Association of hypertension and incident diabetes in Chinese adults: a retrospective cohort study using propensity-score matching

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Abstract

Background
Previous studies have revealed that hypertension is one of major risk factors of incident diabetes. However, reliable quantification of the relationship between hypertension and diabetes risk is limited, especially in Chinese people. We aimed to investigate the association between hypertension and risk of incident diabetes in a large cohort of Chinese population.

Methods
This was a retrospective propensity score-matched cohort study. We enrolled 211809 Chinese adults without diabetes at baseline between 2010 and 2016. The target independent and dependent variable were hypertension at baseline and incident diabetes during follow-up respectively. The one to one propensity score matching using a non-parsimonious multivariable logistic regression was conducted to balance the confounders between 28,946 hypertensive patients and 28,946 non-hypertensive participants. The doubly robust estimation method was used to investigate the association between hypertension and incident diabetes.

Result
After propensity-score matching, the cumulative incidence of diabetes among hypertensive and non-hypertensive participants were 1627.690 per 100,000 person-years and 1414.422 per 100,000 person-years, respectively. In the propensity-score matching cohort, compared to the non-hypertensive participants, the risk of incident diabetes increased by 14.0% among hypertensive subjects (HR = 1.140, 95% confidence interval (CI): 1.058–1.229, P = 0.00063). After adjusting for the demographic and clinical covariates, diabetes risk increased by 13.1% in the hypertensive group (HR = 1.131, 95%CI: 1.049–1.220, P = 0.00143). And diabetes risk increased by 15.4% among hypertensive subjects after adjusting for the propensity score (HR = 1.154, 95%CI:1.070–1.244, P = 0.00019). In the subgroup analysis, compared to non-hypertensive participants with low propensity score, the risk of incident diabetes increased by 2.6 times among hypertensive patients with high propensity score (HR = 3.610,95%CI: 2.604–5.005,P < 0.00001). In the sensitivity analysis, the risk of diabetes in the hypertensive group increased by 11.7% in the original cohort (HR = 1.117,95%CI: 1.044–1.196, P = 0.00134) and 19.9% in the weighted cohort (HR = 1.199,95%CI: 1.149–1.250, P <
Conclusion

Hypertension was associated with a 13.1% increase in the risk of developing diabetes in Chinese adults. Additionally, compared to non-hypertensive participants with low propensity score, the risk of incident diabetes increased by 2.6 times among hypertensive patients with high propensity score.

Background

Diabetes mellitus is an important global public health problem with high morbidity and disability. The World Health Organization estimated that the prevalence of diabetes in adults was 8.5% in 2016[1]. As the population ages and unhealthy lifestyles, the prevalence of diabetes worldwide tends to continue to rise. The International Diabetes Federation estimated that the number of people aged 20–79 years with diabetes will rise to 10.4% in 2040, reaching close to 642 million[2]. It is a debilitating chronic epidemic with potentially various complications. Diabetes can mediate multiple organ damage, leading to cardiovascular events, kidney disease and cerebrovascular complications [3-5]. Consequently, the high morbidity of diabetes has important social, financial and development implications worldwide.

Hypertension and diabetes often co-exist in the same individual [6-8]. The two diseases have etiological aspects in common such as obesity, inflammation, oxidative stress, insulin resistance, and factors associated with increased microvascular and macrovascular impairment [9]. Diabetes mellitus is more frequent in hypertensive than normotensive subjects [10-12]. Therefore, there is a rationale to suspect that hypertension may cause incident diabetes. Furthermore, uncontrolled blood pressure was associated with a two-fold increased risk of incident diabetes in treated hypertensive patients [13]. A study extending the findings showed the presence of hypertensive target organ damage increased the risk of developing diabetes [14]. Despite the evidences linking hypertension and incident diabetes, published studies on the impact of hypertension on development of diabetes have provided conflicting findings. Although some studies have demonstrated increased risk of diabetes in patients with hypertension, others have observed that after adjustment for some covariates, blood pressure has no significant effect on the risk of the subsequent development of diabetes [15-18].
view of these discrepant findings, most of these studies recruited relatively small number of patients from a single center, and they did not ensure balance in measured confounders. Given the traditional parsimonious regression model used in previous studies could result in bias because of unmeasured or residual confounding or the overfitting of the model, potentially preventing identification of the association between hypertension and incident diabetes. However, the propensity score is a conditional probability of having a particular exposure given a set of measured covariates at baseline. Propensity score matching is useful in such studies in which there are many covariates potentially confounding a rare outcome, and there are resource constraints prevent the conduction of randomized clinical trials [19]. Therefore, a large cohort-based study, using propensity score–matched (PSM) data to estimate the association between hypertension and incident diabetes should be conducted, using real-world data from 211,809 Chinese adults across 32 sites and 11 cities between 2010 and 2016.

Methods

**Study Design and Date Source**

This retrospective cohort study was based on a computerized database stablished by the Rich Healthcare Group in China, namely, ‘DATADRYAD’ database (www.Datadryad.org). We downloaded the raw data for free from the site provided by Chen et al [20] from: Association of body mass index and age with incident diabetes in Chinese adults: a population-based cohort study. Dryad Digital Repository. http://dx.doi.org/10.1136/bmjopen-2018-021768). The original study enrolled a total of 685,277 Chinese persons ≥20 years old with at least two visits from 2010 to 2016 across 32 sites and 11 cities in China (Shanghai, Beijing, Nanjing, Suzhou, Shenzhen, Changzhou, Chengdu, Guangzhou, Hefei, Wuhan, Nantong). Cohort entry was defined as the date of the initial visit. In each visit to the health check center, participants completed a detailed questionnaire assessing demographic, lifestyle and family history of chronic disease. The trained staff conducted the clinical measurements, including body weight, height, blood pressure. Biochemical tests about fasting plasma glucose, triglyceride (TG), total cholesterol(TC), high-density lipoprotein cholesterol(HDL-C), low-density lipoprotein cholesterol (LDL-C), serum creatinine(Scr), alanine aminotransferase(ALT), aspartate
aminotransferase (AST) were performed on an autoanalyzer (Beckman 5800). The data were collected under standardized conditions and performed in accordance with uniform procedures. Laboratory methods also were carefully standardized through stringent internal and external quality controls. Authors of the original study have waived all copyright and related ownership of the raw data. Therefore, we could use these data for secondary analysis without infringing on the authors’ rights. Furthermore, research ethics approved was obtained in previous research, no longer needed this secondary research. This was a retrospective cohort study, which means it decreased the risk of selection bias and observation bias.

**Study Sample**

Consistent with the original study, participants were eligible for inclusion in our study aged 20-99 years old with at least two visits between 2010 and 2016. Participants were excluded at baseline in the original study, as follows: (1) no available information on weight, height and gender; (2) extreme BMI values (<15 kg/m2 or >55 kg/m2); (3) visit intervals < 2 years; (4) no available fasting plasma glucose value; (5) participants diagnosed with diabetes at baseline and participants with undefined diabetes status at follow-up. The original study clearly explained trial inclusion / exclusion criteria [20]. In the present study, we further excluded participants with incomplete blood pressure (n = 24). Fig. 1 depicted the participants selection process.

**Outcome Measures**

The outcome of interest was incident diabetes. Diabetes mellitus was defined as fasting plasma glucose ≥7.00 mmol/L and/or self-reported diabetes during the follow-up period [20]. Patients were censored at the time of diagnosis of diabetes or the last visit, whichever came first. Fasting venous blood samples were collected after at least 10 hours fast at each visit. Plasma glucose levels were measured by the glucose oxidase method.

**Exposure of Interest and Covariates**

The exposure of interest was hypertension. Hypertension was defined as systolic blood pressure (SBP) values ≥140 mmHg and/or diastolic blood pressure (DBP) values ≥90 mmHg [21-23]. Blood pressure was measured by trained staff using standard mercury sphygmomanometers. Covariates of interest
included as follows: age, gender, body mass index (BMI), FPG, TG, TC, HDL-C, LDL-C, Scr, ALT, AST; smoking status, drinking status, family history of diabetes, year of follow up.

**Statistical Analyses**

Continuous variables were expressed as the means ± standard deviations (normal distribution) or medians (quartiles) (skewed distribution), and categorical variables were expressed as a frequency or percentages. Two-sample t-tests were used for normally distributed continuous variables, Wilcoxon rank-sum tests for non-normally distributed continuous variables, and chi-square tests for categorical variables. Missing continuous variables were mainly supplemented by means. As the missing values of HDL-C, LDL-C and AST were about 50%, we converted them as categorical variables based on the tertile. Besides missing categorical variables in each covariate are considered as a group.

Considering the differences in the baseline characteristics between eligible participants in the hypertension and non-hypertension group (Table 1), propensity-score (PS) matching was used to identify a cohort of patients with similar baseline characteristics. The propensity score was estimated with the use of a non-parsimonious multivariable logistic-regression model [24], with hypertension as the independent variable and all the baseline characteristics outlined in Table 1 as covariates. Matching was performed with the use of a 1:1 matching protocol without replacement (greedy-matching algorithm), with a caliper width equal to 0.005. Standardized differences (SD) were estimated for all the baseline covariates before and after matching to assess pre-matched imbalance and post-matched balance [25]. Standardized differences of less than 10.0% for a given covariate indicate a relatively small imbalance [25]. The person-years of follow-up were calculated from the baseline interview to the date of incident diabetes or follow-up interview, whichever came first [26]. We used cumulative incidence and person-years incidence to describe the incidence rate [27]. Besides, we also used the log-rank test to compare the Kaplan–Meier hazard ratios (HR) for incident diabetes. The doubly robust estimation method, the combination of multivariate regression model and a propensity score model, was also applied to infer the independent associations between blood pressure status and risk of diabetes [28, 29]. A Cox proportional-hazards regression model was performed by adjusting for the variables that remained imbalanced between the two groups in the PS
matched cohort. Prespecified subgroup analyses were performed on the basis of two types of characteristics. Subgroups were based on age, BMI, FPG, Scr, ALT, TC, TG, propensity score. For the continuous variables, we converted them to a categorical variable according to the clinical cut point or binary. Each stratification was adjusted for all the factors, except for the stratification factor itself. In the subgroup analyses, to maintain the baseline balance between the hypertension group and the non-hypertension group, only the corresponding matched pairs in a subgroup were chosen. For example, in the subgroup of participants with FPG<6.1 mmol/L, only the matched pairs of patients with FPG<6.1 mmol/L in the hypertensive group and in the non-hypertensive group were included in the analysis. The modifications and interactions of subgroups were inspected by likelihood ratio tests.

For sensitivity analyses, inverse probability of treatment weights (IPTW) were also calculated with the estimated propensity scores. IPTW was calculated as the inverse of the propensity score for hypertensive patients and as the inverse of (1- propensity score) for the non-hypertensive patients. IPTW model was used to generate a weighted cohort [29]. We conducted a series of sensitivity analyses to evaluate the robustness of the findings of the study and how our conclusions can be affected by applying various association inference models. In the sensitivity analysis, we added two association inference models in the original cohort and the weighted cohort. The calculated effect sizes and p values from all these models were reported and compared. All results are reported according to the STROBE statement[30].

All of the analyses were performed with the statistical software package R (http://www.R-project.org, The R Foundation) and Empower-Stats (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA). The tests were 2-tailed, and P < 0.05 was taken as statistically significant.

Results

Study population

We identified 211,809 participates (54.82% men and 45.18% women) who met our inclusion criteria (Fig. 1) of whom 29,377 (13.87%) with hypertension and 182,432 (86.13%) without hypertension. The mean age of the population was 42.10±12.65 years. A total of 4173 participants developed diabetes
during the median follow-up of 3.12±0.94 years. The number of participants with missing value of TC, TG, HDL-C and LDL-C were 4854, 4887, 94556 and 93415, respectively. Besides, the missing value of Scr, ALT and AST were 11173, 1782 and 123279, respectively. In addition, the missing value of smoking and drinking status were 151,583 and 151583. Before propensity-score matching, there were differences between the two groups in several of the baseline variables (Table 1). We found that participants with hypertension generally had higher age, BMI, FPG, Scr, ALT, TC and TG. Participants with hypertension also had a higher percentage of male and higher rates of current smoker and drinker. With the use of one to one propensity-score matching, 28,946 hypertensive patients matched with 28,946 non-hypertensive subjects. After matching, the standardized differences were less than 10.0% for almost all variables, indicating that the propensity scores were well matched. Namely, there were only small differences in baseline characteristics between the two groups.

**Incidence rate of diabetes**

Table 2 showed the incidence of diabetes by hypertension exposure before and after propensity-score matching. Before propensity-score matching, a total of 4173 participants developed incident diabetes during follow-up. The morbidity rate in the overall population was 630.947 per 100,000 person-years, specifically, 1693.144 per 100,000 person-years in the hypertensive group and 460.303 per 100,000 person-years in the non-hypertensive group, respectively. The corresponding cumulative incidence of diabetes in the hypertension and non-hypertension group were 5.276(5.021-5.532) and 1.438(1.383-1.492), respectively. This crude difference in the morbidity rate between the two groups changed significantly after the PS-matching procedure (1521.335 per 100,000 person-years among the overall population, 1627.690 per 100,000 person-years among the hypertensive subjects and 1414.422 per 100,000 person-years among the non-hypertensive subjects). The corresponding cumulative incidence in the hypertension and non-hypertension group were 5.072(4.819-5.324) and 4.384(4.148-4.620), respectively. Besides, we assigned participants into subgroup based on propensity score tertile. In comparison with those in a low propensity score level, participants with an increased propensity score level had a higher cumulative incidence in the original cohort (p for trend＜0.00001 ) . The correlation still exists in the propensity-score matching cohort (p for trend＜0.00001 ).
Kaplan–Meier analysis demonstrated that participants with hypertension had a higher incidence of diabetes than those without hypertension in the original cohort. (log-rank test; \( P < 0.0001 \); Fig. 2). After propensity-score matching, the difference of morbidity rate between the two groups reduced significantly. In addition, there was a significant higher incidence of diabetes in the population with high propensity score, especially in the propensity-score matching cohort (Fig. 3).

**Association between hypertension and incident diabetes**

We used cox proportional hazard regression model to evaluate the associations between hypertension and incident diabetes in the propensity-score–matched cohort. We simultaneously showed the results from unadjusted, minimally adjusted analysis, fully adjusted analysis and propensity-score adjusted analysis. (Table 3) In crude model, hypertension had a significant correlation with incident diabetes (HR=1.140, 95% confidence interval (CI): 1.058-1.229, \( P=0.00063 \)). That is, the risk of developing diabetes increased by 14.0% among hypertensive participants than those without hypertension. In minimally adjusted model (adjusted age, gender, BMI, family history of diabetes, smoking and drinking status), the result did not have obvious changes (HR: 1.147, 95%CI: 1.064-1.237, \( P=0.00034 \)). After adjusting for the full covariates (age, gender, BMI, FPG, TC, TG, HDL-C, LDL-C, ALT, AST, Scr, family history of diabetes, smoking and drinking status), we could also detect the connection (HR=1.131, 95%CI: 1.049-1.220, \( P=0.00143 \)). In other words, compared to the non-hypertensive group in the full model, the risk of incident diabetes increased by 13.1% in the hypertensive group. In the propensity-score adjusted model, this correlation still exists, and the risk of developing diabetes increased by 15.4% in the population with hypertension (HR=1.154, 95%CI:1.070-1.244, \( P=0.00019 \)).

**Subgroup analysis**

We used a subgroup analysis to detect the effect of potential confounders which may affect the relationship between hypertension and incident diabetes. We treated age, BMI, FPG, Scr, ALT, TC, TG as the stratification variables to evaluate the trend of effect sizes in these variables. Table 4 showed that none of the interactions were observed based on our priori specification. The analysis revealed that the variables listed above will not affect the association between hypertension and incident
diabetes after propensity-score matching. However, we detected the interaction based on propensity score tertile (Fig.4). Specifically, with reference to the non-hypertensive population with the low propensity score level, the hazard ratios of low, medium and high propensity score level in the hypertensive population were 1.231 (0.870, 1.742), 3.399 (2.529, 4.568) and 3.610 (2.604, 5.005), respectively. Thus, there was a stronger association between hypertension and incident diabetes in the population with high propensity score level.

**Sensitivity analysis**

We used inverse probability of treatment weights [IPTW] to generate a weighted cohort. To ensure the robustness of the results, we performed the cox proportional hazard regression model to assess the relationship between hypertension and incident diabetes in the original cohort and the weighted cohort, respectively. Table 5 simultaneously showed the unadjusted, minimally and fully adjusted models in these two cohorts. We found that hypertension was associated with the likelihood of developing diabetes in both the original cohort and the weighted cohort. Compared with the non-hypertensive group in the full model, the risk of diabetes in the hypertensive group increased by 11.7% in the original cohort (HR=1.117 [95%CI: 1.044-1.196], P= 0.00134) and 19.9% in the weighted cohort (HR=1.199 [95%CI: 1.149-1.250], P < 0.00001), respectively.

**Discussion**

The one to one propensity score-matched cohort study showed hypertension was related to a higher risk of developing diabetes after adjusting for the demographic and clinical covariates. In addition, hypertension was associated with a 13.1% increase in diabetes risk. Subgroup analysis helped us to better understand the relationship between hypertension and incident diabetes in different populations. We found a stronger association in the population with high propensity score level. In contrast, the weaker association between hypertension and incident diabetes were detected in the population with low propensity score level. The correlation also exists both in the original cohort and the weighted cohort.

Hypertension and diabetes share common risk factors and frequently coexist. However, there is no consensus on the association between high blood pressure and the risk of new-onset diabetes.
Meanwhile, few such studies have been conducted in the Chinese population. In a study based on a cohort of 4.1 million adults published in the Journal of the American College of Cardiology, every 20 mmHg higher systolic blood pressure (SBP) was associated with a 58% higher risk of type 2 diabetes mellitus (T2DM) (HR: 1.58; 95% CI: 1.56–1.59), whereas every 10 mmHg higher diastolic blood pressure (DBP) was associated with a 52% higher risk of new onset T2DM (HR: 1.52; 95% CI: 1.51–1.54) [31]. In the Korean genome and epidemiology study, after adjusting for some anthropometric factors, family history of diabetes and biochemical parameters, people with baseline hypertension were at higher risk of developing diabetes than normotensive population. Specifically, in the Grade 1 hypertension group (SBP/DBP 140–159/90–99 mmHg), people had a 26% increased risk of developing diabetes (HR 1.26; 95% CI, 1.04–1.54), in the Grade 2 and 3 hypertension group (SBP/DBP ≥ 160/100 mmHg), people increase their risk of diabetes by 60% (HR 1.60 ; 95% CI,1.30–1.96) [32]. In a population-based prospective cohort study among 10,038 participants in Korea, the researchers found that compared with subjects with normal baseline blood pressure, people with baseline hypertension had a 51% higher risk of developing diabetes [33]. To the best of our knowledge, antihypertensive drugs may associate with the risk of incident diabetes [34]. However, several studies demonstrated that the increased risk of developing diabetes in people with hypertension is due to hypertension itself, given that the increased risk of diabetes persist after adjusting for specific antihypertensive treatments [6, 13]. In contrast, other studies reached inconsistent results that there was no significant association between blood pressure and the risk of incident diabetes after adjusting for some covariates [35–37]. We analyzed these inconsistent findings, and we speculate that the reasons for the different results may be caused by the following factors: (1) the research population was different, including race, gender and age. (2) sample sizes in these studies varied widely. (3) these studies adjusted for different covariates which may affect the relationship between high blood pressure and diabetes risk. (4) The follow-up years varied greatly, affecting the incidence of incident diabetes. Our findings add to the existing literature, which supported the hypothesis that hypertension increased the risk of incident diabetes.

In the present study, the doubly robust estimation method in the propensity-score matched cohort
showed a significant association between hypertension and incident diabetes. Hypertension increased the risk of developing diabetes by 13.1%. The diabetes risk in our study was relatively lower than previous researches. The difference may be that we carried out a propensity-score matching analysis which minimized the effect of potential confounders, thus the results better showed the relationship between hypertension and diabetes in the real world. Besides, the covariates we adjusted were different. We adjusted more biochemical parameters, including FPG, TC, TG, HDL-C, LDL-C, ALT, AST and Scr. Evidence showed that those parameters were associated with hypertension and incident diabetes[38-40]. Furthermore, our research sample is larger (210,809) and they were from 32 sites and 11 cities in China, more representative of the Chinese population. Our results supported the adverse effect of hypertension on the occurrence of diabetes. A detailed understanding of hypertension as a potential risk factor for diabetes will help us better understand and communicate risks with patients and can lead to more personalized prevention and management protocols. And the propensity-score matching analysis has been mainly used for comparison of different treatment methods in the past[41, 42], our research is helpful for the promotion of propensity score methods in correlation studies.

It is still unclear whether there is direct causal relationship between high blood pressure and diabetes risk. However, there is a substantial overlap between hypertension and diabetes in etiology and disease mechanisms. The two diseases share common mediators, including obesity, endothelial dysfunction, inflammation, oxidative stress and insulin resistance [9]. In hypertensive people, the presence of obesity leads to overactivation of the sympathetic nervous and renin-angiotensin-aldosterone systems, as well as proinflammatory/pro-oxidative mechanisms, which are related to diabetes [43, 44]. As we know, hypertension could induce endothelial dysfunction [45]. The Framingham Offspring Study revealed that some plasma markers of endothelial dysfunction (such as plasminogen activator inhibitor-1 antigen and von Willebrand factor antigen) were associated with an increased risk of new onset diabetes independent of other diabetes risk factors including obesity, insulin resistance, and inflammation[46]. Besides, endothelial dysfunction could inhibit NO synthase and reduce NO bioavailability which is a crucial factor for the vasodilator action [47]. Therefore,
endothelial dysfunction reduces vasodilation, increases vascular resistance, thus, limit insulin and glucose delivery in the sensitive tissues (ie, skeletal muscle, liver, and adipose tissue) and blunts insulin-stimulated glucose uptake [9, 48]. There was a low-grade inflammatory reaction in patients with diabetes and hypertension [49, 50]. High blood pressure increases the level of inflammatory markers, such as C-reactive protein, interleukin 6 and adhesion molecules which related to the insulin signaling pathway and β-cell function and further lead to the incident diabetes [51, 52]. In addition, oxidative stress-related cytokines (interleukin-1, interleukin-6 and tumor necrosis factor-a) could modify glucose metabolism which may contribute to the pathophysiology of diabetes mellitus [53]. Our study has some strengths. To our knowledge, this is the first propensity score-matched cohort study to explore the risk of hypertension for incident diabetes. Propensity score matching balances the distribution of measured baseline covariates to minimize measured confounding factors. Compared with other statistical methods, since the effectiveness of propensity score matching is calculated based on the average difference between matched individuals, it does not need to make any assumptions about the correlation between the dependent and explanatory variables. Meanwhile, we evaluate the relationship among comparable individuals so that our results were relatively more convincing. Furthermore, as the study was an observational study which was susceptible to potential confusion, we also used strict statistical adjustment to further minimize the effect of residual confounders. So far, the propensity score adjustment model we conducted are rarely used. Additionally, we performed the effect modifier factor analysis to explore other potential risk of the associations between hypertension and incident diabetes in different subgroups. It is worth mentioning that we conducted a set of sensitivity analysis to ensure the reliability of the results, especially we used the inverse probability of treatment weights(IPTW) to generate a weighted cohort and further detected the association between hypertension and diabetes in the weighted cohort. Moreover, our sample size was relatively large compared to most previous similar studies, and the participants came from multiple centers. Conversely, some limitations of our study should be noted. First of all, as the study participants were Chinese, studies of other races are needed in order to confirm that our findings can be extended to
other populations. Second, we cannot obtain data on other diabetes risk factors from the electronic
database, such as medical history and other diseases. Third, the researchers did not conduct 2-hour
oral glucose tolerance test. A study showed that just 55% of diabetic patients were diagnosed by
testing fasting blood glucose alone in Asians [54]. Thus, the diagnostic criteria for diabetes in our
study may underestimate the true prevalence of diabetes. However, 2-hour oral glucose tolerance
test for all participants were not feasible in a such large cohort. Fourth, propensity score matching
can ensure balance of measured confounding factors but not unmeasured confounding factors. And
although propensity score matching was performed based on baseline covariates to minimize
measured confounders, it does not ensure that all measured baseline characteristics will match, such
as the gender. But we reduced the caliper width to 0.005 to minimize the interference of gender on
the results. Fifth, this is an observational study that provides an inference of association rather than
establishes a causal relationship between hypertension and diabetes. Therefore, our findings need to
be interpreted cautiously and need to be further validated by prospective research.

Conclusion
After propensity-score matching, hypertension was associated with a 13.1% increase in the risk of
developing diabetes in Chinese adults after adjusting for some demographic and clinical covariates. In
addition, there was a stronger association in the population with high propensity score level.
Compared to non-hypertensive participants with low propensity score, the risk of incident diabetes
increased by 2.6 times among hypertensive patients with high propensity score. Blood pressure is a
potential modifiable risk factor in terms of interventions aiming to prevent incident diabetes.

Abbreviations
BMI, Body mass index; FPG; Fasting plasma glucose; Scr, Serum creatinine; TC, Total cholesterol; TG,
Triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipid cholesterol; ALT,
Alanine aminotransferase; AST, Aspartate aminotransferase; T2DM, type 2 diabetes mellitus; DM,
diabetes mellitus; SD, Standardized difference; HR, hazard ratios; CI, Confidence intervals; Ref,
reference; PS, propensity score; IPTW, inverse probability of treatment weights; HBP, hypertension;
NHBP, non-hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Declarations
Authors’ contributions
Yang Wu and Haofei Hu conceived and designed the research, drafted the manuscript. Jinlin Cai and Runtian Chen did statistical analysis. Xin Zuo and Heng Cheng took part in the discussion. Dewen Yan revised the manuscript. All authors read and approved the final manuscript.

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Not applicable

Competing interests
The authors declare that they have no competing interests

Availability of data and materials
Data can be downloaded from ‘DATADRYAD’ database (www.Datadryad.org).

Consent for publication
Not applicable.

Ethics approval and consent to participate
The previously published article [20] has stated the study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all Participants.

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Tables

Table 1 Baseline characteristics before and after propensity-score matching.

| Characteristic | Hypertension | Before Matching | SD(100%) | Hypertension | After Matching |
|----------------|--------------|----------------|----------|--------------|---------------|
| Participants   | 29,377       | 182,432        | 28,946   | 28,946       |
| Age (years)    | ±14.84       | 40.58 ± 11.56  | 51.21 ± 14.65 | 52.16 ± 13.54 |
| Gender         |              |                | 47.7     |              |
| Male           | 20410(69.48%) | 95702(52.46%)  | 20048 (69.26%) | 18293 (63.20%) |
| Female         | 8967(30.52%)  | 86730(47.54%)  | 8898 (30.74%) | 10653 (36.80%) |
| BMI (Kg/m²)    | 25.29 ± 3.42 | 22.91 ± 3.21   | 71.9     | 25.23 ± 3.37 | 24.95 ± 3.39 |
| FPG (mmol/L)   | 5.15 ± 0.67  | 4.88 ± 0.59    | 42.6     | 5.14 ± 0.66  | 5.124 ± 0.63 |
| Scr (mmol/L)   | 73.93 ± 17.27| 69.44 ± 14.96  | 27.8     | 73.83 ± 17.25| 72.76 ± 16.49 |
| ALT (U/L)      | 17.50 (12.50-26.10) | 27.2 |
| AST (U/L)      |              | 26.8           |          |              |
| Low            | 2548 (8.67%) | 26851 (14.72%) | 2520 (8.71%) | 3014 (10.41%) |
| Medium         | 4025 (13.70%)| 25371 (13.91%) | 3975 (13.73%) | 4066 (14.05%) |
| High           | 6177 (21.03%)| 23558 (12.91%) | 6056 (20.92%) | 5391 (18.62%) |
| Not recorded   | 16627 (56.60%)| 106652 (58.46%)| 16395 (56.64%)| 16475 (56.92%)|
| TC (mmol/L)    | 5.00 ± 0.93  | 4.66 ± 0.87    | 37.0     | 4.99 ± 0.93  | 4.98 ± 0.96 |
| TG (mmol/L)    | 1.43 (1.00-2.11) | 1.03(0.71-1.50)| 43.8     | 1.43 (1.00-2.10)| 1.300(0.90-1.97) |
| HDL-C (mmol/L) |              | 13.4           |          |              |
| Low            | 6556 (22.32%)| 32300 (17.71%) | 6464 (22.33%) | 6384 (22.06%) |
| Medium         | 5628 (19.16%)| 32613 (17.88%) | 5540 (19.14%) | 5334 (18.43%) |
| High           | 5369 (18.28%)| 34787 (19.07%) | 5288 (18.27%) | 5638 (19.48%) |
| Not recorded   | 11824 (40.25%)| 82732 (45.35%) | 11654 (40.26%)| 11590 (40.04%)|
| LDL-C (mmol/L) |              | 24.4           |          |              |
| Low            | 4269 (14.53%)| 34785 (19.07%) | 4211 (14.55%) | 4493 (15.52%) |
| Medium         | 5810 (19.78%)| 33624 (18.43%) | 5714 (19.74%) | 5677 (19.61%) |
| High           | 7836 (26.67%)| 32070 (17.58%) | 7708 (26.63%) | 7766 (26.83%) |
| Smoking status          | Current smoker | Ever smoker | Never smoker | Not recorded |
|-------------------------|----------------|-------------|--------------|--------------|
|                         | 1974 (6.82%)   | 363 (1.25%) | 5347 (18.47%)| 21597 (74.52%)|
| Current smoker          | 1984 (6.75%)   | 364 (1.24%) | 5432 (18.49%)| 21597 (74.52%)|
| Ever smoker             | 10090 (5.53%)  | 2195 (1.20%)| 40161 (22.01%)| 129986 (71.25%)|
| Never smoker            | 11462 (39.02%) | 81953 (44.92%)| 11313 (39.08%)| 129986 (71.25%)|
| Not recorded            | 11010 (38.04%) | 1677 (5.79%) | 4819 (16.65%) | 22192 (76.67%) |

| Drinking status         | Current drinker | Ever drinker | Never drinker | Not recorded |
|-------------------------|-----------------|-------------|---------------|--------------|
| Current drinker         | 332 (1.15%)     | 1209 (4.18%)| 6143 (21.22%) | 21597 (74.52%)|
| Ever drinker            | 1016 (0.56%)    | 7739 (4.24%)| 43691 (23.95%)| 129986 (71.25%)|
| Never drinker           | 335 (1.14%)     | 1217 (4.14%)| 6228 (21.20%) | 21597 (74.52%)|
| Not recorded            | 229 (0.79%)     | 1010 (3.49%)| 5515 (19.05%) | 22192 (76.67%) |

| Family history of diabetes | NO  | YES |
|-----------------------------|-----|-----|
|                             | 28934 (98.49%) | 443 (1.51%) |
|                             | 178532 (97.86%)| 3900 (2.14%) |

Values are n (%) or mean ± SD

SD, Standardized differences; BMI, Body mass index; FPG, Fasting plasma glucose; Scr, Serum creatinine; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; TC, Total cholesterol; TG, Triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipid cholesterol.

Table 2 Incidence rate of incident diabetes before and after propensity-score matching.
| Variable                  | Participant\(s(n)\) | DM events\(n)\) | Cumulative incidence (95% CI) | Per person-year | 100,000 |
|--------------------------|----------------------|-----------------|------------------------------|----------------|---------|
| **Before Matching**      |                      |                 |                              |                |         |
| Total                    | 211,809              | 4173            | 1.970(1.911-2.029)           | 630.947        |         |
| Hypertension             | 29,377               | 1550            | 5.276(5.021-5.532)           | 1,693.144      |         |
| Non-hypertension         | 182,432              | 2623            | 1.438(1.383-1.492)           | 460.303        |         |
| PS Tertile               |                      |                 |                              |                |         |
| Low                      | 70,603               | 75              | 0.106(0.082-0.130)           | 34.009         |         |
| Medium                   | 70,603               | 393             | 0.557(0.502-0.612)           | 177.986        |         |
| High                     | 70,603               | 3705            | 5.248(5.083-5.412)           | 1,683.684      |         |
| **After Matching**       |                      |                 |                              |                |         |
| Total                    | 57,892               | 2737            | 4.728(4.555-4.901)           | 1,521.335      |         |
| Hypertension             | 28,946               | 1468            | 5.072(4.819-5.324)           | 1,627.690      |         |
| Non-hypertension         | 28,946               | 1269            | 4.384(4.148-4.620)           | 1,414.422      |         |
| PS Tertile               |                      |                 |                              |                |         |
| Low                      | 19,297               | 131             | 0.679(0.563-0.795)           | 218.835        |         |
| Medium                   | 19,297               | 693             | 3.591(3.329-3.854)           | 1,153.609      |         |
| High                     | 19,298               | 1913            | 9.913(9.491-10.335)          | 3,189.768      |         |

CI, confidence interval; DM, diabetes mellitus; PS, propensity score.

Table 3 Relationship hypertension and incident diabetes in different models.

| Variable          | Non-adjusted(HR,95%CI,P) | Model I (HR,95%CI,P) | Model II (HR,95%CI,P) | M     |
|-------------------|---------------------------|----------------------|-----------------------|-------|
|                   | Ref.                      | Ref.                 | Ref.                  |       |
| Non-hypertension  |                          |                      |                       |       |
| Hypertension      | 1.140 (1.058, 1.229)      | 1.147 (1.064, 1.237) | 1.131 (1.049, 1.220)  | 0.0063|
|                   | 0.00063                   | 0.00034              | 0.00143               | 0.01  |

Crude model: we did not adjust other covariates.

Model I: we adjust age, gender, BMI, family history of diabetes, smoking and drinking status.

Model II: we adjust age, gender, BMI, FPG, TC, TG, HDL-C, LDL-C, ALT, AST, Scr, family history of diabetes, smoking and drinking status.

Model III: we adjust propensity score.

HR, Hazard ratios; CI, Confidence interval; Ref, Reference

Table 4 Effect size of hypertension on incident diabetes in prespecified and exploratory
### Table 5 Relationship hypertension and incident diabetes in different models of the original and the weighted cohort.

#### A

| Variable        | Non-adjusted | Model I (HR,95%CI,P) | Model II (HR,95%CI,P) |
|-----------------|--------------|----------------------|-----------------------|
| Non-hypertension| Ref.         | Ref.                 | Ref.                  |
| Hypertension    | 3.745 (3.517, 3.988) | 1.388 (1.296, 1.486) | 1.117 (1.044, 1.196) |
|                 | <0.00001     | <0.00001             | 0.00134               |

#### B

| Variable        | Non-adjusted | Model I (HR,95%CI,P) | Model II (HR,95%CI,P) |
|-----------------|--------------|----------------------|-----------------------|
| Non-hypertension| Ref.         | Ref.                 | Ref.                  |
| Hypertension    | 1.152 (1.105, 1.201) | 1.192 (1.143, 1.243) | 1.199 (1.149, 1.250) |
|                 | <0.00001     | <0.00001             | <0.00001              |

A In the original cohort; B In the weighted cohort.

Note 1: Above models adjusted for age, gender, BMI, FPG, TC, TG, HDL-C, LDL-C, ALT, AST, Scr, family history of diabetes, smoking and drinking status.

Note 2: In each case, the model is not adjusted for the stratification variable.

BMI, Body mass index; FPG, Fasting plasma glucose; Scr, Serum creatinine; ALT, Alanine aminotransferase; TC, Total cholesterol; TG, Triglyceride; HR, Hazard ratios; CI, Confidence interval.
Crude model: we did not adjust other covariates.

Model I: we adjust age, gender, BMI, family history of diabetes, smoking and drinking status.

Model II: we adjust age, gender, BMI, FPG, TC, TG, HDL-C, LDL-C, ALT, AST, Scr, family history of diabetes, smoking and drinking status.

HR, Hazard ratios; CI, Confidence interval; Ref, Reference

Figures
According to the data source article:

685,277 Chinese participants ≥20 years old with at least two visits in 2010 - 2016

- 473,444 Were excluded
  - 103,946 Had available weight and height measurements
    - 1 Had no available information on gender
    - 152 Had extreme BMI values (<15 kg/m² or >55 kg/m²)
  - 31,370 Had no available fasting plasma glucose value
  - 324,233 Had visit intervals less than 2 years
  - 7,112 Diagnosed with diabetes at baseline
  - 6,630 Undefined diabetes status at follow-up

211,833 Were included in the original study.

According to our studying:

- 24 Had incomplete blood pressure

211,809 Were included in study analysis
- 29,377 With hypertension
- 182,432 Without hypertension

57,892 Were included in propensity-score-matched analysis
- 28,946 With hypertension
- 28,946 Without hypertension
Figure 1

Study Population
According to the data source article:

- 685,277 Chinese participants ≥20 years old with at least two visits in 2010 - 2016

  - 473,444 Were excluded
  - 103,946 Had available weight and height measurements
    - 1 Had no available information on gender
    - 152 Had extreme BMI values (<15 kg/m² or >55 kg/m²)
    - 31,370 Had no available fasting plasma glucose value
    - 324,233 Had visit intervals less than 2 years
    - 7,112 Diagnosed with diabetes at baseline
    - 6,650 Undefined diabetes status at follow-up

  - 211,833 Were included in the original study.

According to our studying:

  - 24 Had incomplete blood pressure

  - 211,809 Were included in study analysis
    - 29,377 With hypertension
    - 182,432 Without hypertension

  - 57,892 Were included in propensity-score-matched analysis
    - 28,946 With hypertension
    - 28,946 Without hypertension
Figure 1
Study Population

Figure 2
Kaplan–Meier event-free survival curve based on hypertension and non-hypertension. Fig. 2a Kaplan–Meier analysis of incident diabetes based on hypertension (HBP) and non-hypertension (NHB) in the original cohort (log-rank, P < 0.0001). Fig. 2b Kaplan–Meier analysis of incident diabetes based on hypertension (HBP) and non-hypertension (NHB) in the propensity-score matching cohort (log-rank, P < 0.0001).
Figure 2

Kaplan–Meier event-free survival curve based on hypertension and non-hypertension. Fig. 2a Kaplan–Meier analysis of incident diabetes based on hypertension (HBP) and non-hypertension (NHBP) in the original cohort (log-rank, P < 0.0001). Fig. 2b Kaplan–Meier analysis of incident diabetes based on hypertension (HBP) and non-hypertension (NHBP) in the propensity-score matching cohort (log-rank, P < 0.0001).
Figure 3

Kaplan–Meier event-free survival curve based on propensity score tertile. Fig. 3a Kaplan–Meier analysis of incident diabetes based on propensity score (PS) tertile in the original cohort (log-rank, P < 0.0001). Fig. 3b Kaplan–Meier analysis of incident diabetes based on propensity score(PS) tertile in the propensity-score matching cohort (log-rank, P < 0.0001).
Figure 4

Three-dimensional bar graph for association between hypertension and non-hypertension with diabetes based on propensity score. A three-dimensional bar graph for association between hypertension and non-hypertension with diabetes based on propensity score in the propensity-score matching cohort. PS, Propensity-score; HR, Hazard ratios; CI, Confidence interval; Ref, reference.
Figure 4

Three-dimensional bar graph for association between hypertension and non-hypertension with diabetes based on propensity score. A three-dimensional bar graph for association between hypertension and non-hypertension with diabetes based on propensity score in the propensity-score matching cohort. PS, Propensity-score; HR, Hazard ratios; CI, Confidence interval; Ref, reference.