No	5408 (91.4)	4662(93.9)	2342(98.7)	12,412 (93.7)

Table 1 (continued)

Characteristic		Controls, No. (%)	Cases, No. (%)		Total ($n=13,252$)
		Cognitively normal ($n=5916$)	MCI ($n=4964$)	Dementia ($n=2372$)	
	Yes	508 (8.6)	302(6.1)	30(1.3)	840 (6.3)
	Reading				
	No	4290 (72.5)	3907(78.7)	2142(90.3)	10,339 (78.0)
	Yes	1626 (27.5)	1057(21.3)	230(9.7)	2913 (22.0)
	Neighbor interaction				
	No	899 (15.2)	1001(20.2)	609(25.7)	2509 (18.9)
	Yes	5017 (84.8)	3963(79.8)	1763(74.3)	10,743 (81.1)
Environmental factors [a]	Residence location				
	Rural	3020 (51.0)	2425(48.9)	1500(63.2)	6945 (52.4)
	Urban	2896 (49.0)	2539(51.1)	872(36.8)	6307 (47.6)
	Region				
	Northern China	2265 (38.3)	2141(43.1)	719(30.3)	5125 (38.7)
	Southern China	3651 (61.7)	2823(56.9)	1653(69.7)	8127 (61.3)
	$PM_{2.5}$ [c]				
	Pollution	4152 (70.2)	3447(69.4)	1748(73.7)	9347 (70.5)
	Normal	1764 (29.8)	1517(30.6)	624(26.3)	3905 (29.5)

Abbreviations: *MCI* mild cognitive impairment, $PM_{2.5}$, *SCD* subjective cognitive decline, *SD* sensory dysfunction

[a] The distribution of different groups of subjects in different cognitive statuses in the table was tested by Wilcoxon, $p<0.05$

[b] Manual workers refer to farmers, fishermen, and herders; mental workers refer to teachers, research or medical workers, and office workers. The data of occupation do not include those whose occupations cannot be distinguished

[c] $PM_{2.5}$ pollution level refers to the annual average concentration of $PM_{2.5}$ is greater than 35.00ug / m^3; the normal level refers to the annual average concentration of $PM_{2.5} \leq 35.00$ug / m^3

on the development of MCI and dementia, we analyzed the survey data and found that in subjects initially diagnosed with hypertension at middle age (45–64 years old), the influence of hypertension was most remarkable on dementia development (OR = 1.22; 95%CI, 1.04–1.44) but less significant on MCI (OR = 1.12; 95%CI, 1.00–1.26). Meanwhile, we found that the influence of diabetes was more significant on MCI and dementia for subjects diagnosed with diabetes for the first-time at an age < 45 than those ≥ 45, and the extent of such an impact declined as the age of first-time diagnosis increased (Fig. 3).

It is also noteworthy that compared with individuals without hypertension, for those initially diagnosed with hypertension at middle age (45–64 years old), their OR values for the impact on dementia and MCI were 1.22 (95%CI, 1.04–1.44) and 1.12 (95%CI, 1.00–1.26), respectively (Fig. 3). Moreover, compared to individuals without diabetes, for the subjects with their first diagnoses of diabetes were made before 45 years old or at ages between 45 and 64, the OR values of their influence on dementia were 4.55 (95%CI, 1.71–12.11) and 1.29 (95%CI, 1.01–1.66), respectively; while for their influence on MCI, the OR values corresponding to the two age groups, respectively, were 3.20 (95%CI, 1.43–7.18) and 1.27 (95%CI, 1.07–1.51) (Fig. 3), together suggesting that for patients first-time diagnosed with diabetes at a younger age, particularly those under 45 years old, the risk of becoming cognitively impaired is higher than that in older-age diabetes patients, with even more prominent impact on dementia than on MCI.

Impact of HD and its duration on MCI and dementia

Next, analyses were performed to investigate possible associations of hypertension, diabetes or the HD comorbidity with MCI or dementia. Specifically, four groups of subjects exposed to the following factors were analyzed, namely, those with neither hypertension nor diabetes, with hypertension alone, with diabetes alone and with the HD comorbidity. Our data revealed that compared with subjects without hypertension or diabetes, the OR values for dementia in patients with hypertension only, diabetes only and HD, respectively, were 1.18 (95%CI, 1.03–1.36), 1.26 (95%CI, 0.91–1.75) and 1.53 (95%CI, 1.20–1.95), while for MCI the ORs, correspondingly, were 1.11 (95%CI, 1.00–1.24), 1.32 (95%CI, 1.06–1.64) and 1.27 (95%CI, 1.06–1.52) (Fig. 2), suggesting that the impact of diabetes as a mono-factor on the development

Table 2 Prevalence conditions of hypertension and diabetes of participants

Exposure factors	Controls, No. (%)	Cases, No. (%)		Total ($n=13,252$)
	Cognitively normal ($n=5916$)	MCI ($n=4964$)	Dementia ($n=2372$)	
Hypertension [a]				
No	4164(70.4)	3266(65.8)	1499(63.2)	8929(67.4)
Yes	1752(29.6)	1698(34.2)	873(36.8)	4323(32.6)
Diabetes [a]				
No	5351(90.4)	4285(86.3)	2074(87.4)	11,710(88.4)
Yes	565(9.6)	679(13.7)	298(12.6)	1542(11.6)
Comorbidity conditions of HTN and diabetes [a]				
Non-HTN with non-diabetes	3953(66.8)	3013(60.7)	1415(59.7)	8381(63.2)
HTN only	1398(23.6)	1272(25.6)	659(27.8)	3329(25.1)
Diabetes only	211(3.6)	253(5.1)	84(3.5)	548(4.1)
HD	354(6)	426(8.6)	214(9)	994(7.5)
Years of the first-time diagnosis of HD to the first-time diagnosis of CI or the date of the survey [a]				
1 to 2	90(1.5)	92(1.9)	37(1.6)	219(1.7)
3 to 4	66(1.1)	75(1.5)	35(1.5)	176(1.3)
5 to 9	96(1.6)	118(2.4)	73(3.1)	287(2.2)
10 +	102(1.7)	141(2.8)	69(2.9)	312(2.4)
Treatment conditions of HTN [a]				
Non-HTN	4164(70.4)	3266(65.8)	1499(63.2)	8929(67.4)
HTN undergoing standard treatment	1551(26.2)	1465(29.5)	741(31.2)	3757(28.4)
HTN undergoing treatment occasionally	108(1.8)	121(2.4)	68(2.9)	297(2.2)
HTN without treatment	93(1.6)	112(2.3)	64(2.7)	269(2.0)
Treatment conditions of diabetes [a]				
Non-diabetes	5351(90.4)	4285(86.3)	2074(87.4)	11,710(88.4)
Diabetes undergoing standard treatment	507(8.6)	604(12.2)	271(11.4)	1382(10.4)
Diabetes undergoing treatment occasionally	20(0.3)	24(0.5)	9(0.4)	53(0.4)
Diabetes without treatment	38(0.6)	51(1)	18(0.8)	107(0.8)
Treatment conditions of HD [a]				
Non-HTN and non-DM	3953(66.8)	3013(60.7)	1415(59.7)	8381(63.2)
HTN only with standard treatment	1226(20.7)	1089(21.9)	542(22.8)	2857(21.6)
HTN only with treatment occasionally	90(1.5)	94(1.9)	57(2.4)	241(1.8)
HTN only without treatment	82(1.4)	89(1.8)	60(2.5)	231(1.7)
Diabetes only with standard treatment	191(3.2)	222(4.5)	76(3.2)	489(3.7)
Diabetes only with treatment occasionally	6(0.1)	11(0.2)	3(0.1)	20(0.2)
Diabetes only without treatment	14(0.2)	20(0.4)	5(0.2)	39(0.3)
HD with standard treatment	301(5.1)	350(7.1)	184(7.8)	835(6.3)
HD with treatment occasionally	46(0.8)	70(1.4)	29(1.2)	145(1.1)
HD without treatment	7(0.1)	6(0.1)	1(0.0)	14(0.1)

Abbreviations: *CI* cognitive impairment, *HD* hypertension combined with diabetes, *HTN* hypertension, *MCI* mild cognitive impairment

[a] The distribution of cognitive status of people with HTN(no/yes),diabetes(no/yes), comorbidity conditions of HTN and diabetes, years of the first-time diagnosis of HD to the first-time diagnosis of cognitive impairment or the date of the survey, treatment conditions of HTN, treatment conditions of diabetes, treatment conditions of HD in Table 2 were tested by Wilcoxon or Kruskal–Wallis test, $p<0.05$

of MCI was more significant than those of the other three exposures, while dementia was most markedly influenced by the HD comorbidity.

We then further investigated whether the duration length of HD has a cumulative impact on MCI and dementia. Our results showed that compared with individuals without hypertension or diabetes, individuals with HD for 5–9 years and ≥ 10 years, respectively, had OR values for their impact on MCI of 1.37 (95%CI, 1.00–1.89) and 1.43(95%CI, 1.04–1.96), whereas the

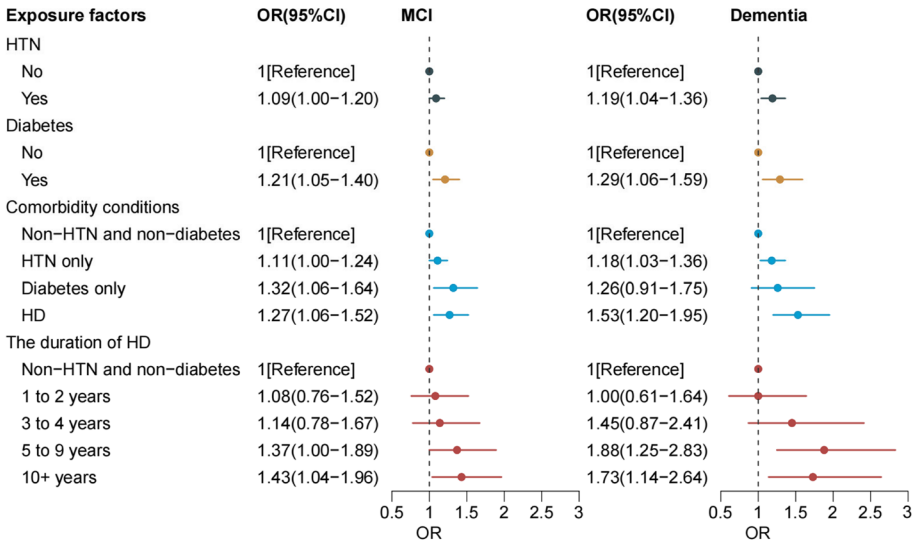

Fig. 2 ORs for HTN, diabetes, and their comorbidity for MCI, and dementia. Abbreviations: HD, hypertension combined with diabetes; HTN, hypertension; MCI, mild cognitive impairment; OR, odds ratio

corresponding OR values for the impact on dementia were 1.88 (95%CI, 1.25–2.83) and 1.73 (95%CI, 1.14–2.64) (Fig. 2), suggesting that when lasting for longer than five years, HD significantly impacted the development of MCI and dementia, moreover, its impact on dementia was more significant than that on MCI.

Impact of treatment of hypertension and diabetes on MCI and dementia

To understand whether treatments for hypertension or diabetes affect the development of cognitive impairment, we compared MCI and dementia occurrence between patients with hypertension and/or diabetes who did and did not adhere, respectively, to prescribed medication. Our data showed that patients with hypertension who consistently adhered to their medication had an OR of 1.16 for developing dementia, whereas those not or only occasionally taking hypertension treatment faced a significantly higher risk, with an OR of 1.51. Similarly, diabetes patients who undergone standard, occasional, and without treatment, had ORs of 1.28, 1.43 and 1.42, respectively, although the difference was not statistically significant. For patients with HD, inconsistent treatment was linked to a significantly higher risk of developing dementia (OR = 1.81) as opposed to those who strictly adhered to their medication (OR = 1.54) (Table S6).

Similar findings were made for MCI. Patients with hypertension who consistently adhered to their medication had an OR of 1.07 for developing MCI. In contrast, those with occasional and without hypertension treatment had a notably higher risk, with ORs of 1.18 and 1.28, respectively. For individuals with diabetes, adherence to medication or not, respectively, gave rise to ORs of 1.20 and 1.39 for the development of MCI, despite that the difference was not statistically significant. For patients with both hypertension and diabetes, inconsistent treatment was associated with a significantly higher risk of developing MCI (OR = 1.64) compared to those who consistently adhered to their medication (OR = 1.22) (Table S6).

Impact of hypertension, diabetes and their comorbidity on MCI and dementia in subject subgroups

To investigate the influences of hypertension and diabetes on cognitive impairment occurrence in different socioeconomic populations, we further subgrouped our participants based on their demographic parameters as shown in Fig. S1 in Additional file 1. Our analyses demonstrated that in the female subgroup, the risk of developing dementia associated with HD increased as compared with those without hypertension and diabetes, with a corresponding OR value of 1.55 (95%CI, 1.15–2.08), while the male subgroup displayed an increased risk of developing MCI in those with diabetes alone compared to those without hypertension and diabetes, with a corresponding OR value of 1.39 (95%CI, 1.00–1.94) (Additional file 1: Fig. S1). Furthermore, when the subgroup of age > 65 was examined, we found that the risk of dementia associated with HD increased compared with those without hypertension and diabetes, with a corresponding OR value of 1.51(95%CI, 1.16–1.96), whereas the 60–64 year age group exhibited an increased risk of developing MCI for the HD subjects when compared with corresponding control subjects, with a corresponding OR value of

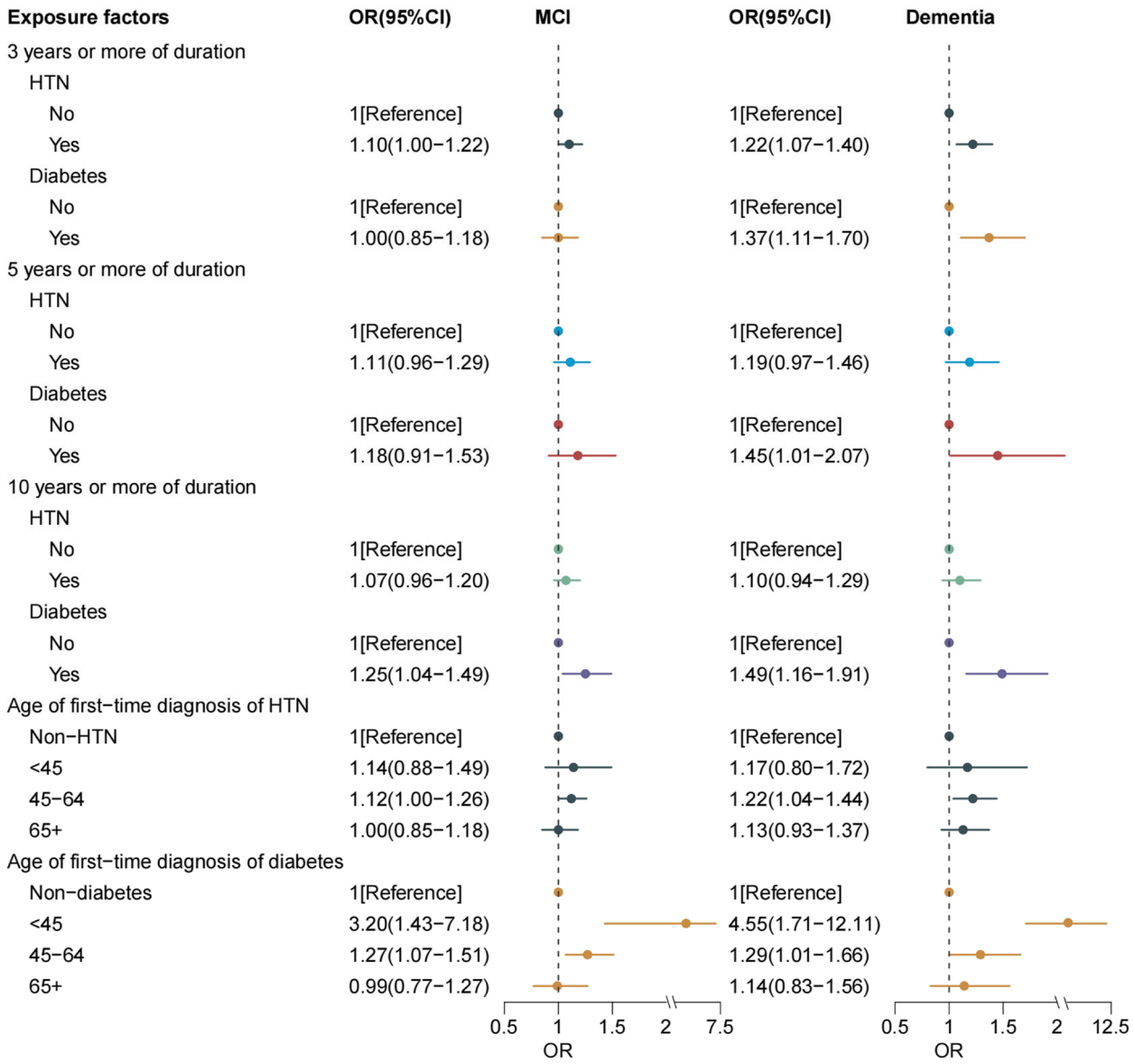

Fig. 3 ORs for cumulative years after, and age of the first-time diagnosis of HTN and diabetes for MCI, and dementia. Abbreviations: HTN, hypertension; MCI, mild cognitive impairment; OR, odds ratio

1.86 (95%CI, 1.28–2.70). Moreover, this age subgroup (60–64 years old) developed MCI or dementia at higher risks when they had diabetes alone than those without hypertension and diabetes, with corresponding OR values being 1.97 (95%CI, 1.27–3.05) and 2.06 (95%CI, 1.01–4.20), respectively (Additional file 1: Fig. S1).

Interestingly, in the low education subgroup based on the years of education, compared to those without hypertension and diabetes, HD presented an OR of 1.42 (95%CI, 1.07–1.89) for dementia, whereas the corresponding OR value for those who had HD in the high education subgroup was 1.61 (95%CI, 0.95–2.72), despite that the HD subjects in the high education subgroup still revealed a higher risk of developing MCI than those without hypertension and diabetes (Additional file 1: Fig. S1), largely suggesting that patient with HD had a higher risk to develop dementia in low education subgroup than those in not low education subgroup.

Subjects were also subgrouped according to their residence in urban or rural area. It is noteworthy that

increased dementia risks for HD were found in both subgroups in comparison with those without hypertension and diabetes, and the corresponding OR values were 1.50 (95%CI, 1.07–2.11) and 1.68 (95%CI, 1.17–2.43), respectively. Interestingly, rural residents with diabetes alone presented a higher risk of developing MCI than people without hypertension and diabetes (OR = 1.65; 95%CI, 1.14–2.40), whereas those with hypertension alone living in urban areas developed dementia at an increased probability than the subjects without hypertension and diabetes, with a corresponding OR value of 1.26 (95%CI, 1.01–1.58) (Additional file 1: Fig. S1), indicating that people with HD living in the rural areas had a higher dementia risk than those in urban areas, while individuals having hypertension alone in urban areas presented a higher risk of developing dementia than those living in rural areas.

Impact of HD duration on MCI and dementia in subgroups

Next, we analyzed our data in order to clarify the impacts of HD duration in different subgroups divided based on sex, educational level and residence area. Compared to individuals without hypertension and diabetes, the risks of developing MCI and dementia for male subjects with HD for 10 years or more increased as the corresponding OR values were 1.98 (95%CI, 1.16–3.40) and 2.46 (95%CI, 1.20–5.03), respectively. Similarly, individuals in the female subgroup who had had HD for 5 to 9 years also showed an elevated risk to develop MCI or dementia compared to those without hypertension and diabetes, with OR values of 1.57 (95%CI, 1.06–2.31) and 1.94 (95%CI, 1.17–3.21), respectively (Additional file 1: Fig. S2). The results suggested that males with HD for 10 years or more and females with HD for 5 to 9 years faced a higher risk of developing dementia than the risk of developing MCI.

In the subgroup with less education, compared to individuals without hypertension and diabetes, the risk of developing dementia increased with a duration of HD for 5 to 9 years and for 10 years or more, with OR values of 1.63 (95%CI, 1.02–2.62) and 1.87 (95%CI, 1.10–3.15), respectively (Additional file 1: Fig. S2). Moreover, in rural areas, compared to individuals without hypertension and diabetes, the risk of developing dementia elevated for those with a history of HD for 3 to 4 years, presenting an OR of 2.20 (95%CI, 1.06–4.59). In the urban subgroup, the risk to develop dementia increased for individuals with HD for 5 to 9 years, with an OR of 2.56 (95%CI, 1.49–4.40), as compared to those without hypertension and diabetes (Additional file 1: Fig. S2). The findings indicated that patients with HD for 3 to 4 years in rural areas had a higher risk of dementia than those in urban areas, whereas individuals with HD for 5 to 9 years in urban areas faced a greater risk compared to their rural counterparts.

Sensitivity analysis

Sensitivity analyses were performed to test the reliability and robustness of our case control study. Our results revealed cumulative effects of hypertension, diabetes and their comorbidity on cognitive impairment (Figs. 2 and 3). In model 1, when we used each exposure factor as a single factor, among subjects with hypertension alone, diabetes alone and HD, the OR values of the impact on dementia were 1.32 (95% CI, 1.18–1.47), 1.11 (95%CI, 0.86–1.44), and 1.69 (95%CI, 1.41–2.02), respectively. In model 2, after we adjusted for sex, age, marital status, educational level, and occupation, the corresponding OR values of the impact on developing dementia were 1.34 (95%CI, 1.19–1.50), 1.47 (95%CI, 1.12–1.92), and 2.11 (95%CI, 1.75–2.55), respectively (Additional file 1: Tables S4 to S5), together demonstrating that the outcomes derived from model 1 or model 2 and those of model 3 were primarily stable.

Discussion

This current case–control study has identified hypertension, diabetes and their comorbidity HD as risk factors for cognitive impairment in the elderly. Furthermore, our data suggest that they exert significant cumulative promoting impacts on the development of cognitive impairment. The study therefore provides epidemiological evidence for future optimized design and implementation of strategies for alleviating the burden of cognitive impairment in the elderly.

Notably, while previous studies examined the association between HD and cognition in high-income countries [18, 19], to our knowledge, such a correlation has not been clarified in LMICs thus far. In such a context, our results reveal that in LMICs such as China, compared with elderly individuals with hypertension or diabetes alone, those with both conditions combined face a significantly elevated risk of developing cognitive impairment. This finding suggests that in LMICs, population prevention and control of hypertension and diabetes, especially the HD comorbidity, may be essential to mitigating the risk of developing cognitive impairment.

Interestingly, previous studies indicated that the disease curse of hypertension or diabetes alone might impact on dementia occurrence. For instance, it was suggested that blood pressure first increased and then started to decrease 5 years before diagnosis of dementia, and that long illness duration of diabetes increased the risk of dementia [11, 15]. Nevertheless, the effect of duration of HD on cognitive impairment has not been reported. Hence, our observation that HD cumulatively impact on

cognitive impairment development, as the length of HD duration positively correlates with the risk of developing dementia and MCI, further underscores the importance of improving prevention and control against HD, particularly in LMICs. Additionally, we found that the impact of diabetes on cognitive impairment—particularly mild cognitive impairment (MCI)—is stronger than that of hypertension. This finding aligns with the conclusions of the 2024 Lancet review [11], which also emphasized the greater influence of diabetes compared to hypertension on dementia risk.

It is noteworthy that whether standard treatments for hypertension and/or diabetes might affect the impact of the disease(s) on the occurrence of cognitive impairment remains somewhat obscure. A meta-analysis including 12 trials with 4.1 years follow-up period (n = 92,135) showed that lowering blood pressure may be associated with a lower risk of dementia or cognitive impairment [27]. Another meta-analysis of diabetes cohort studies found that compared to diabetic patients taking other medications or no medication, OR value for the impact of taking metformin on cognitive impairment was 0.6 (95%CI, 0.4–0.8) [28]. Whereas, a Cochrane review suggested that intensive diabetes control did not significantly improve cognitive function compared to standard diabetes control [29]. Moreover, the effect of medication adherence on cognition status in patients with HD remains unclear, as previous studies mainly focused on numerical reductions in blood pressure and blood sugar, along with specific antihypertensive and antidiabetic medications' impact on cognitive function [27–29]. In this current study, we observed that subjects practicing consistent standard medication against HD displayed improved cognitive function than those receiving no or only occasional HD treatments, highlighting the importance of proper management for hypertension and/or diabetes in mitigating the risk of developing cognitive impairment in the elderly. In such a context, our research results support implementation of more effective clinical and public health measures, such as screening for HD, ensuring consistent standard treatment for HD, and developing practical and feasible programs to promote awareness of the association between HD and cognitive impairment, to reduce the burden of cognitive impairment and achieve goals set by the Sustainable Development Goals and the Healthy China Action (2019–2030) [30, 31].

Also of note is that the pathophysiologic mechanisms via which hypertension or diabetes might promote pathogenesis of cognitive impairment is still incompletely understood, although multi-layer mechanistic explanations have been suggested by numerous experimental studies on the adverse biologic effects of high blood pressure and high blood sugar, including impeded brain blood supply due to hampered integrity of the brain's microcirculation; neuroinflammation and amyloid-related pathologic changes, which may contribute to amyloid buildup and Alzheimer's disease, caused by breached blood–brain barrier; and damaged myelin sheaths that can lead to signal processing errors and neuron death; in addition to other alterations associated with hypertension or diabetes (for reviews, see references [32–36]. Furthermore, these mechanistic studies also illustrate pathological processes and biological outcomes shared by the two diseases, i.e., hypertension and diabetes, thereby consequently and rationally connecting the comorbidity, to a larger extent than either disease alone, to cognitive impairment [32, 36]. In consistence with this notion, it has been previously reported that presence of HD may speed up hippocampal shrinkage and brain aging, increasing the risk of developing cognitive impairment [18]. In such context, further mechanistic investigation to elaborate how hypertension and diabetes, as a singly disease alone or in combination, promote pathogenesis of cognitive impairment, will help develop more effective clinical and public health strategies against this medically as well as socially important condition.

Our study confirms the lifelong approach of risk factors for dementia in population from LMIC. On one hand the number of years of the first-time diagnosis of dementia is important for the prevention of dementia, on the other hand the age at first-time diagnosis is also important. Furthermore, their impact in some conditions are different for MCI and dementia. Early identification and sustained management of risk factors across the life course are essential for effective dementia prevention strategies in LMICs. Our results support the need for long-term investment in community-based screening programs, early intervention policies, and age-targeted health promotion strategies.

Strengths and limitations

The strengths of this current study include a rigorous sampling design, standardized procedures, comprehensive quality control, large sample sizes, detailed covariate information, and robust statistical analysis methods.

Limitations of this study are a potential recall bias in obtaining information. Our strategies to minimize the drawbacks of such limitations are implementing medical records to validate self-reported information, conducting structured interviews with standardized questions, and training data collectors to recognize and mitigate recall bias during interviews, as we adopted a rigorous survey protocol that can effectively control recall bias. Furthermore, our study focused on individuals aged 60 and older, as they bear a relatively heavier burden of cognitive impairment compared to those under the age of 60.

Abbreviations

CI	Confidence interval
HD	Hypertension combined with diabetes
HTN	Hypertension
LMICs	Low- and middle-income countries
MCI	Mild cognitive impairment
OR	Odds ratio
PINDEC	Prevention and Intervention on Neurodegenerative Disease for Elderly in China
SCD	Subjective cognitive decline
SD	Sensory dysfunction

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13195-025-01761-3.

Additional file 1.

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Authors' contributions
QD, JW, XY, CX, WJ, YL, HZ, SQ had full access to all of the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. JW, XY, WJ and YL are co-first authors. JW, QD and CX are co-corresponding authors. Concept and design: JW, XY, QD; acquisition, analysis, or interpretation of data: QD, JW, XY, CX, WJ, YL, HZ, SQ; drafting of the manuscript: WJ, YL, JT, NL, XY; critical revision of the manuscript for important intellectual content: JW, XY, QD, CX, JL; statistical analysis: QD, WJ, CX; obtained funding: JW, QD; administrative, technical, or material support: JW, QD, XY, CX; supervision: JW, QD, XY.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study was approved by the Ethics Review Committee of the National Center for Chronic and Noncommunicable Disease Control and Prevention, the Chinese Center for Disease Control and Prevention (Batch No.: 201620; 201902), and all participants provided informed consent before enrollment.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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