# Prevalence, Awareness, and Treatment of Isolated Diastolic Hypertension: Insights From the China PEACE Million Persons Project 

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Background-Characterizing and assessing the prevalence, awareness, and treatment patterns of patients with isolated diastolic hypertension (IDH) can generate new knowledge and highlight opportunities to improve their care.

Methods and Results-We used data from the China PEACE (Patient-centered Evaluative Assessment of Cardiac Events) Million Persons Project, which screened 2351035 participants aged 35 to 75 years between 2014 and 2018. IDH was defined as systolic and diastolic blood pressure of $<140$ and $\geq 90 \mathrm{~mm} \mathrm{Hg}$; awareness as self-reported diagnosis of hypertension; and treatment as current use of antihypertensive medications. Of the 2310184 participants included (mean age 55.7 years; $59.5 \%$ women); $73279(3.2 \%)$ had IDH, of whom $63112(86.1 \%)$ were untreated, and only $6512(10.3 \%)$ of the untreated were aware of having hypertension. When compared with normotensives, participants who were $<60$ years, men, at least college educated, had body mass index of $>28 \mathrm{~kg} / \mathrm{m}^{2}$, consumed alcohol, had diabetes mellitus, and prior cardiovascular events were more likely to have IDH (all $P<0.01$ ). Among those with IDH, higher likelihood of awareness was associated with increased age, women, college education, body mass index of $>28 \mathrm{~kg} / \mathrm{m}^{2}$, higher income, diabetes mellitus, prior cardiovascular events, and Central or Eastern region (all $P<0.05$ ). Most treated participants with IDH reported taking only 1 class of antihypertensive medication.

Conclusions-IDH affects a substantial number of people in China, however, few are aware of having hypertension and most treated participants are poorly managed, which suggests the need to improve the diagnosis and treatment of people with IDH. (J Am Heart Assoc. 2019;8:e012954. DOI: 10.1161/JAHA.119.012954.)

Key Words: awareness • hypertension subtypes • isolated diastolic hypertension • prevalence • treatment

Isolated diastolic hypertension (IDH), whether in treated or untreated patients, is an uncommon type of hypertension accounting for $<20 \%$ of hypertension cases. ${ }^{1-4}$ Nevertheless,

IDH is independently associated with an increased risk of stroke, heart disease, and the other sequelae of hypertension. ${ }^{5-14}$ However, the most recent US, Chinese, and

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## Clinical Perspective

## What Is New?

- This is one of the largest population-based studies to evaluate the characteristics, prevalence, awareness, and treatment patterns of individuals with isolated diastolic hypertension (IDH) in China, allowing us to draw robust conclusions across diverse subgroups.
- We found that IDH affected a large number of adults in China, and these patients had some unique characteristics as compared with people without hypertension as well as those with other types of hypertension.
- Awareness of hypertension was significantly lower among people with IDH as compared with other types of hypertension, and most participants with IDH despite treatment had scope for further intensification of therapy.


## What Are the Clinical Implications?

- Given that diastolic hypertension can independently influence the risk of adverse cardiovascular events, identifying characteristics that may be associated with IDH and understanding the current awareness and treatment patterns among those with IDH can help identify the patients at increased cardiovascular risk and highlight opportunities to improve their care.
- Focusing on people with IDH and improving their diagnosis and treatment, may be critical to mitigate the burden of hypertension, especially in the young- and middle-aged population.

European high blood pressure guidelines do not specifically address IDH as a distinct phenotype or provide any specific guidance for its management. ${ }^{15-17}$

Although many studies have focused on patient characteristics, knowledge, and treatment, patients with IDH constitute a small subset of all patients with hypertension, and have traditionally been included within the total population of hypertensive patients, ${ }^{1,18-20}$ even though they may have unique features. ${ }^{20,21}$ Given its low prevalence, a large sample size would be required to fully capture the range of attributes of individuals with IDH across diverse population subgroups, and draw robust conclusions with high precision. Characterizing these patients specifically and assessing their awareness and treatment patterns can generate new knowledge about this distinct subtype of hypertension. This information will not only expand our knowledge about the IDH phenotype, but could also equip us to identify targets for improvement of care.

Accordingly, we sought to identify and study patients with IDH, whether treated or untreated, using data from the China PEACE (Patient-centered Evaluative Assessment of Cardiac Events) Million Persons Project, a large-scale population-
based screening project which was initiated with the aim of providing detailed information on smaller subgroups of patients who have traditionally been hard to identify in the population. We sought to describe the characteristics and prevalence of individuals with IDH across diverse population subgroups among both untreated and treated hypertensives; assess awareness of having hypertension among untreated IDH participants; assess the number and classes of medications used by treated participants with IDH; and identify the associations between individual characteristics with prevalence of, and awareness among those with IDH. Although some of the treated patients may be individuals who initially had systolic and diastolic hypertension, but with medications have only diastolic hypertension, this does represent the spectrum of patients who would be seen in practice with IDH, either as a de novo condition or as inadequately treated diastolic hypertension. Moreover, the treatment rates in China are sufficiently low that the population with IDH largely represents those with the de novo condition.

## Methods

The China PEACE Million Persons Project is a major national program, and as the government policy stipulates, it is not permissible for the researchers to make the raw data publicly available at this time.

## Study Design and Population

Details of the China PEACE Million Persons Project have been described previously. ${ }^{22,23}$ Briefly, we used a convenience sampling strategy to select 184 sites (111 rural counties and 73 urban districts) from all 31 provinces in mainland China. People were encouraged to participate in the project through publicity campaigns in the newspaper and on the television. Of the 2351035 participants aged 35 to 75 years enrolled at these sites between September 15, 2014 and May 29, 2018, we excluded 14904 participants because of missing or extreme blood pressure values (systolic blood pressure [SBP] $<70$ or $>270 \mathrm{~mm} \mathrm{Hg}$; diastolic blood pressure [DBP] $<30$ or $>150 \mathrm{~mm} \mathrm{Hg}$ ), 142 participants due to missing or extreme body mass index values (<10 or $>50 \mathrm{~kg} / \mathrm{m}^{2}$ ), and 25805 participants due to missing data on covariates, including geographical region, education, occupation, marital status, household income, and alcohol use (Figure S1).

## Blood Pressure Collection and Classification

For every participant, blood pressure was measured twice at enrollment, at an interval of 1 minute, on their right upper arm using an electronic blood pressure monitor (Omron HEM-7430;

Omron Corporation, Kyoto, Japan) after 5 minutes of rest in the seated position. The values of both the readings as well as their mean were recorded. If the difference between the 2 SBP measurements was $>10 \mathrm{~mm} \mathrm{Hg}$, a third blood pressure reading was taken and the mean SBP and DBP was calculated using the last 2 readings in such cases. The mean SBP and DBP were used for all calculations. Additionally, information was collected on any prescription drugs taken by the participants in the past 2 weeks for antiplatelet, blood pressure, lipid, or glucose control during an in-person interview.

Since this study was done in a Chinese cohort, we used the Chinese Guidelines for the Management of Hypertension to define hypertension and classify patients with hypertension into different hypertension subtypes. ${ }^{15}$ Participants were considered to have hypertension if they had an average SBP of at least 140 mm Hg or an average DBP of at least 90 mm Hg or self-reported use of an antihypertensive medication in the past 2 weeks. IDH was defined as an average SBP of $<140 \mathrm{~mm} \mathrm{Hg}$ but a DBP of at least 90 mm Hg . We defined IDH based on the participant's SBP and DBP at the time of screening, and the IDH group included both untreated IDH participants and those with IDH despite antihypertensive medication. The "other hypertensive subtypes" group included all hypertensives, except those with IDH, including participants with isolated systolic hypertension (ISH; SBP $\geq 140 \mathrm{~mm} \mathrm{Hg}$ and DBP $<90 \mathrm{~mm} \mathrm{Hg}$ ), combined systolic-diastolic hypertension (SDH; SBP $\geq 140 \mathrm{~mm} \mathrm{Hg}$ and DBP $\geq 90 \mathrm{~mm} \mathrm{Hg}$ ), and controlled hypertensives (participants who reported having a history of hypertension or taking antihypertensive medications but had an SBP $<140 \mathrm{~mm} \mathrm{Hg}$ and a DBP $<90 \mathrm{~mm} \mathrm{Hg}$ ). Participants who did not have a history of hypertension or antihypertensive medication use and who had an SBP $<140 \mathrm{~mm} \mathrm{Hg}$ and a DBP $<90 \mathrm{~mm} \mathrm{Hg}$ were defined as normotensives.

Participants were considered to be aware of their hypertension if they responded "yes" to the question "Have you ever been diagnosed with hypertension?". Participants were considered to be receiving treatment for hypertension if they reported using antihypertensive medication (Western or traditional Chinese medication) currently or within the last 2 weeks.

## Independent Variables

Information on the participants' sociodemographic characteristics, health behaviors, medical history, and cardiovascular risk factors was recorded during in-person interviews as described previously. ${ }^{22}$ Height and weight were collected using standard protocols, and body mass index (BMI) was calculated by dividing the weight in kilograms by the square of height in meters. Obesity was defined as a BMI of at least $28 \mathrm{~kg} / \mathrm{m}^{2}$, which was in accordance with the recommendations of the Working Group on Obesity in China. ${ }^{24}$

We also formed diverse, mutually exclusive subgroups, to assess if some population subgroups had higher or lower rates of prevalence and awareness compared with the average rates of the total population. These subgroups were defined a priori by all possible combinations of 10 characteristics: age group (35-44, 45-54, 55-64, and 65-75 years), sex (men, women), geographic region (Western, Central, Eastern), urbanity (urban, rural), occupation (farmer, nonfarmer), annual household income ( $<10000,10000-$ 50 000, and >50 000 Yuan/year), education (primary school and below, middle school, high school, college and above), prior cardiovascular events (myocardial infarction or stroke; yes versus no), current smoker (yes versus no), and diabetes mellitus (yes versus no).

## Statistical Analysis

We assessed the prevalence of IDH among the overall study population and among hypertensive participants (both overall and among untreated and treated hypertensives) and compared the prevalence of IDH with other hypertension subtypes across different age groups. We also calculated age- and sexstandardized prevalence of IDH at the national level, standardizing against data from all 31 provinces in the 2010 Chinese Census. We then described the characteristics of participants with IDH and compared these with normotensive as well as with other hypertensive subgroups, and described the characteristics of untreated and treated participants with IDH separately. Next, we assessed the awareness of hypertension among untreated IDH participants across different population characteristics; and compared the awareness rates of untreated IDH participants with those of untreated ISH and SDH participants across different age groups. We assessed awareness only among untreated IDH participants as some treated participants with IDH may have adequately lowered their DBP and moved to the controlled hypertensive group, thus underestimating awareness rates among those having IDH despite treatment. The statistical significance of the differences between groups was assessed using Pearson Chisquared test.

We retained 1198 mutually exclusive subgroups of at least 200 participants each, which included $84.1 \%$ of the participants with IDH, and calculated the prevalence of IDH among all study participants and the awareness rates among untreated IDH participants. We also used histograms to show the rate distributions, and repeated the analysis by restricting to 731 subgroups containing at least 500 participants each (which included $77.6 \%$ of the participants with IDH).

Among participants who had IDH despite treatment, we assessed the number and class of medications reported by them. Medication usage was divided into 6 medication classes defined by the 2010 Chinese guidelines for the

Table 1. Baseline Characteristics of Participants With Isolated Diastolic Hypertension Compared With Normotensives and Other Hypertensives

| Characteristics, n (\%) | Normotensives | Isolated Diastolic Hypertension | Other Hypertensives |
| :---: | :---: | :---: | :---: |
| n (\%) | 1286404 (55.7\%) | 73279 (3.2\%) | 950501 (41.1\%) |
| Age, y |  |  |  |
| 35 to 39 | 91686 (7.1\%) | 4603 (6.3\%) | 14056 (1.5\%) |
| 40 to 44 | 181177 (14.1\%) | 10538 (14.4\%) | 45006 (4.7\%) |
| 45 to 49 | 229912 (17.9\%) | 15328 (20.9\%) | 91801 (9.7\%) |
| 50 to 54 | 235412 (18.3\%) | 16479 (22.5\%) | 149641 (15.7\%) |
| 55 to 59 | 170190 (13.2\%) | 10082 (13.8\%) | 147992 (15.6\%) |
| 60 to 64 | 182963 (14.2\%) | 8910 (12.2\%) | 205833 (21.7\%) |
| 65 to 69 | 123906 (9.6\%) | 4985 (6.8\%) | 176376 (18.6\%) |
| 70 to 75 | 71158 (5.5\%) | 2354 (3.2\%) | 119796 (12.6\%) |
| Sex |  |  |  |
| Men | 501100 (39.0\%) | 42360 (57.8\%) | 392040 (41.2\%) |
| Women | 785304 (61.0\%) | 30919 (42.2\%) | 558461 (58.8\%) |
| Urbanity |  |  |  |
| Urban | 517420 (40.2\%) | 26309 (35.9\%) | 345720 (36.4\%) |
| Rural | 768984 (59.8\%) | 46970 (64.1\%) | 604781 (63.6\%) |
| Region |  |  |  |
| Eastern | 416104 (32.3\%) | 23902 (32.6\%) | 352929 (37.1\%) |
| Western | 494433 (38.4\%) | 28156 (38.4\%) | 308351 (32.4\%) |
| Central | 375867 (29.2\%) | 21221 (29.0\%) | 289221 (30.4\%) |
| Education |  |  |  |
| Primary school or lower | 512301 (39.8\%) | 26212 (35.8\%) | 473213 (49.8\%) |
| Middle school | 432275 (33.6\%) | 25959 (35.4\%) | 288724 (30.4\%) |
| High school | 211349 (16.4\%) | 12368 (16.9\%) | 126468 (13.3\%) |
| College or above | 111560 (8.7\%) | 7602 (10.4\%) | 49895 (5.2\%) |
| Unknown* | 18919 (1.5\%) | 1138 (1.6\%) | 12201 (1.3\%) |
| Employment |  |  |  |
| Employed | 963858 (74.9\%) | 57582 (78.6\%) | 649247 (68.3\%) |
| Unemployed | 17294 (1.3\%) | 1345 (1.8\%) | 11630 (1.2\%) |
| Retired | 185763 (14.4\%) | 8342 (11.4\%) | 191626 (20.2\%) |
| Housework | 95722 (7.4\%) | 4470 (6.1\%) | 83403 (8.8\%) |
| Unknown* | 23767 (1.8\%) | 1540 (2.1\%) | 14595 (1.5\%) |
| Occupation |  |  |  |
| Farmer | 602369 (46.8\%) | 34562 (47.2\%) | 492275 (51.8\%) |
| Non-farmer | 660268 (51.3\%) | 37177 (50.7\%) | 443631 (46.7\%) |
| Unknown* | 23767 (1.8\%) | 1540 (2.1\%) | 14595 (1.5\%) |
| Household income, Yuan/y |  |  |  |
| $<10000$ | 256630 (19.9\%) | 14307 (19.5\%) | 216481 (22.8\%) |
| 10000 to 50000 | 711228 (55.3\%) | 40359 (55.1\%) | 521951 (54.9\%) |
| $>50000$ | 199441 (15.5\%) | 11908 (16.3\%) | 128457 (13.5\%) |
| Unknown* | 119105 (9.3\%) | 6705 (9.1\%) | 83612 (8.8\%) |

Continued

Table 1. Continued

| Characteristics, n (\%) | Normotensives | Isolated Diastolic Hypertension | Other Hypertensives |
| :---: | :---: | :---: | :---: |
| Marital status |  |  |  |
| Married | 1208737 (94.0\%) | 69159 (94.4\%) | 869211 (91.4\%) |
| Widowed, separated, divorced, single | 61396 (4.8\%) | 3192 (4.4\%) | 70389 (7.4\%) |
| Unknown* | 16271 (1.3\%) | 928 (1.3\%) | 10901 (1.1\%) |
| Health insurance status |  |  |  |
| Insured | 1258190 (97.8\%) | 71580 (97.7\%) | 932199 (98.1\%) |
| Uninsured | 8388 (0.7\%) | 502 (0.7\%) | 4890 (0.5\%) |
| Unknown* | 19826 (1.5\%) | 1197 (1.6\%) | 13412 (1.4\%) |
| Medical history |  |  |  |
| Myocardial infarction | 6281 (0.5\%) | 496 (0.7\%) | 10447 (1.1\%) |
| Stroke | 15628 (1.2\%) | 1614 (2.2\%) | 38626 (4.1\%) |
| Diabetes mellitus | 51410 (4.0\%) | 3499 (4.8\%) | 93329 (9.8\%) |
| Cardiovascular disease risk factor |  |  |  |
| Current smoker | 249422 (19.4\%) | 20667 (28.2\%) | 185778 (19.5\%) |
| Current drinker | 292489 (22.7\%) | 26529 (36.2\%) | 240183 (25.3\%) |
| Obesity | 134244 (10.4\%) | 17241 (23.5\%) | 214058 (22.5\%) |

$P$-value $<0.001$ for all comparisons among the 3 groups.
*Participants either refused to answer the question or did not know the answer.
management of hypertension ${ }^{15}$ and included angiotensinconverting enzyme inhibitors or angiotensin receptor blockers, beta-blockers, calcium channel blockers, diuretics, and fixed-dose combination drugs. We also collected information on the traditional Chinese medications (TCMs) used for hypertension. To assess whether the management of IDH patients varied by severity, we stratified them into 3 groups based on the degree DBP elevation (90-95, 96-100, and $>100 \mathrm{~mm} \mathrm{Hg}$ ) and compared the most frequently used antihypertensive medication class and the number of antihypertensive medications used by patients in each of these groups.

Finally, we developed 2 multivariable generalized linear mixed models with a logit link function and township-specific random intercepts (to account for geographic autocorrelation) to identify individual characteristics associated with prevalence of IDH, and the awareness of hypertension among untreated IDH participants (details in Data S1). For identifying the characteristics associated with IDH, we compared IDH participants with both normotensives as well as other hypertensives using 2 separate models. Explanatory variables included participants' age, sex, marital status, annual household income, education level, occupation, geographical region, health insurance status, smoking, alcohol use, obesity, physician-diagnosed diabetes mellitus (DM), and prior cardiovascular events (myocardial infarction or stroke).

All analyses were conducted using R 3.33 (The R Foundation for Statistical Computing, Vienna, Austria) and SAS 9.4
(SAS Institute Inc, Cary, NC). The central ethics committee at the China National Center for Cardiovascular Disease and the Internal Review Board at Yale University approved this project, and written informed consent was obtained from all enrolled participants.

## Results

## Population Characteristics

Our sample included 2310184 participants with a mean age of 55.7 (SD 9.8) years; 1374684 (59.5\%) were women; and 1023780 (44.3\%) had hypertension. Compared with the population aged 35 to 75 years in the 2010 Chinese Census, our sample contained more people from older age groups (70.4\% of people with age 50 and older in the Million Persons Project versus $46.1 \%$ in Census).

## Prevalence and Characteristics of Participants With IDH

Overall, 73279 (3.2\% of the study population and $7.2 \%$ of hypertensives) participants had IDH and 950501 ( $41.1 \%$ of the study population) participants had other types of hypertension (including, 469349 [20.3\%] with ISH, 403912 [17.5\%] with SDH, and 77240 [3.3\%] with controlled hypertension). When we standardized our results to national census-based estimates, we found a higher prevalence of


Figure 1. Prevalence of isolated diastolic hypertension and other types of hypertension (isolated systolic hypertension, systolic-diastolic hypertension, and controlled hypertension), by age group.

IDH (3.8\%) but a lower prevalence of other hypertension subgroups (34.0\%). Overall, participants with IDH were more likely to be younger, men, employed, married, more educated, have higher income, consume alcohol, be current smoker, and obese than those who were normotensive or who had other types of hypertension (all $P<0.001$; Table 1). Additionally, participants with IDH were more likely to have a history of myocardial infarction, stroke, and DM $(0.7 \%, 2.2 \%$, and $4.8 \%$ respectively) when compared with normotensive participants $(0.5 \%, 1.2 \%$, and $4.0 \%$ respectively), and less likely to have a history of myocardial infarction, stroke, and DM compared with participants with other types of hypertension $(1.1 \%, 4.1 \%$, and $9.8 \%$ respectively). Both untreated and treated IDH participants had similar characteristics (Table S1).

The prevalence of IDH decreased with age, whereas the prevalence of other hypertension subtypes (including ISH, SDH and controlled hypertensives) increased with age (Figure 1). The prevalence of IDH was significantly higher for men (4.5\% of overall population and $9.8 \%$ of hypertensives) as compared with women ( $2.2 \%$ of overall population and $5.2 \%$ of hypertensives; Table 2). The prevalence was also significantly higher among those living in rural areas and Western regions, who were at
least college educated, and had a higher income (Table 2). Prevalence of IDH showed a similar distribution across different population subgroups in both treated and untreated hypertensive participants (Table 3 and Table S2).

The 1198 subgroups varied with respect to the prevalence of participants with IDH (median: 2.9\%, [IOR: 1.7-4.7]; Figure S2). The prevalence of IDH was substantially higher in subgroups with participants who were younger, men, without prior cardiovascular event, and without DM as compared with participants who were older, women, with prior cardiovascular event, and with DM (Figure 2). Subgroups with at least 500 participants had similar results (Figures S3 and S4).

In mixed effects multivariable logistic regression analysis assessing independent predictors of IDH, we identified several individual characteristics associated with the prevalence of IDH (Table 4). When compared with normotensives, participants who were young- and middle-aged, men, were at least college educated, consumed alcohol, had DM, were obese, and had prior cardiovascular events were more likely to have IDH than those who were older, women, less educated, did not consume alcohol, were not obese, and did not have DM or prior cardiovascular events (all $P<0.01$ ). Participants who

Table 2. Prevalence of Isolated Diastolic Hypertension Among All Participants and Hypertensive Participants, by Population Characteristics

| Characteristics | All Participants |  | Hypertensive Participants |  |
| :---: | :---: | :---: | :---: | :---: |
|  | n | Prevalence of IDH $\mathrm{n}(\%, 95 \% \mathrm{Cl})$ | n | Prevalence of IDH n (\%, 95\% CI) |
| n (\%, 95\% CI) | 2310184 | 73279 (3.2\%, 3.1-3.2) | 1023780 | 73279 (7.2\%, 7.1-7.2) |
| Age, y |  |  |  |  |
| 35 to 39 | 110345 | 4603 (4.2\%, 4.1-4.3) | 18659 | 4603 (24.7\%, 24.1-25.3) |
| 40 to 44 | 236721 | 10538 (4.5\%, 4.4-4.5) | 55544 | 10538 (19.0\%, 18.6-19.3) |
| 45 to 49 | 337041 | 15328 (4.5\%, 4.5-4.6) | 107129 | 15328 (14.3\%, 14.1-14.5) |
| 50 to 54 | 401532 | 16479 (4.1\%, 4.0-4.2) | 166120 | 16479 (9.9\%, 9.8-10.1) |
| 55 to 59 | 328264 | 10082 (3.1\%, 3.0-3.1) | 158074 | 10082 (6.4\%, 6.3-6.5) |
| 60 to 64 | 397706 | 8910 (2.2\%, 2.2-2.3) | 214743 | 8910 (4.1\%, 4.1-4.2) |
| 65 to 69 | 305267 | 4985 (1.6\%, 1.6-1.7) | 181361 | 4985 (2.7\%, 2.7-2.8) |
| 70 to 75 | 193308 | 2354 (1.2\%, 1.2-1.3) | 122150 | 2354 (1.9\%, 1.9-2.0) |
| Sex |  |  |  |  |
| Men | 935500 | 42360 (4.5\%, 4.5-4.6) | 434400 | 42360 (9.8\%, 9.7-9.8) |
| Women | 1374684 | 30919 (2.2\%, 2.2-2.3) | 589380 | 30919 (5.2\%, 5.2-5.3) |
| Urbanity |  |  |  |  |
| Urban | 889449 | 26309 (3.0\%, 2.9-3.0) | 372029 | 26309 (7.1\%, 7.0-7.2) |
| Rural | 1420735 | 46970 (3.3\%, 3.3-3.3) | 651751 | 46970 (7.2\%, 7.1-7.3) |
| Region |  |  |  |  |
| Eastern | 792935 | 23902 (3.0\%, 3.0-3.1) | 376831 | 23902 (6.3\%, 6.3-6.4) |
| Western | 830940 | 28156 (3.4\%, 3.3-3.4) | 336507 | 28156 (8.4\%, 8.3-8.5) |
| Central | 686309 | 21221 (3.1\%, 3.1-3.1) | 310442 | 21221 (6.8\%, 6.7-6.9) |
| Education |  |  |  |  |
| Primary school or lower | 1011726 | 26212 (2.6\%, 2.6-2.6) | 499425 | 26212 (5.2\%, 5.2-5.3) |
| Middle school | 746958 | 25959 (3.5\%, 3.4-3.5) | 314683 | 25959 (8.2\%, 8.2-8.3) |
| High school | 350185 | 12368 (3.5\%, 3.5-3.6) | 138836 | 12368 (8.9\%, 8.8-9.1) |
| College or above | 169057 | 7602 (4.5\%, 4.4-4.6) | 57497 | 7602 (13.2\%, 12.9-13.5) |
| Unknown* | 32258 | 1138 (3.5\%, 3.3-3.7) | 13339 | 1138 (8.5\%, 8.1-9.0) |
| Employment |  |  |  |  |
| Employed | 1670687 | 57582 (3.4\%, 3.4-3.5) | 706829 | 57582 (8.1\%, 8.1-8.2) |
| Unemployed | 30269 | 1345 (4.4\%, 4.2-4.7) | 12975 | 1345 (10.4\%, 9.8-10.9) |
| Retired | 385731 | 8342 (2.2\%, 2.1-2.2) | 199968 | 8342 (4.2\%, 4.1-4.3) |
| Housework | 183595 | 4470 (2.4\%, 2.4-2.5) | 87873 | 4470 (5.1\%, 4.9-5.2) |
| Unknown* | 39902 | 1540 (3.9\%, 3.7-4.0) | 16135 | 1540 (9.5\%, 9.1-10.0) |
| Occupation |  |  |  |  |
| Farmer | 1129206 | 34562 (3.1\%, 3.0-3.1) | 526837 | 34562 (6.6\%, 6.5-6.6) |
| Non-farmer | 1141076 | 37177 (3.3\%, 3.2-3.3) | 480808 | 37177 (7.7\%, 7.7-7.8) |
| Unknown* | 39902 | 1540 (3.9\%, 3.7-4.0) | 16135 | 1540 (9.5\%, 9.1-10.0) |
| Household income, Yuan/y |  |  |  |  |
| $<10000$ | 487418 | 14307 (2.9\%, 2.9-3.0) | 230788 | 14307 (6.2\%, 6.1-6.3) |
| 10000 to 50000 | 1273538 | 40359 (3.2\%, 3.1-3.2) | 562310 | 40359 (7.2\%, 7.1-7.2) |

Continued

Table 2. Continued

| Characteristics | All Participants |  | Hypertensive Participants |  |
| :---: | :---: | :---: | :---: | :---: |
|  | n | Prevalence of IDH <br> n (\%, 95\% CI) | n | Prevalence of IDH <br> n (\%, 95\% CI) |
| >50 000 | 339806 | 11908 (3.5\%, 3.4-3.6) | 140365 | 11908 (8.5\%, 8.3-8.6) |
| Unknown* | 209422 | 6705 (3.2\%, 3.1-3.3) | 90317 | 6705 (7.4\%, 7.3-7.6) |
| Marital status |  |  |  |  |
| Married | 2147107 | 69159 (3.2\%, 3.2-3.2) | 938370 | 69159 (7.4\%, 7.3-7.4) |
| Widowed, separated, divorced, single | 134977 | 3192 (2.4\%, 2.3-2.4) | 73581 | 3192 (4.3\%, 4.2-4.5) |
| Unknown* | 28100 | 928 (3.3\%, 3.1-3.5) | 11829 | 928 (7.8\%, 7.4-8.3) |
| Health insurance status |  |  |  |  |
| Insured | 2261969 | 71580 (3.2\%, 3.1-3.2) | 1003779 | 71580 (7.1\%, 7.1-7.2) |
| Uninsured | 13780 | 502 (3.6\%, 3.3-4.0) | 5392 | 502 (9.3\%, 8.5-10.1) |
| Unknown* | 34435 | 1197 (3.5\%, 3.3-3.7) | 14609 | 1197 (8.2\%, 7.7-8.6) |
| Medical history |  |  |  |  |
| Myocardial infarction | 17224 | 496 (2.9\%, 2.6-3.1) | 10943 | 496 (4.5\%, 4.1-4.9) |
| Stroke | 55868 | 1614 (2.9\%, 2.8-3.0) | 40240 | 1614 (4.0\%, 3.8-4.2) |
| Diabetes mellitus | 148238 | 3499 (2.4\%, 2.3-2.4) | 96828 | 3499 (3.6\%, 3.5-3.7) |
| CVD risk factor |  |  |  |  |
| Current smoker | 455867 | 20667 (4.5\%, 4.5-4.6) | 206445 | 20667 (10.0\%, 9.9-10.1) |
| Current drinker | 559201 | 26529 (4.7\%, 4.7-4.8) | 266712 | 26529 (9.9\%, 9.8-10.1) |
| Obesity | 365543 | 17241 (4.7\%, 4.6-4.8) | 231299 | 17241 (7.5\%, 7.3-7.6) |

CVD indicates cardiovascular disease; IDH, isolated diastolic hypertension.
*Participants either refused to answer the question or did not know the answer.
were married, farmers, and current smokers were less likely to have IDH (all $P<0.001$ ). Income and health insurance did not have a significant association with prevalence of IDH. Similarly, when compared with participants with other hypertension subtypes, participants who were younger, men, were at least college educated, and consumed alcohol were more likely to have IDH (all $P<0.001$ ); whereas, participants who were older, farmer, current smokers, had DM, were obese, had prior cardiovascular events, and belonged to the Central or Eastern regions were more likely to have other types of hypertension (all $P<0.001$ ).

## Awareness of Having Hypertension Among Untreated Participants

Among untreated IDH participants ( $n=63112$ or $86.1 \%$ of the overall IDH group), only 6512 (or $10.3 \%$ ) were aware of having hypertension, whereas 72220 (or 24.8\%) of the 290645 untreated ISH and 89516 (or $44.1 \%$ ) of the 203173 untreated SDH participants were aware of having hypertension. Awareness among untreated participants across all subtypes of hypertension increased with age; however, awareness among
participants with IDH was significantly lower than other hypertensives (ISH and SDH), across all age groups (Figure 3; $P<0.005$ for all age -groups). The awareness rates were higher among those who lived in rural areas or Eastern or Central regions, were retired, had a higher income, and were widowed/ separated/or divorced (Table 3). Fewer than $15 \%$ of the IDH participants with at least 1 or more cardiovascular risk factors (including smoking, alcohol use, and obesity) and $<33 \%$ of IDH participants with a prior cardiovascular event or DM were aware of having hypertension. The 1198 subgroups varied with respect to awareness of having hypertension among untreated IDH participants (median: 9.7\% [IQR: 4.0-17.6]; Figure S2). Awareness was higher in subgroups of participants who were older, had prior cardiovascular event, and had prior DM (Figure 4). Awareness rates were similar among men and women and in rural and urban areas. Subgroups with at least 500 participants had similar results (Figures S3 and S4).

We identified several independent factors associated with awareness of having hypertension among untreated IDH participants (Table 4). Awareness was significantly higher among IDH participants who were older, women, had higher income (>50 000 Yuan/year), were at least college educated,

Table 3. Prevalence and Awareness of Isolated Diastolic Hypertension Among Untreated Hypertensives, by Population Characteristics

| Characteristics | Untreated Hypertensive <br> Participants ( n ) | Prevalence of IDH $\mathrm{n}(\%, 95 \% \mathrm{Cl})$ | Awareness Among IDH Participants $\mathrm{n}(\%, 95 \% \mathrm{Cl})$ |
| :---: | :---: | :---: | :---: |
| n (\%, 95\% CI) | 718666 | 63112 (8.8\%, 8.7-8.8) | 6512 (10.3\%, 10.1-10.6) |
| Age, y |  |  |  |
| 35 to 39 | 16425 | 4361 (26.6\%, 25.9-27.2) | 274 (6.3\%, 5.6-7.0) |
| 40 to 44 | 46923 | 9658 (20.6\%, 20.2-20.9) | 633 (6.6\%, 6.1-7.0) |
| 45 to 49 | 84788 | 13560 (16.0\%, 15.7-16.2) | 1179 (8.7\%, 8.2-9.2) |
| 50 to 54 | 121131 | 13939 (11.5\%, 11.3-11.7) | 1551 (11.1\%, 10.6-11.6) |
| 55 to 59 | 109324 | 8354 (7.6\%, 7.5-7.8) | 1022 (12.2\%, 11.5-12.9) |
| 60 to 64 | 144370 | 7258 (5.0\%, 4.9-5.1) | 969 (13.4\%, 12.6-14.1) |
| 65 to 69 | 117786 | 4062 (3.4\%, 3.3-3.6) | 619 (15.2\%, 14.1-16.3) |
| 70 to 75 | 77919 | 1920 (2.5\%, 2.4-2.6) | 265 (13.8\%, 12.3-15.3) |
| Sex |  |  |  |
| Men | 311796 | 36421 (11.7\%, 11.6-11.8) | 3777 (10.4\%, 10.1-10.7) |
| Women | 406870 | 26691 (6.6\%, 6.5-6.6) | 2735 (10.2\%, 9.9-10.6) |
| Urbanity |  |  |  |
| Urban | 250233 | 22345 (8.9\%, 8.8-9.0) | 2187 (9.8\%, 9.4-10.2) |
| Rural | 468433 | 40767 (8.7\%, 8.6-8.8) | 4325 (10.6\%, 10.3-10.9) |
| Region |  |  |  |
| Eastern | 259305 | 20374 (7.9\%, 7.8-8.0) | 2432 (11.9\%, 11.5-12.4) |
| Western | 240487 | 24697 (10.3\%, 10.1-10.4) | 1998 (8.1\%, 7.7-8.4) |
| Central | 218874 | 18041 (8.2\%, 8.1-8.4) | 2082 (11.5\%, 11.1-12.0) |
| Education |  |  |  |
| Primary school or lower | 357641 | 23063 (6.4\%, 6.4-6.5) | 2450 (10.6\%, 10.2-11.0) |
| Middle school | 220050 | 22377 (10.2\%, 10.0-10.3) | 2292 (10.2\%, 9.8-10.6) |
| High school | 92551 | 10333 (11.2\%, 11.0-11.4) | 1035 (10.0\%, 9.4-10.6) |
| College or above | 38218 | 6314 (16.5\%, 16.1-16.9) | 673 (10.7\%, 9.9-11.4) |
| Unknown* | 10206 | 1025 (10.0\%, 9.5-10.6) | 62 (6.0\%, 4.6-7.5) |
| Employment |  |  |  |
| Employed | 522751 | 50534 (9.7\%, 9.6-9.7) | 4909 (9.7\%, 9.5-10.0) |
| Unemployed | 8739 | 1109 (12.7\%, 12.0-13.4) | 147 (13.3\%, 11.3-15.3) |
| Retired | 116143 | 6351 (5.5\%, 5.3-5.6) | 897 (14.1\%, 13.3-15.0) |
| Housework | 58954 | 3761 (6.4\%, 6.2-6.6) | 441 (11.7\%, 10.7-12.8) |
| Unknown* | 12079 | 1357 (11.2\%, 10.7-11.8) | 118 (8.7\%, 7.2-10.2) |
| Occupation |  |  |  |
| Famer | 387791 | 30616 (7.9\%, 7.8-8.0) | 3040 (9.9\%, 9.6-10.3) |
| Non-farmer | 318796 | 31139 (9.8\%, 9.7-9.9) | 3354 (10.8\%, 10.4-11.1) |
| Unknown* | 12079 | 1357 (11.2\%, 10.7-11.8) | 118 (8.7\%, 7.2-10.2) |
| Household income, Yuan/y |  |  |  |
| $<10000$ | 168343 | 12725 (7.6\%, 7.4-7.7) | 1222 (9.6\%, 9.1-10.1) |
| 10000 to 50000 | 390550 | 34601 (8.9\%, 8.8-8.9) | 3462 (10.0\%, 9.7-10.3) |
| >50 000 | 92258 | 9903 (10.7\%, 10.5-10.9) | 1186 (12.0\%, 11.3-12.6) |

Continued

Table 3. Continued

| Characteristics | Untreated Hypertensive <br> Participants ( n ) | Prevalence of IDH $\mathrm{n}(\%, 95 \% \mathrm{Cl})$ | Awareness Among IDH Participants n (\%, 95\% CI) |
| :---: | :---: | :---: | :---: |
| Unknown* | 67515 | 5883 (8.7\%, 8.5-8.9) | 642 (10.9\%, 10.1-11.7) |
| Marital status |  |  |  |
| Married | 662083 | 59671 (9.0\%, 8.9-9.1) | 6141 (10.3\%, 10.0-10.5) |
| Widowed, separated, divorced, single | 47873 | 2629 (5.5\%, 5.3-5.7) | 321 (12.2\%, 11.0-13.5) |
| Unknown* | 8710 | 812 (9.3\%, 8.7-9.9) | 50 (6.2\%, 4.5-7.8) |
| Health insurance status |  |  |  |
| Insured | 704139 | 61637 (8.8\%, 8.7-8.8) | 6371 (10.3\%, 10.1-10.6) |
| Uninsured | 4130 | 448 (10.8\%, 9.9-11.8) | 48 (10.7\%, 7.9-13.6) |
| Unknown* | 10397 | 1027 (9.9\%, 9.3-10.5) | 93 (9.1\%, 7.3-10.8) |
| Medical history |  |  |  |
| Myocardial infarction | 5167 | 334 (6.5\%, 5.8-7.1) | 99 (29.6\%, 24.7-34.5) |
| Stroke | 18897 | 986 (5.2\%, 4.9-5.5) | 309 (31.3\%, 28.4-34.2) |
| Diabetes mellitus | 51296 | 2521 (4.9\%, 4.7-5.1) | 650 (25.8\%, 24.1-27.5) |
| CVD risk factor |  |  |  |
| Current smoker | 149972 | 17842 (11.9\%, 11.7-12.1) | 1847 (10.4\%, 9.9-10.8) |
| Current drinker | 193777 | 22740 (11.7\%, 11.6-11.9) | 2389 (10.5\%, 10.1-10.9) |
| Obesity | 146456 | 13970 (9.5\%, 9.4-9.7) | 1908 (13.7\%, 13.1-14.2) |

CVD indicates cardiovascular disease; IDH, isolated diastolic hypertension.
*Participants either refused to answer the question or did not know the answer.
obese, had DM, prior cardiovascular event, and belonged to Central or Eastern region (all $P<0.05$ ). Participant's marital status, occupation, health insurance status, and health behaviors like smoking and alcohol use, were not independently associated with their awareness of having hypertension.

## Treatment Patterns Among Treated Participants With IDH

Most treated participants with IDH reported taking 1 antihypertensive medication in both urban and rural areas (Figure 5). Even though use of combination therapy increased slightly with age, $<5 \%$ of the participants received $\geq 3$ drugs across all age groups. Most treated participants with IDH reported taking Western antihypertensive medications (9969 or $98 \%$ ). Among IDH participants using 2 or fewer classes of medications, calcium channel blockers (42\%) were the most frequent class of medication used, followed by angiotensinconverting enzyme inhibitors or angiotensin receptor blockers (20\%), and diuretics (7\%), respectively (Table 5). On stratification of IDH patients based on their degree of DBP elevation, we found that the majority ( $74.7 \%$ ) had DBP of 90 to 95 mm Hg , followed by 96 to 100 mm Hg (19.6\%), and $>100 \mathrm{~mm} \mathrm{Hg}(5.7 \%)$, respectively. The most frequently used
antihypertensive medication class and the number of antihypertensive medications used did not vary significantly between 3 groups (both $P>0.05$; Figure 55 ).

## Discussion

In this large study, we report the characteristics, prevalence, awareness, and treatment patterns of people with IDH in China, and how these differ from other hypertensives and vary across diverse population subgroups. We found that IDH affected almost $4 \%$ of adults between 35 and 75 years in China (and represents nearly $25 \%$ of the hypertensive population aged $<45$ years). Awareness of hypertension was significantly lower among people with IDH as compared with other types of hypertension and was lowest among youngand middle-aged adults in whom IDH was most prevalent. Additionally, among those with IDH despite treatment, the vast majority were treated with only 1 class of antihypertensive medication.

This study extends the scientific literature in several ways. First, this is one of the largest population-based studies, to our knowledge, to evaluate the characteristics and prevalence of IDH, allowing us to draw robust conclusions across a wide variety of diverse subgroups. Our findings that young age, male sex, obesity, DM, alcohol


Figure 2. Density plots of prevalence of isolated diastolic hypertension among all study participants in 1198 mutually exclusive population subgroups (of at least 200 participants), by age, sex, prior cardiovascular events, history of diabetes mellitus, and urbanity.
consumption, and prior cardiovascular events are positively associated with IDH prevalence supports and expands on the associations previously described in the literature but with smaller numbers of patients with IDH. ${ }^{1,3,20,25-27}$ For example, Franklin et $\mathrm{al}^{20}$ and Liu et $\mathrm{al}^{25}$ showed that younger age, male sex, and BMI were predictors of IDH in a small population of IDH patients. In this study, we identified additional factors associated with IDH including DM, alcohol consumption, history of prior cardiovascular event, and showed that these associations were consistent across tens of thousands of individuals with IDH and across diverse population subgroups. The prevalence rates of IDH found in our study were also comparable with those reported previously in studies not only from Chinese cohorts (for example, Huang et $\mathrm{al}^{3}$ found a prevalence of $4.4 \%$ among adults aged 35 to 74 and Sun et al ${ }^{11}$ found a prevalence of $5.8 \%$ among adults $>35$ years), but also from other lowand middle-income countries. ${ }^{26,27}$

Second, to the best of our knowledge, our study is the first to assess the awareness of having hypertension among a large Chinese population with IDH compared with other hypertension subtypes, and to identify characteristics that are
associated with awareness. Our findings suggest that even though awareness among participants with IDH increases with age, it is significantly lower as compared with awareness among participants with other hypertension subtypes, across all age groups. These findings are consistent with previous reports from other countries which have shown $26 \%$ lower diagnosis (hazard ratio 0.74 ; $\mathrm{Cl} 0.60-0.92$ ) and $31 \%$ lower medication initiation (hazard ratio 0.69 ; $\mathrm{Cl} 0.55-0.86$ ) among younger patients with IDH as compared with systolic/diastolic hypertension. ${ }^{18}$

Third, our assessment of the antihypertensive medications among treated participants with IDH provides information on what medications may not be effectively treating IDH or that people are not taking. We found that the majority of these patients were treated with only 1 class of antihypertensive medication. Calcium channel blockers was the most frequently used class of antihypertensive medication among these patients, even though they may not be most effective for this phenotype, which could be due to the prescription habits of the physicians, availability, and cost-related factors of other classes of antihypertensive medications. ${ }^{28}$

Table 4. Mixed Effects Multivariable Regression Models for Association Between Individual Characteristics and the Prevalence of Isolated Diastolic Hypertension and the Awareness Among Untreated Participants With Isolated Diastolic Hypertension

|  | Prevalence of IDH |  |  |  | Awareness Among IDH Participants |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Model 1 <br> Odds Ratio <br> (95\% CI) | $P$ Value | Model 2 <br> Odds Ratio <br> (95\% CI) | $P$ Value | Odds Ratio ( $95 \% \mathrm{Cl}$ ) | $P$ Value |
| Age, y |  |  |  |  |  |  |
| 35 to 39 | 1 |  | 1 |  | 1 |  |
| 40 to 44 | 1.27 (1.22-1.32) | $<0.001$ | 0.81 (0.78-0.84) | $<0.001$ | 1.24 (1.08-1.43) | 0.003 |
| 45 to 49 | 1.46 (1.41-1.52) | $<0.001$ | 0.59 (0.57-0.62) | $<0.001$ | 1.65 (1.45-1.88) | $<0.001$ |
| 50 to 54 | 1.54 (1.48-1.60) | $<0.001$ | 0.40 (0.38-0.42) | $<0.001$ | 2.13 (1.87-2.43) | $<0.001$ |
| 55 to 59 | 1.29 (1.25-1.35) | $<0.001$ | 0.25 (0.24-0.26) | $<0.001$ | 2.37 (2.07-2.72) | $<0.001$ |
| 60 to 64 | 0.99 (0.95-1.03) | 0.534 | 0.15 (0.14-0.15) | $<0.001$ | 2.75 (2.40-3.17) | $<0.001$ |
| 65 to 69 | 0.79 (0.75-0.83) | $<0.001$ | 0.09 (0.09-0.10) | $<0.001$ | 3.26 (2.80-3.79) | $<0.001$ |
| 70 to 75 | 0.64 (0.61-0.68) | $<0.001$ | 0.06 (0.06-0.07) | $<0.001$ | 3.05 (2.53-3.68) | $<0.001$ |
| Sex |  |  |  |  |  |  |
| Men | 1 |  | 1 |  | 1 |  |
| Women | 0.45 (0.44-0.45) | $<0.001$ | 0.50 (0.49-0.51) | $<0.001$ | 1.07 (1.00-1.14) | 0.052 |
| Marital status |  |  |  |  |  |  |
| Not married | 1 |  | 1 |  | 1 |  |
| Married | 0.91 (0.88-0.95) | $<0.001$ | 1.02 (0.98-1.07) | 0.279 | 0.88 (0.78-1.00) | 0.057 |
| Household income, Yuan/y |  |  |  |  |  |  |
| $<10000$ | 1 |  | 1 |  | 1 |  |
| 10000 to 50000 | 0.97 (0.95-1.00) | 0.031 | 1.01 (0.99-1.04) | 0.277 | 1.04 (0.97-1.13) | 0.264 |
| >50 000 | 0.99 (0.95-1.02) | 0.417 | 1.05 (1.01-1.08) | 0.014 | 1.17 (1.06-1.30) | 0.003 |
| Education level |  |  |  |  |  |  |
| Lower than college | 1 |  | 1 |  | 1 |  |
| College or above | 1.08 (1.04-1.11) | $<0.001$ | 1.10 (1.07-1.14) | $<0.001$ | 1.16 (1.05-1.28) | 0.003 |
| Occupation |  |  |  |  |  |  |
| Not farmer | 1 |  | 1 |  | 1 |  |
| Farmer | 0.95 (0.92-0.97) | $<0.001$ | 0.92 (0.89-0.94) | $<0.001$ | 0.94 (0.87-1.00) | 0.066 |
| Health insurance status |  |  |  |  |  |  |
| Uninsured | 1 |  | 1 |  | 1 |  |
| Insured | 1.07 (0.98-1.15) | 0.115 | 1.02 (0.94-1.10) | 0.699 | 0.87 (0.69-1.10) | 0.259 |
| CVD risk factor |  |  |  |  |  |  |
| Current smoker | 0.88 (0.86-0.90) | $<0.001$ | 0.96 (0.94-0.99) | 0.001 | 1.02 (0.95-1.09) | 0.656 |
| Current drinker | 1.38 (1.35-1.41) | $<0.001$ | 1.07 (1.04-1.09) | $<0.001$ | 1.02 (0.96-1.09) | 0.529 |
| Diabetes mellitus | 1.05 (1.01-1.09) | 0.012 | 0.63 (0.60-0.65) | $<0.001$ | 2.31 (2.09-2.55) | $<0.001$ |
| Obesity | 2.49 (2.44-2.54) | $<0.001$ | 0.92 (0.90-0.94) | $<0.001$ | 1.50 (1.41-1.59) | $<0.001$ |
| Prior CVE | 1.65 (1.57-1.74) | $<0.001$ | 0.80 (0.76-0.84) | $<0.001$ | 3.14 (2.75-3.59) | $<0.001$ |
| Geographic region |  |  |  |  |  |  |
| Western | 1 |  | 1 |  | 1 |  |
| Eastern | 0.91 (0.88-0.95) | $<0.001$ | 0.78 (0.75-0.81) | $<0.001$ | 1.52 (1.38-1.67) | $<0.001$ |
| Central | 0.97 (0.93-1.01) | 0.167 | 0.82 (0.79-0.86) | $<0.001$ | 1.43 (1.30-1.58) | $<0.001$ |

Model 1 includes normotensive participants and participants with isolated diastolic hypertension. Model 2 includes participants with isolated diastolic hypertension and participants with other types of hypertension (isolated systolic hypertension, systolic diastolic hypertension, controlled hypertension). CVD indicates cardiovascular disease; CVE, cardiovascular event; IDH, isolated diastolic hypertension; ISH, isolated systolic hypertension; SDH, systolic diastolic hypertension.

## Clinical Implications

These findings have important clinical implications as IDH is independently associated with a higher risk of incident heart failure and cardiovascular mortality as compared with normal

BP, and BP lowering in patients with IDH has been shown to protect against major vascular events. ${ }^{29-31}$ As such, identifying characteristics that may be associated with IDH and understanding the current awareness and treatment patterns


Figure 3. Awareness of having hypertension among untreated participants with isolated diastolic hypertension (IDH), isolated systolic hypertension (ISH), and systolic-diastolic hypertension (SDH), by age group.
among those with IDH can help identify the patients at increased cardiovascular risk and highlight the opportunities for improving their care. Current hypertension management guidelines ${ }^{15-17}$ lack guidance on management of patients with IDH and the recent randomized clinical trials ${ }^{32,33}$ focused only on SBP targets for improving outcomes, resulting in lack of contemporary guidance on optimal DBP targets for management of patients with IDH. As clinicians and public health professionals develop and implement strategies to help prevent and control hypertension, our findings suggest the need to target people with IDH among other hypertension subtypes for reducing the burden of hypertension.

Considering that patients with IDH are much younger and often without additional cardiovascular risk factors as compared with other hypertension subtypes, they are less likely to come in contact with the health system and hence, more likely to not to be diagnosed. These patients could benefit from more targeted hypertension screening initiatives focusing on the young- and middle-aged adults. For example, promoting free BP screenings at work places and in schools and colleges could result in early diagnosis of those with IDH,
and prevent the catastrophic sequelae of hypertension in these patients. Additionally, given the growing burden of obesity in China and its strong association with IDH, it is critical to slow the increase in BMI through public health interventions, to prevent the development of IDH in unaffected individuals. Moreover, increasing awareness of the clinical significance of an elevated DBP in the young and providing clear guidance on management of patients with IDH could also ensure better management of these patients. The point is that the emphasis on SBP should not lead to the neglect of people with IDH.

This study was derived from a large Chinese population. China is of special interest because it represents $25 \%$ of the world's population and hypertension is a major public health challenge in China. However, given that China is more recent in the epidemiological transition, and treatment rates are much lower than many Western countries, similar large-scale studies in other countries are warranted to understand impact of nation-specific characteristics on the epidemiology of IDH. Nevertheless, these findings are relevant for several low- and middle-income countries where hypertension is growing in importance, treatment rates tend


Figure 4. Density plots of awareness of having hypertension among untreated participants with isolated diastolic hypertension in 1198 mutually exclusive population subgroups (of at least 200 participants), by age, sex, prior cardiovascular events, history of diabetes mellitus, and urbanity.
to be lower, and fewer evidence exists to guide public health programs.

## Limitations

Our study has several potential limitations. First, for estimation of characteristics and prevalence of participants with IDH, we classified patients into different hypertension subgroups based on the value of the SBP and DBP at enrollment, irrespective of their medication use. As such, some treated hypertensive participants may have had their SBP controlled with medication, and may have been included in the IDH group. However, the vast majority ( $86 \%$ ) of the participants in the IDH group were untreated. Moreover, since the treated participants with IDH had persistent elevation of their DBP even after treatment, they were not much different from the untreated IDH group, as shown in Table S1. Second, treated IDH patients who had their DBP $<90 \mathrm{~mm} \mathrm{Hg}$ were classified as having "controlled hypertension" instead of IDH, which could have underestimated the prevalence of IDH of China. However, considering that less than one third of the people with hypertension receive
treatment in China and an even fewer proportion actually have controlled hypertension, and that these rates are even lower for younger age groups where IDH is most prevalent, ${ }^{23}$ few individuals in the IDH group would have been classified as having "controlled hypertension". Third, our study used convenience rather than a nationally representative sample for large-scale recruitment. This could have resulted in a sampling bias resulting in overestimation of the awareness and treatment rates since these participants would be more likely to be in contact with the health system. Fourth, awareness and treatment rates could also have been affected by a participant's access to and use of healthcare services, however, we did not collect this information in this study. Fifth, since we also used "self-reported use of an antihypertensive medication in the past 2 weeks" as a criterion for defining hypertension, some patients taking hypertensive medication might not have reported that use, possibly underestimating the burden of hypertension in China. Lastly, for individuals who were aware of having hypertension, our study did not collect information on the duration of hypertension, which could have influenced the treatment patterns seen among these participants.


Figure 5. Number of antihypertensive medications used by treated participants with isolated diastolic hypertension, by age and urbanity.

## Conclusions

IDH affects a large number of adults in China, and these patients may have some unique characteristics as compared with people without hypertension as well as those with other types of hypertension. However, patients with IDH have the lowest rate of awareness compared with other hypertension subtypes, and most participants with IDH despite treatment had scope for further increase in the intensity of therapy. Our findings suggest the need to specifically focus public health and clinical strategies on people with IDH and improve their diagnosis and treatment, to mitigate the
burden of hypertension, especially in the young- and middleaged population.

## Appendix

## Members of the Provincial Coordinating Office in China PEACE Million Persons Project

Beijing Center for Diseases Prevention and Control: Chun Huang, Zhong Dong, Bo Jiang; Tianjin Chest Hospital: Zhigang Guo, YingYi Zhang; Hebei Center for Diseases Prevention and Control: Jixin Sun, Yuhuan Liu; Shanxi Center for Diseases

Table 5. Classes of Antihypertensive Medications Used by Treated Participants With Isolated Diastolic Hypertension

|  | A | B | C | D | F |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| A | $1808(20.08 \%)$ | $136(1.51 \%)$ | $602(6.69 \%)$ | $276(3.07 \%)$ | $10(0.11 \%)$ | $4(0.04 \%)$ |
| B |  | $331(3.68 \%)$ | $224(2.49 \%)$ | $27(0.30 \%)$ | $13(0.14 \%)$ | $3(0.03 \%)$ |
| C |  |  | $3780(41.99 \%)$ | $71(0.79 \%)$ | $43(0.48 \%)$ | $14(0.16 \%)$ |
| D |  |  |  | $638(7.09 \%)$ | $11(0.12 \%)$ | $0(0 \%)$ |
| F |  |  |  |  | $563(6.25 \%)$ | $1(0.01 \%)$ |
| T |  |  |  |  | $19(2.20 \%)$ |  |

A indicates angiotensin converting enzyme inhibitors or angiotensin receptor blockers; B, beta-blockers; C, calcium channel blockers; D, diuretics; F, fixed-dose combination drugs; T, traditional Chinese medication.

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## SUPPLEMENTAL MATERIAL

## Data S1.

## Supplemental Methods

Equation for the generalized linear mixed effects multivariable regression models used to study the association between individual characteristics and the prevalence of isolated diastolic hypertension and the awareness among untreated participants with isolated diastolic hypertension.

If $\mathrm{Y}_{\mathrm{ij}}$ indicates that the $\mathrm{i}^{\text {th }}$ patient in the $\mathrm{j}^{\text {th }}$ township is hypertensive, then we estimated

$$
\operatorname{logit}\left(\operatorname{Pr}\left[\mathrm{Y}_{\mathrm{ij}}=1\right]\right)=\alpha_{\mathrm{j}}+\Sigma \mathrm{BX}_{\mathrm{ij}}
$$

where $\alpha_{j} \sim N\left(0, \tau^{2}\right)$ is a random intercept over townships and $X_{i j}$ is a vector of patient risk factors.

We used age, sex, marital status, annual household income, education level, occupation, health insurance status, smoking, alcohol use, obesity, diabetes mellitus, prior cardiovascular events, and geographical region as risk factors.

Table S1. Baseline characteristics of participants with isolated diastolic hypertension, by treatment status.

| Characteristics, n (\%,95\% CI) | Untreated participants with IDH | Treated participants with IDH |
| :---: | :---: | :---: |
| N (\%) | 63112 | 10167 |
| Age (years) |  |  |
| 35-39 | 4361 (6.9\%, 6.7-7.1) | 242 (2.4\%, 2.1-2.7) |
| 40-44 | 9658 (15.3\%, 15.0-15.6) | 880 (8.7\%, 8.1 - 9.2) |
| 45-49 | 13,560 (21.5\%, 21.2-21.8) | 1768 (17.4\%, 16.7-18.1) |
| 50-54 | 13,939 (22.1\%, 21.8-22.4) | 2540 (25.0\%, 24.1-25.8) |
| 55-59 | 8354 (13.2\%, 13.0-13.5) | 1728 (17.0\%, 16.3-17.7) |
| 60-64 | 7258 (11.5\%, 11.3-11.7) | 1652 (16.2\%, 15.5-17.0) |
| 65-69 | 4062 (6.4\%, 6.2-6.6) | 923 (9.1\%, 8.5-9.6) |
| 70-75 | 1920 (3.0\%, 2.9-3.2) | 434 (4.3\%, 3.9 - 4.7) |
| Sex |  |  |
| Men | 36,421 (57.7\%, 57.3-58.1) | 5939 (58.4\%, 57.5-59.4) |
| Women | 26,691 (42.3\%, 41.9-42.7) | 4228 (41.6\%, 40.6-42.5) |
| Urbanity |  |  |
| Urban | 22,345 (35.4\%, 35.0-35.8) | 3964 (39.0\%, 38.0-39.9) |
| Rural | 40,767 (64.6\%, 64.2-65.0) | 6203 (61.0\%, 60.1-62.0) |
| Region |  |  |
| Eastern | 20,374 (32.3\%, 31.9-32.6) | 3528 (34.7\%, 33.8-35.6) |
| Western | 24,697 (39.1\%, 38.8-39.5) | 3459 (34.0\%, 33.1-34.9) |
| Central | 18,041 (28.6\%, 28.2-28.9) | 3180 (31.3\%, 30.4-32.2) |
| Education |  |  |
| Primary school or lower | 23,063 (36.5\%, 36.2-36.9) | 3149 (31.0\%, 30.1-31.9) |
| Middle school | 22,377 (35.5\%, 35.1-35.8) | 3582 (35.2\%, 34.3-36.2) |
| High school | 10,333 (16.4\%, 16.1-16.7) | 2035 (20.0\%, 19.2-20.8) |
| College or above | 6314 (10.0\%, 9.8-10.2) | 1288 (12.7\%, 12.0-13.3) |
| Unknown* | 1025 (1.6\%, 1.5-1.7) | 113 (1.1\%, 0.9-1.3) |
| Employment |  |  |
| Employed | 50,534 (80.1\%, 79.8-80.4) | 7048 (69.3\%, 68.4-70.2) |
| Unemployed | 1109 (1.8\%, 1.7-1.9) | 236 (2.3\%, 2.0-2.6) |
| Retired | 6351 (10.1\%, 9.8-10.3) | 1991 (19.6\%, 18.8-20.4) |
| Housework | 3761 (6.0\%, 5.8-6.1) | 709 (7.0\%, 6.5-7.5) |
| Unknown* | 1357 (2.2\%, 2.0-2.3) | 183 (1.8\%, 1.5-2.1) |
| Occupation |  |  |
| Famer | 30,616 (48.5\%, 48.1-48.9) | 3946 (38.8\%, 37.9-39.8) |
| Nonfarmer | 31,139 (49.3\%, 48.9-49.7) | 6038 (59.4\%, 58.4-60.3) |


| Unknown* | $1357(2.2 \%, 2.0-2.3)$ | $183(1.8 \%, 1.5-2.1)$ |
| :---: | :---: | :---: |
| Household Income (Yuan/year) |  |  |
| $<10,000$ | $12,725(20.2 \%, 19.8-20.5)$ | $1582(15.6 \%, 14.9-16.3)$ |
| $10,000-50,000$ | $34,601(54.8 \%, 54.4-55.2)$ | $5758(56.6 \%, 55.7-57.6)$ |
| $>50,000$ | $9903(15.7 \%, 15.4-16.0)$ | $2005(19.7 \%, 18.9-20.5)$ |
| Unknown* | $5883(9.3 \%, 9.1-9.5)$ | $822(8.1 \%, 7.6-8.6)$ |
| Marital Status | $59,671(94.5 \%, 94.4-94.7)$ | $9488(93.3 \%, 92.8-93.8)$ |
| Married | $2629(4.2 \%, 4.0-4.3)$ | $563(5.5 \%, 5.1-6.0)$ |
| Widowed, separated, divorced, <br> single | $812(1.3 \%, 1.2-1.4)$ | $116(1.1 \%, 0.9-1.3)$ |
| Unknown* | $61,637(97.7 \%, 97.5-97.8)$ | $9943(97.8 \%, 97.5-98.1)$ |
| Health Insurance Status | $448(0.7 \%, 0.6-0.8)$ | $54(0.5 \%, 0.4-0.7)$ |
| Insured | $1027(1.6 \%, 1.5-1.7)$ | $170(1.7 \%, 1.4-1.9)$ |
| Uninsured | $334(0.5 \%, 0.5-0.6)$ | $162(1.6 \%, 1.3-1.8)$ |
| Unknown* | $986(1.6 \%, 1.5-1.7)$ | $628(6.2 \%, 5.7-6.6)$ |
| Medical History | $2521(4.0 \%, 3.8-4.1)$ | $978(9.6 \%, 9.0-10.2)$ |
| Myocardial Infarction |  |  |
| Stroke | $17,842(28.3 \%, 27.9-28.6)$ | $2825(27.8 \%, 26.9-28.7)$ |
| Diabetes Mellitus | $22,740(36.0 \%, 35.7-36.4)$ | $3789(37.3 \%, 36.3-38.2)$ |
| CVD Risk Factor | $13,970(22.1 \%, 21.8-22.5)$ | $3271(32.2 \%, 31.3-33.1)$ |
| Current smoker |  |  |

CI, Confidence Interval; CVD, Cardiovascular Disease; IDH, Isolated Diastolic Hypertension

* Participants either refused to answer the question or did not know the answer.

Table S2. Prevalence of isolated diastolic hypertension among treated hypertensive participants, by population characteristics.

| Characteristics, n (\%, 95\% CI) | Treated Hypertensives | Prevalence of IDH |
| :---: | :---: | :---: |
| N (\%) | 305,114 | 10,167 (3.3\%, 3.3 - 3.4) |
| Age (years) |  |  |
| 35-39 | 2234 | 242 (10.8\%, 9.5-12.1) |
| 40-44 | 8621 | 880 (10.2\%, 9.6-10.8) |
| 45-49 | 22,341 | 1768 (7.9\%, 7.6-8.3) |
| 50-54 | 44,989 | 2540 (5.6\%, 5.4-5.9) |
| 55-59 | 48,750 | 1728 (3.5\%, 3.4-3.7) |
| 60-64 | 70,373 | 1652 (2.3\%, 2.2-2.5) |
| 65-69 | 63,575 | 923 (1.5\%, 1.4-1.5) |
| 70-75 | 44,231 | 434 (1.0\%, 0.9-1.1) |
| Sex |  |  |
| Men | 122,604 | 5939 (4.8\%, 4.7-5.0) |
| Women | 182,510 | 4228 (2.3\%, 2.2-2.4) |
| Urbanity |  |  |
| Urban | 121,796 | 3964 (3.3\%, 3.2-3.4) |
| Rural | 183,318 | 6203 (3.4\%, 3.3-3.5) |
| Region |  |  |
| Eastern | 117,526 | 3528 (3.0\%, 2.9-3.1) |
| Western | 96,020 | 3459 (3.6\%, 3.5-3.7) |
| Central | 91,568 | 3180 (3.5\%, 3.4-3.6) |
| Education |  |  |
| Primary school or lower | 141,784 | 3149 (2.2\%, 2.1-2.3) |
| Middle school | 94,633 | 3582 (3.8\%, 3.7-3.9) |
| High school | 46,285 | 2035 (4.4\%, 4.2-4.6) |
| College or above | 19,279 | 1288 (6.7\%, 6.3-7.0) |
| Unknown* | 3133 | 113 (3.6\%, 3.0-4.3) |
| Employment |  |  |
| Employed | 184,078 | 7048 (3.8\%, 3.7-3.9) |
| Unemployed | 4236 | 236 (5.6\%, 4.9-6.3) |
| Retired | 83,825 | 1991 (2.4\%, 2.3-2.5) |
| Housework | 28,919 | 709 (2.5\%, 2.3-2.6) |
| Unknown* | 4056 | 183 (4.5\%, 3.9 - 5.2) |
| Occupation |  |  |
| Famer | 139,046 | 3946 (2.8\%, 2.8-2.9) |
| Nonfarmer | 162,012 | 6038 (3.7\%, 3.6-3.8) |
| Unknown* | 4056 | 183 (4.5\%, 3.9-5.2) |


| Household Income (Yuan/year) |  |  |
| :--- | :---: | :---: |
| $<10,000$ | 62,445 | $1582(2.5 \%, 2.4-2.7)$ |
| $10,000-50,000$ | 171,760 | $5758(3.4 \%, 3.3-3.4)$ |
| $>50,000$ | 48,107 | $2005(4.2 \%, 4.0-4.3)$ |
| Unknown* | 22,802 | $822(3.6 \%, 3.4-3.8)$ |
| Marital Status | 276,287 | $9488(3.4 \%, 3.4-3.5)$ |
| Married | 25,708 | $563(2.2 \%, 2.0-2.4)$ |
| Widowed, separated, divorced, <br> single | 3119 | $116(3.7 \%, 3.1-4.4)$ |
| Unknown* | 299,640 | $9943(3.3 \%, 3.3-3.4)$ |
| Health Insurance Status | 1262 | $54(4.3 \%, 3.2-5.4)$ |
| Insured | 4212 | $170(4.0 \%, 3.4-4.6)$ |
| Uninsured | 5776 | $162(2.8 \%, 2.4-3.2)$ |
| Unknown* | 21,343 | $628(2.9 \%, 2.7-3.2)$ |
| Medical History | 45,532 | $978(2.1 \%, 2.0-2.3)$ |
| Myocardial Infarction |  |  |
| Stroke | 56,473 | $2825(5.0 \%, 4.8-5.2)$ |
| Diabetes Mellitus | 72,935 | $3789(5.2 \%, 5.0-5.4)$ |
| CVD Risk Factor | 84,843 | $3271(3.9 \%, 3.7-4.0)$ |
| Current smoker |  |  |
| Current drinker |  |  |
| Obesity |  |  |

CI, Confidence Interval; CVD, Cardiovascular Disease; IDH, Isolated Diastolic Hypertension

* Participants either refused to answer the question or did not know the answer.

Figure S1. Flowchart of study participant selection in China Patient-Centered Evaluative Assessment of Cardiac Events Million Persons Project.


BMI, Body Mass Index

Figure S2. Histograms of prevalence of isolated diastolic hypertension (IDH) and awareness among untreated IDH participants in 1,198 mutually exclusive population subgroups (at least $\mathbf{2 0 0}$ participants each) defined priori by $\mathbf{1 0}$ selected characteristics.


Figure S3. Histograms prevalence of isolated diastolic hypertension (IDH) and awareness among untreated IDH participants in 731 mutually exclusive population subgroups (at least 500 participants each) defined priori by $\mathbf{1 0}$ selected characteristics.


Figure S4. Density plots of prevalence of isolated diastolic hypertension (IDH) among all study participants (A) and awareness among untreated IDH participants (B) in 731 mutually exclusive population subgroups (of at least 500 participants), by age, sex, prior cardiovascular events, history of diabetes and urbanity.
A. Prevalence





B. Awareness


Figure S5. Number of antihypertensive medications used by treated participants with isolated diastolic hypertension, by degree of diastolic blood pressure (DBP) elevation.



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